

# Diagnostic Yield of Acid Fast Bacilli in Bronchoalveolar Lavage of Sputum-Negative Pulmonary Tuberculosis Patients

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Abstract: Pulmonary tuberculosis (PTB) remains a significant public health concern, especially in high-burden countries like Pakistan. Diagnosis becomes particularly challenging in sputum-negative patients, leading to delayed treatment and increased transmission. Bronchoalveolar layage (BAL) has emerged as a potential diagnostic tool in such cases. Objective: To determine the diagnostic yield of acid-fast bacilli (AFB) in bronchoalveolar lavage of sputum-negative pulmonary tuberculosis patients. **Methods:** This cross-sectional study was conducted in the Department of Pulmonology, Gulab Devi Hospital, Lahore, over six months from June to December 2024. One hundred fifty sputum-negative PTB patients undergoing BAL were enrolled through consecutive sampling. BAL samples were collected and sent to the pathology laboratory for AFB testing via Ziehl-Neelsen staining. The primary outcome was the proportion of positive AFB results among the study population. Data were analyzed using SPSS version 25. Chi-square test was applied to assess associations between diagnostic yield and demographic or clinical variables; a p-value < 0.05 was considered statistically significant. Results: Among 150 patients, 71.3% (n = 107) were male; the mean age was  $42.81 \pm 11.23$  years. Most participants (72.0%) were aged ≤45 years. A majority (68.0%) resided in rural areas, and 62.7% belonged to a low socioeconomic status. Comorbidities included diabetes (32.7%), hypertension (40.7%), and obesity (9.3%). The mean disease duration was  $2.36 \pm 1.09$  months, with 80.7% having symptoms for  $\leq 3$  Months. Family history of TB and smoking history were noted in 26.0% and 22.0%, respectively. Most patients were unskilled workers (47.3%) or housewives (24.0%). The diagnostic yield of BAL for AFB was 83.3% (n = 125). Diagnostic yield was significantly associated with gender (p < 0.05), residential status (p = 125). < 0.05, disease duration (p < 0.05), and occupation (p < 0.05). Conclusion: Bronchoalveolar lavage demonstrates a high diagnostic yield for AFB in sputum-negative PTB patients and should be incorporated as a standard diagnostic modality in suspected cases. Early and accurate diagnosis through BAL can facilitate timely management, reduce disease transmission, and improve patient outcomes, particularly in resource-limited settings. Keywords: Bronchoalveolar lavage, Pulmonary tuberculosis, Sputum Negative

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## Introduction

Tuberculosis (TB), particularly pulmonary TB, remains a major global health concern. According to the World Health Organization (WHO), over 8.2 million new TB cases were reported worldwide in 2023, the highest number since global monitoring began in 1995 (1,2). Around 1.25 million people died from TB, making it one of the leading causes of death from infectious diseases (3). The South Asian Association for Regional Cooperation (SAARC) countries, which include eight member states, carry a significant share of the global TB burden (4). In 2019, the region accounted for 37% of global TB cases, with about 3.7 million reported cases. India, Pakistan, and Bangladesh were key contributors to the global TB cases, marking them as high-burden countries (5). Pakistan is one of the countries with a high TB burden. In 2019, it recorded around 570,000 TB cases, with an incidence rate of 263 per 100,000 people. This made up approximately 5.7% of global TB cases. Pakistan's efforts to combat TB include the National Guidelines for the Control of Tuberculosis, which focus on diagnosis, treatment, and prevention (6). However, issues such as financial constraints, drug resistance, and unequal access to healthcare facilities continue to pose challenges in the control of TB (7,8). Bronchoalveolar lavage (BAL) is an effective diagnostic tool for diagnosing sputum-negative PTB, particularly when combined with more sensitive diagnostic techniques like culture and molecular tests (Xpert MTB/RIF) (9). While AFB smear microscopy on BAL fluid alone has moderate sensitivity, these advanced methods significantly improve diagnostic accuracy in sputum-negative cases (10). Sputum smear microscopy is less sensitive in detecting Mycobacterium tuberculosis, especially when the bacterial load is low, but BAL can increase the diagnostic yield (11). Culturing Mycobacterium tuberculosis from BAL samples provides a higher diagnostic yield than AFB smear microscopy, offering better sensitivity.BAL significantly enhances diagnostic sensitivity. These tests can rapidly detect TB and rifampicin resistance with much higher sensitivity than smear microscopy (12).

This study was done to determine the diagnostic yield of BAL-AFB of sputum-negative pulmonary tuberculosis patients. Literature showed that the diagnostic yield of BAL-AFB is high. However, culture is still considered a reliable method. This may be due to the scarcity of evidence and data; no such local database is available. Therefore, we conducted this study to get the proof of the local population and also to determine the extent of diagnostic yield of BAL-AFB in comparison with AFB microscopy.

## Methodology

This cross-sectional study was conducted on 150 patients with pulmonary tuberculosis at the Department of Pulmonology, Gulab Devi Hospital, Lahore. The total duration of this study was 6 months from June 2024 to December 2024. Patients aged 16-75 years of either gender admitted with sputum-negative pulmonary tuberculosis and undergoing bronchoalveolar lavage (It was defined as the presence of Mycobacterium tuberculosis on sputum culture, but the sputum sample was negative) were included in our study. Patients with contraindications to bronchoscopy

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(uremia, coagulation disorders, thrombocytopenia, severe pulmonary hypertension, and single lung) and moderate to massive pleural effusion, asthma, and COVID-19 patients who had already taken anti-tuberculous treatment were excluded from our study. A sample size of 150 patients was calculated with a 95% confidence level, a 6.5% margin of error, and a percentage of diagnostic yield, i.e., 80% of BAL-AFB in sputumnegative pulmonary tuberculosis patients.(13)

Informed consent was obtained. Demographic information (name, age, gender, duration of symptoms, diabetes (BSR>200mg/dl), hypertension (BP $\geq$ 140/90mmHg), h/o smoking (>5 pack years), Family history of tuberculosis, occupation, residence, season, socioeconomic status) was also noted. Then, patients had undergone BAL, and the sample was taken. All samples were sent to the pathology department for AFB testing. Reports were assessed, and findings were recorded.

The collected data was analysed statistically by using SPSS version 26. Quantitative variables like age, BMI, and duration of symptoms were presented as mean and standard deviation. Qualitative variables like gender, diabetes, hypertension, smoking, F/h tuberculosis, occupation, residence, season, socioeconomic status, and diagnostic yield were presented in frequency and percentage. Data was stratified for age, gender, BMI, diabetes, hypertension, smoking, family history of tuberculosis, occupation, residence, season, socioeconomic status, and duration of symptoms by applying the chi-square test at 95 % CI. This study included 150 sputum-negative pulmonary tuberculosis patients meeting the inclusion criteria. Of these 150 patients, 71.3 % (n = 107) were male, while 28.7 % (n = 43) were female. The mean age was 42.81  $\pm$  11.23 years (range: 21 years to 65 years), and 72.0 % (n = 108) were aged up to 45 years. One hundred and two (68.0 %) belonged to rural areas, and the majority had poor social background, i.e., 62.7 % (n = 94). Diabetes was reported by 32.7 % (n = 49), hypertension in 40.7 % (n = 61), and 9.3 % (n = 14) were obese (Mean BMI was  $23.82 \pm 2.17$  kg/m 2). Mean duration of pulmonary tuberculosis was  $2.36 \pm 1.09$  months, and 80.7 % (n = 121) had disease duration up to 3 months, and family history of tuberculosis was noted in 26.0 % (n = 39), while history of smoking was positive in 22.0 % (n = 33). Of these 150 study cases, most of the patients i.e. 47.3 % (n = 71) were un - skilled workers, 20.0 % (n =30) were experienced workers, 6.7 % (n = 10) were farmers, 2.0 % (n =3) had office job and 24.0 % (n = 36) were house - wives. The diagnostic yield of acid-fast bacilli in bronchoalveolar lavage of sputum-negative pulmonary tuberculosis patients was positive in 83.3 % (n = 125) of our study cases.

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Factors	Diagnostic Yield		P value
	<b>Positive</b> (n = 125)	Negative $(n = 25)$	
Gender			
Male (n = 107)	96	11	0.001
Female $(n = 43)$	29	14	
Age groups			
$\leq$ 45 Years (n= 108)	90	18	0.998
> 45 Years (n= 42)	35	07	
Residential status		1	
Rural (n= 102)	77	25	0.001
Urban (n= 48)	48	00	
Socioeconomic status	22	11	0.025
Poor (n=94)	83	11	0.035
Middle Income (n=56)	42	14	
Diabetes			
Yes (n=49)	42	07	0.586
No (n=101)	83	18	
Hypertension			
Yes (n=61)	50	11	0.710
No (n = 89)	75	14	
Obesity			
Yes (n = 14)	14	00	0.079
No (n = 136)	111	25	
Disease duration			
Up to 3 months $(n = 121)$	96	25	0.007
> 3 months (n = 29)	25	00	
Family History			
Yes (n =39)	32	07	0.803
No (n = 111)	93	18	
Smoking			
Yes (n = 33)	29	04	0.428
No (n = 117)	96	21	
Occupation			
Unskilled worker (n = )	71	00	0.001
Skilled worker (n = )	19	11	

Results

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Farmer $(n = )$	03	07	
Office worker $(n = )$	03	00	
Housewife (n =)	29	07	

## Discussion

In suspected pulmonary tuberculosis (PTB) cases where patients cannot produce sputum or have negative sputum smears, bronchoalveolar lavage (BAL) is an important diagnostic tool. The diagnostic yield of acid-fast bacilli (AFB) smear microscopy on BAL samples varies across studies but generally shows moderate sensitivity and high specificity (14). Available literature indicates that while AFB smear microscopy on BAL samples is highly specific, its sensitivity is low, meaning a negative result does not definitively rule out PTB. Hence, it is often recommended to use more sensitive diagnostic methods, such as PCR tests, i.e., Xpert MTB/RIF assay, in conjunction with AFB smear microscopy to improve diagnostic accuracy in sputum-negative PTB cases (15).

This study included 150 sputum-negative pulmonary tuberculosis patients meeting the inclusion criteria. Of these 150 patients, 71.3 % (n = 107) were male, while 28.7 % (n = 43) were females. Men are diagnosed with PTB more frequently than women worldwide. According to the World Health Organization (WHO), the male-to-female ratio of TB cases is approximately 2:1. Biological, social, and behavioral factors may influence this disparity. Hormonal differences may affect susceptibility to TB. Among females, estrogen provides some protection, particularly before menopause, whereas serum testosterone has been associated with higher TB risk in men. Alam et al (16) from Multan has also reported 53 % male patients in sputum negative pulmonary TB patients, similar to our results. Koraa et al (17) from Egypt has also reported 56 % male patients with sputum negative pulmonary tuberculosis, similar to our results. Imtiaz et al (13) from Saudi Arabia has also reported 67 % men in sputum negative pulmonary TB patients, similar to our results. Ahmed et al (18) from Qatar has also reported 85 % male gender preponderance in sputum negative pulmonary TB patients, similar to our results. Gaude et al (19) from India has reported 74.83 % male patients in sputum negative pulmonary TB, similar to our results. Ahmmed et al (20) from Bangladesh has also reported 58 % male patients in sputum negative pulmonary TB patients, similar to our results.

Mean age was  $42.81 \pm 11.23$  years (range; 21 years to 65 years) and 72.0 % (n = 108) were aged up to 45 years. Alam et al 16 from Multan has also reported  $39.68 \pm 7.3$  years mean age of the patients with sputum negative pulmonary TB patients, similar to our results. Koraa et al (17) from Egypt has also reported  $37.12 \pm 11.90$  years mean age of the patients with sputum negative pulmonary tuberculosis, similar to our results. Imtiaz et al (13) from Saudi Arabia has also reported  $53 \pm 20$  years mean age of the sputum negative pulmonary TB patients, similar to our results. Ahmed et al (18) from Qatar has also reported  $33.3 \pm 10$  years mean age in sputum negative pulmonary TB patients, similar to our results. Gaude et al (19) from India has reported  $46.38 \pm 17.11$  years mean age of the patients in sputum negative pulmonary TB, similar to our results. Ahmmed et al (20) from Bangladesh has also reported  $36.56 \pm 12.05$  years mean age of the sputum negative pulmonary TB patients, similar to our results.

One hundred and two (68.0 %) belonged to rural areas and majority had poor social background i.e. 62.7 % (n = 94). Alam et al 16 from Multan has also reported 63% patients with sputum negative pulmonary TB patients belonged to rural areas.Koraa et al (17) from Egypt has reported 84% urban patients with sputum negative pulmonary tuberculosis which is different from our findings.

Diabetes was reported by 32.7 % (n = 49), hypertension in 40.7 % (n = 61) and 9.3 % (n = 14) were obese (Mean BMI was  $23.82 \pm 2.17$  kg/m 2). Alam et al (16) from Multan has also reported similar findings. Koraa et al (17) from Egypt has also reported 28.6 % diabetes in patients with

sputum negative pulmonary tuberculosis, similar to our results.Imtiaz et al (13) from Saudi Arabia has also reported 31 % diabetes in the sputum negative pulmonary TB patients, similar to our results. Gaude et al (19) from India has reported 28.7 % diabetic patients in sputum negative pulmonary TB, similar to our results.

Mean duration of pulmonary tuberculosis was  $2.36 \pm 1.09$  months and 80.7 % (n = 121) had disease duration up to 3 months and family history of tuberculosis was noted in 26.0 % (n = 39). Imtiaz et al (13) from Saudi Arabia has also reported 20 % positive family history in the sputum negative pulmonary TB patients, similar to our results.

History of smoking was positive in 22.0 % (n = 33). Alam et al (16) from Multan has also reported 45 % smoking among patients with sputum negative pulmonary TB patients, similar to our results.Imtiaz et al (13) from Saudi Arabia has also reported 39 % history of smoking in sputum negative pulmonary TB patients, similar to our results. Gaude et al (19) from India has reported 8.39 % positive family history which is quite less than that of our study results.

Of these 150 study cases, most of the patients i.e. 47.3 % (n = 71) were un - skilled workers, (20).0 % (n = 30) were skilled workers, 6.7 % (n = 10) were farmers, 2.0 % (n = 3) had office job and 24.0 % (n = 36) were house - wives. Koraa et al (17) from Egypt has also reported 70 % patients with sputum negative pulmonary tuberculosis were workers while 30 % were non - workers, similar to our results. Ahmed et al (18) from Qatar has also reported 85.6 % sputum negative pulmonary TB patients were unskilled workers, similar to our results.

Diagnostic yield of acid fast bacillus in bronchoalveolar lavage of sputum negative pulmonary tuberculosis patients was positive in 83.3 % (n = 125) of our study cases. Alam et al (16) from Multan has also reported 88.3 % positive predictive value in sputum negative pulmonary TB patients, similar to our results. Koraa et al (17) from Egypt has also reported 100 % diagnostic yield of bronchoalveolar lavage in patients with sputum negative pulmonary tuberculosis, similar to our results. Imtiaz et al (13) from Saudi Arabia has also reported 80 % positive diagnostic yield in sputum negative pulmonary TB patients, similar to our results. Ahmmed et al (20) from Bangladesh has also reported 66 % diagnostic yield of BAL in sputum negative pulmonary TB patients, similar to our results.

## Conclusion

The diagnostic Yield of Bronchoalveolar lavage was very high and was found effective and reliable in the diagnosis of sputum negative pulmonary tuberculosis. Bronchoalveolar lavage can be used to increase diagnostic rate of PTB and hence prevention of transmission. The diagnostic yield of bronchoalveolar lavage was significantly associated with gender, residential status, disease duration and occupation. All clinicians treating such patients can effectively employ bronchoalveolar lavage for timely diagnosis followed by effective management to safeguard these patients from future adverse outcomes. This will improve their quality of life and relieve suffering families from disease stigma and social isolation.

## Declarations

#### Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-MS-038-23) **Consent for publication** 

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#### **Conflict of interest**

The authors declared the absence of a conflict of interest.

#### **Author Contribution**

#### TZJ (Resident)

Manuscript drafting, Study Design, SM (Associate Professor)

*Review of Literature, Data entry, Data analysis, and drafting articles.* **AZJ (Resident)** 

Conception of Study, Development of Research Methodology Design, FHZC (Assistant professor)

Study Design, manuscript review, critical input. **FB** (**Resident**),

Manuscript drafting, Study Design,

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Conception of Study, Development of Research Methodology Design,

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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