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ORIGINAL ARTICLE

Spirometry results after treatment for pulmonary tuberculosis: comparison between patients with and without previous lung disease: a multicenter study

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ABSTRACT

Objective: To compare patients with and without previous lung disease, in terms of the spirometry results after they had been treated for pulmonary tuberculosis (PTB) and cured, as well as to analyze risk factors related to functional severity. **Methods:** This was a cross-sectional, multicenter study conducted at four referral centers in Brazil. Patients were divided into two groups: those with a history of lung disease or smoking (LDS+ group); and those with no such history (LDS– group). Patients underwent spirometry (at least six months after being cured). Sociodemographic and clinical data were collected. **Results:** A total of 378 patients were included: 174 (46.1%) in the LDS+ group and 204 (53.9%) in the LDS– group. In the sample as a whole, 238 patients (62.7%) had spirometric changes. In the LDS+ group, there was a predominance of obstructive lung disease (in 33.3%), whereas restrictive lung disease predominated in the LDS– group (in 24.7%). Radiological changes were less common in the LDS– group than in the LDS+ group ($p < 0.01$), as were functional changes ($p < 0.05$). However, of the 140 (79.1%) LDS– group patients with a normal or minimally altered chest X-ray, 76 (54%) had functional changes ($p < 0.01$). The risk factors associated with functional severity in the LDS– group were degree of dyspnea ($p = 0.03$) and moderate or severe radiological changes ($p = 0.01$). **Conclusions:** Impaired pulmonary function is common after treatment for PTB, regardless of the history of lung disease or smoking. Spirometry should be suggested for patients who develop moderate/severe dyspnea or relevant radiological changes after treatment for PTB.

Keywords: Tuberculosis, pulmonary; Respiratory function tests; Airway obstruction/complications.

INTRODUCTION

Tuberculosis is recognized as a global public health problem, and its control has been a challenge in recent decades.[1] In 2015, Brazil met the millennium goals by decreasing the incidence of and mortality from tuberculosis. Among the so-called BRICS countries (Brazil, Russia, India, China, and South Africa), Brazil has the lowest tuberculosis incidence rate, although the prevalence of the disease remains steady.[2] However, there are still major obstacles to controlling tuberculosis in Brazil, such as impediments to investigating contacts, to making an early diagnosis, and to initiating antituberculosis therapy in primary care.[2]

Delayed diagnosis and the low effectiveness of antituberculosis therapy, which may be due to sociocultural factors associated with patients, physicians, and the organization of the health care system, promote the spread of the disease and increase the risk of progression of lung lesions.[3-5]

One of the aspects rarely addressed in the literature is the clinical and social impact of pulmonary sequelae among patients who have completed the treatment

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regimen. Pulmonary tuberculosis (PTB) can lead to chronic airflow obstruction, depending on the degree of anatomical distortion present, and to restricted ventilation caused by fibrotic scarring associated with reduced TLC. Greater lung injury, related to disability and impaired quality of life, has been associated with delayed diagnosis of tuberculosis, quantity of previous treatments, smoking, malnutrition, and a high bacillary load at the initiation of antituberculosis therapy.[6-10]

The functional changes resulting from PTB that are observed after treatment manifest as restrictive lung disease (RLD), obstructive lung disease (OLD), or mixed obstructive-restrictive lung disease (MORLD), regardless of the history of exposure to smoking.[11] The most commonly described functional change is OLD.[6,7,12] The prevalence of OLD after treatment for PTB is estimated to range from 15% to 77%,[10,12] whereas that of MORLD, the second most prevalent, is estimated to range from 9% to 34%.[9,12] At one center in Brazil, MORLD was reported to be the most common functional change, with a prevalence of 34%.[11] However, OLD was observed in 33% of the patients evaluated by Di Naso et al.[13] and in 49% of those evaluated by Nihues et al.[14] At another center, RLD was the most prevalent (in 41%).[15]

In Brazil, there have been few studies reporting the proportion of patients with radiological and functional changes after treatment for PTB, and in those few studies[9-15] there was no exclusion of patients with a history of lung disease or smoking prior to treatment for PTB. Therefore, given the prevalence of PTB in Brazil, it is relevant to have knowledge of the magnitude of spirometric changes in this population.

The objective of the present study was to compare patients with a history of lung disease or smoking and those with no such history, on the basis of the spirometry results after treatment for PTB, at one of four referral centers in Brazil, as well as to analyze risk factors related to functional severity in the patients with no history of lung disease or smoking.

METHODS

Study design

This was a cross-sectional, multicenter study involving non-probability purposive sampling. The study population consisted of 418 patients recruited between 2014 and 2015 from one of the following referral centers in Brazil: the Federal University of Minas Gerais *Hospital das Clínicas* (a tertiary referral center), in the city of Belo Horizonte; the Brazilian Institute for Tuberculosis Research (a secondary referral center), in the city of Salvador; the Dourados Municipal Program for Tuberculosis Control (a secondary referral center), in the city of Dourados; and the Thoracic Diseases Institute of the Federal University of Rio de Janeiro School of Medicine Clementino Fraga Filho University Hospital, (a tertiary referral center), in the city of Rio de Janeiro.

We included patients who were ≥ 18 years of age; had been diagnosed with PTB, confirmed by sputum smear microscopy or mycobacterial culture; had received a single treatment for PTB at one of the four referral centers; had been cured; and had undergone spirometry. We excluded patients whose spirometry results did not meet the *Sociedade Brasileira de Pneumologia e Tisiologia* (SBPT, Brazilian Thoracic Association) acceptability and reproducibility criteria[16] or who had a condition that made it impossible to perform the test or was a contraindication to it, such as hemoptysis, an altered level of consciousness, acute myocardial infarction or ischemic stroke in the last 3 months, uncontrolled systemic arterial hypertension, and aortic aneurysm.

All patients who had been cured of PTB were invited to participate in the study. Participants completed a standardized questionnaire that collected information on sociodemographic and clinical characteristics, such as gender, age, smoking, alcoholism, and comorbidities. In addition, the time from symptom onset to diagnosis of PTB was determined. Smokers were defined as individuals who had smoked at least 100 cigarettes (or equivalent) in their lifetime, and former smokers were defined as those who had quit smoking more than 12 months prior.[17] Alcoholism was assessed with the Cut down, Annoyed, Guilty, and Eye-opener questionnaire.[18]

Sociodemographic and clinical characteristics were categorized as follows: skin color, defined as White or Non-White; marital status, defined as married/living as married or other (widowed, separated/divorced, or single); level of education, defined as ≤ 9 or > 9 years of schooling; and self-reported comorbidities. Diagnoses of lung disease (asthma, COPD, bronchiectasis, interstitial lung disease, and silicosis) prior to treatment for PTB were reviewed by the pulmonologists involved in the present study, who followed the definitions proposed in the Global Initiative for Asthma guidelines and the Global Initiative for Chronic Obstructive Lung Disease guidelines, as well as in a national practice guideline.[19-21]

With regard to signs and symptoms, participants were evaluated for the presence of dyspnea, as classified by the modified Medical Research Council (mMRC) scale,[22] cough, expectoration, and wheezing. These data were obtained on the day of the spirometry.

Patients were divided into two groups: those with a history of lung disease or smoking prior to treatment for PTB (LDS+ group); and those with no such history (LDS− group). Spirometry was performed at least 6 months after the PTB had been cured.

Functional assessment

Spirometry was performed with a Koko spirometer (Pulmonary Data Service Inc., Louisville, CO, USA). All tests were performed and interpreted following the recommendations of the SBPT guidelines.[16]

Post-bronchodilator values were compared with pre-bronchodilator values and were expressed as absolute values and as a percentage of predicted values, according to Knudson et al.[23] for female and male patients under 20 and 25 years of age, respectively, and according to Pereira et al.[24] for patients older than that. The technicians who performed the tests were certified by the SBPT. Spirometry results were classified as follows: normal spirometry; OLD; OLD with reduced (F)VC; and RLD. The severity of obstruction was graded on the basis of FEV_1 and FEV_1/FVC, in % of predicted, as follows[16]: mild, ≥ 60%; moderate, 41-59%; and severe, ≤ 40%. The severity of restriction was graded on the basis of (F)VC, in percentage of predicted, as follows[16]: mild, ≥ 60%; moderate, 51-59%; and severe, ≤ 50%.

Radiological assessment

Chest X-rays were performed on dates close to those on which spirometry was performed, were evaluated by radiologists, and were classified by pulmonologists. Chest X-rays showing no changes were classified as normal. The remaining chest X-rays were classified as defined in the National Tuberculosis Association (NTA) classification[25]: NTA-I, or minimal; NTA-II, or moderately advanced (in one or both lungs, there may be lesions, the total extent of which should not exceed the total volume of one lung if the lesions are not confluent and should not exceed one third of the volume of one lung if they are confluent); and NTA-III, or far advanced (if the lesions are even more extensive).

Statistical analysis

The study variables were entered into an Excel database and were analyzed using the IBM SPSS Statistics software package, version 22.0 (IBM Corporation, Armonk, NY, USA). The distribution of the variables was assessed by the Kolmogorov-Smirnov test. Continuous variables are expressed as means and standard deviations or as medians and interquartile ranges, whereas categorical variables are expressed as absolute and relative frequencies. Clinical, demographic, radiological, and functional characteristics were compared between the two groups by using the chi-square test or the Student's t-test, as appropriate. The spirometric classifications of the LDS− group patients were analyzed, in terms of clinical, demographic, and radiological characteristics, with Pearson's chi-square test and were divided into two groups: no disease (normal spirometry results) or mild disease; and moderate or severe disease. Values of $p < 0.05$ were considered significant.

Ethical considerations

The study was approved by the Research Ethics Committee of the Federal University of Minas Gerais (Reference no. 14606113.7.0000.5149). All participating patients gave written informed consent.

RESULTS

Of the 418 patients initially recruited, 40 (10.5%) were excluded because the spirometry tests did not meet acceptability and reproducibility criteria. There were no significant clinical, demographic, or radiological differences between the patients who were included in the study and those who were excluded.

Therefore, the final sample comprised 378 patients, of whom 174 (46%) were in the LDS+ group and 204 (54%) were in the LDS− group. The characteristics of the patients are described in Table 1. The proportions of patients who were male, were > 49 years of age, had completed ≤ 9 years of schooling, had at least one comorbidity (systemic arterial hypertension, heart disease, or diabetes mellitus), were alcoholics, and had respiratory symptoms were significantly higher in the LDS+ group than in the LDS− group (Table 1).

Chest X-rays classified as normal or NTA-I were more common in the LDS− group than in the LDS+ group ($p < 0.01$; Table 1). Pre- and post-bronchodilator absolute and percentage of predicted FEV_1, $FEF_{25-75\%}$, FEV_1/FVC, and $FEF_{25-75\%}$/FVC were significantly higher in the LDS− group than in the LDS+ group (Table 2).

Of the 378 patients evaluated, 238 (62.7%) had spirometric changes. Normal spirometry was more common in the LDS− group ($p < 0.01$). As can be seen in Table 3, the most common spirometric changes in the LDS+ group were OLD, in 58 patients (33.3%) and OLD with reduced FVC, in 49 (28.2%), whereas the most common spirometric changes in the LDS− group were RLD, in 50 (24.7%) and OLD, in 42 (20.6%).

With regard to the severity of OLD and RLD, there was a predominance of mild disease in both groups. Among the patients who had OLD with reduced FVC, severe disease was more common in those in the LDS+ group, whereas moderate disease was more common in those in the LDS− group (Table 3).

Table 4 shows the radiological grading and spirometric classification of the LDS− group patients (n = 177). Of the 140 (79.1%) LDS− group patients whose chest X-ray was classified as normal or NTA-I, 76 (54.0%) had functional changes ($p < 0.01$).

Analysis of the classification of the LDS− group patients, based on spirometry results and clinical, demographic, and radiological characteristics, revealed that age > 49 years, mMRC grade 2-4 dyspnea, and radiological changes classified as NTA-II/III were associated with moderate and severe functional changes. There was no significant association between the time from symptom onset to diagnosis of tuberculosis and the severity of spirometric changes (Table 5).

DISCUSSION

The main finding of the present study is that, after having been treated for PTB and cured, 238

Table 1. Clinical, demographic, and radiological characteristics of patients treated for pulmonary tuberculosis (N = 378) who had a history of lung disease or smoking or who had no such history; 2014-2015.

Characteristic	LDS+ group (n = 174)		LDS− group (n = 204)		p
	n	%	n	%	
Gender					
Male	115	66.1	82	40.2	< 0,01
Female	59	33.9	122	59.8	
Age, years					
18-29	15	8.6	54	26.5	< 0.01
30-49	56	32.2	89	43.6	
> 49	103	59.2	61	29.9	
Skin color					
White	32	18.4	33	16.3	0.60
Non-White	142	81.6	169	83.7	
Marital status					
Married/living as married	106	61.3	100	51.0	0.05
Other[a]	67	38.7	96	49.0	
Level of education					
≤ 9 years of schooling	105	80.8	96	60.0	< 0.01
> 9 years of schooling	25	19.2	64	40.0	
HIV/AIDS					
Yes	8	6.0	5	3.3	0.30
No	126	94.0	145	96.7	
Systemic arterial hypertension					
Yes	57	33.3	34	16.7	< 0.01
No	114	66.7	170	83.3	
Heart disease					
Yes	13	7.5	3	1.5	< 0.01
No	161	92.5	201	98.5	
Diabetes mellitus					
Yes	25	14.6	15	7.6	0.03
No	146	85.4	182	92.4	
Chronic kidney disease					
Yes	10	5.7	11	5.4	0.88
No	164	94.3	193	94.6	
Cancer					
Yes	7	4.0	3	1.5	0.12
No	167	96.0	201	98.5	
Smoking					
No	25	14.4	204	100	< 0.01
Smoker	71	40.8			
Former smoker	78	44.8			
Alcoholism					
Yes	63	36.8	36	18.4	< 0.01
No	108	63.2	160	81.6	
Dyspnea, mMRC					
0-1	142	84.0	181	93.3	< 0.01
2-4	27	16.0	13	6.7	
Cough					
Yes	92	52.9	50	25.5	< 0.01
No	82	47.1	146	74.5	
Expectoration					
Yes	68	39.1	32	16.3	< 0.01
No	106	60.9	164	83.7	
Wheezing					
Yes	40	23.1	10	5.1	< 0.01
No	133	76.9	186	94.9	
Chest X-ray					
Normal/NTA-I	87	55.4	140	79.1	< 0.01
NTA-II/III	70	44.6	87	20.9	
Disease duration to diagnosis					
< 30 days	24	20.9	37	23.6	0.59
≥ 30 days	91	79.1	120	76.4	

LDS: history of lung disease or smoking; mMRC: modified Medical Research Council (scale); and NTA: National Tuberculosis Association (classification system).[25] [a]Widowed, separated/divorced, or single.

Table 2. Spirometric variables of patients treated for pulmonary tuberculosis (N = 378) who had a history of lung disease or smoking or who had no such history; 2014-2015.[a]

Variable	LDS+ group (n = 174)	LDS− group (n = 204)	p*
IC, L	2.29 ± 0.82	2.40 ± 0.68	< 0.01
IC, % of predicted	78.8 ± 23.9	82.5 ± 16.3	
Post-BD IC, L	2.44 ± 0.83	2.43 ± 0.60	0.04
VC, L	3.35 ± 1.05	3.37 ± 0.91	0.01
VC, % of predicted	83.9 ± 20.6	84.9 ± 1.5	
Post-BD VC, L	3.50 ± 0.97	3.45 ± 0.93	< 0.01
FVC, L	3.36 ± 1.13	3.31 ± 0.86	0.01
FVC, % of predicted	82.9 ± 20.4	84.3 ± 15.1	
Post-BD FVC, L	3.44 ± 1.11	3.34 ± 0.87	< 0.01
FEV_1, L	2.39 ± 1.00	2.66 ± 0.74	0.01
FEV_1, % of predicted	72.2 ± 24.2	82.2 ± 17.5	
Post-BD FEV_1, L	2.54 ± 1.03	2.74 ± 0.75	0.01
$FEF_{25-75\%}$, L/s	1.92 ± 1.28	2.69 ± 1.18	< 0.01
$FEF_{25-75\%}$, % of predicted	58.3 ± 35.3	80.5 ± 34.2	
Post-BD $FEF_{25-75\%}$, L/s	2.21 ± 1.40	2.95 ± 1.22	< 0.01
FEV_1/FVC, %	69.7 ± 14.2	80.4 ± 11.1	< 0.01
FEV_1/FVC, % of predicted	86.0 ± 16.8	97.0 ± 12.5	
$FEF_{25-75\%}$/FVC, %	54.8 ± 30.9	82.5 ± 35.2	< 0.01
$FEF_{25-75\%}$/FVC, % of predicted	67.8 ± 36.0	95.7 ± 39.8	

LDS: history of lung disease or smoking; IC: inspiratory capacity; and BD: bronchodilator. [a]Values expressed as mean ± SD. *Chi-square test.

Table 3. Spirometric classification of patients treated for pulmonary tuberculosis (N = 378) who had a history of lung disease or smoking or who had no such history; 2014-2015.[a]

Classification	LDS+ group (n = 174)		LDS− group (n = 204)		p*
	n	%	n	%	
Normal spirometry	48	27.6	92	45.8	0.01
Obstructive lung disease	58	33.3	42	20.6	0.99
Mild	44	75.9	37	88.1	
Moderate	13	22.4	4	9.5	
Severe	1	1.7	1	2.4	
Obstructive lung disease with reduced FVC	49	28.2	18	8.9	0.03
Mild	8	16.3	4	20.0	
Moderate	17	34.7	12	60.0	
Severe	24	49.0	4	20.0	
Restrictive lung disease	19	10.9	50	24.7	0.54
Mild	17	89.5	46	92.0	
Moderate	0	0.0	1	2.0	
Severe	2	10.5	3	6.0	

LDS: history of lung disease or smoking. [a]According to the recommendations of the Brazilian Thoracic Association guidelines.[16] *Chi-square test for linear association.

(62.7%) of the patients had spirometric changes. Comparison of the two groups revealed that functional and radiological changes were less common in the LDS− group. However, of the 140 (79.1%) LDS− group patients whose chest X-ray was classified as normal or NTA-I, 76 (54.0%) had functional changes. These data suggest that impaired pulmonary function after PTB is a major cause of chronic lung disease. The risk factors related to functional severity in this group were age > 49 years, mMRC grade 2-4 dyspnea, and radiological changes classified as NTA-II/III.

Investigation of changes in pulmonary function after completion of treatment for PTB has been gaining prominence in the literature.[6,7,9,11-15,26,27] In our study, the most common functional change in the LDS− group was RLD (24.7%). Cruz et al.[15] also described RLD as the main functional change after treatment for PTB; however, that study included patients who underwent more than one treatment for PTB.

In the literature, the reported frequency of OLD ranges from 15% to 77%.[6,7,9,12,28,29] The combination

Table 4. Comparison between spirometry results and chest X-ray results of patients treated for pulmonary tuberculosis who had no history of lung disease or smoking (n = 177); 2014-2015.

Spirometry results[b]	Chest X-ray results[a]							
	Normal (n = 68)		NTA-I (n = 72)		NTA-II (n = 31)		NTA-III (n = 6)	
	n	%	n	%	n	%	n	%
Normal spirometry	35	46.7	29	38.7	10	13.3	1	1.3
Obstructive lung disease	11	28.9	19	50.0	8	21.1	0	0.0
Restrictive lung disease	17	37.0	18	39.1	9	19.6	2	4.3
Obstructive lung disease with reduced FVC	5	27.8	6	33.3	4	22.2	3	16.7

[a]According to the National Tuberculosis Association (NTA) classification system.[25] [b]According to the recommendations of the Brazilian Thoracic Association guidelines.[16] Chi-square test; p = 0.01.

of PTB and airflow obstruction can occur regardless of the presence of smoking,[30] suggesting that the obstruction found in the LDS− group patients may be due to their PTB lesions. Some population-based studies have also described OLD as the most common functional change; however, those studies included smokers, former smokers, and patients with a history of lung disease,[28,29] similar to what was observed in the LDS+ group in the present study.

PTB can affect the airways and lung parenchyma, leading to mucosal edema, hypertrophy/hyperplasia of the mucous glands, increased mucus secretion, smooth muscle layer hypertrophy, and increased activity of metalloproteinases. Consequently, there can be changes in airway caliber (caused by stenosis, distortion, bronchiectasis, and emphysema), increased airway resistance, and reduced airflow.[31] In addition, fibrotic scarring can reduce lung compliance, leading to restriction.[27] This heterogeneity of lung lesions should be more extensively studied, especially with regard to pathophysiology and inflammatory phenomena.

Functional changes, which may persist after PTB has been cured, are associated with disability and reduced quality of life.[32,33] Lee et al.[4] stated that early diagnosis and prompt initiation of therapy translate to a lower likelihood of significant functional changes. In our study, there was no association between the time from symptom onset to diagnosis of PTB and the severity of spirometric changes, suggesting that PTB may lead to functional changes, regardless of the timing of the initiation of therapy, as also reported by Manji et al.[34]

Specifically in the LDS− group patients, dyspnea can be explained by structural (NTA-II and NTA-III) lesions leading to airway obstruction, with small airways involvement and bronchiectasis,[10] as well as destruction of the lung parenchyma. Other studies have identified an association between the extent of radiographic changes and changes in pulmonary function.[13,15,32,34-36] Those studies suggest that greater lesion extent translates to greater tissue damage, these sequelae being reflected in changes in pulmonary function. However, those studies did not assess the severity of spirometric changes.[13,15,32,34-36] Disease overlap could explain the higher frequency of symptoms (dyspnea, cough, expectoration, and wheezing) in the LDS+ group. Some limitations of the present study should be noted. The first limitation is that functional changes were not assessed longitudinally, rather being assessed 24 months after completion of the antituberculosis therapy. That could provide different results if the lesions have yet to stabilize.[37] The second limitation is the use of chest X-ray, a method that may underestimate the extent of sequelae. Chest CT can more accurately characterize the changes caused by PTB sequelae. However, in a recent study, chest CT and chest X-ray were in disagreement in only 7% of the examinations in patients with PTB sequelae.[26] In addition, chest X-ray is inexpensive and is available at tuberculosis treatment centers in Brazil, in contrast to chest CT, to which access is limited. Another limitation is that pulmonary function was assessed by spirometry only, without plethysmography or DLCO measurement. However, the equipment needed for those tests is unavailable at most centers in Brazil. Finally, the relationship between greater functional severity and being > 49 years of age was not investigated.

Functional changes constitute knowledge gaps that warrant further studies, especially studies aimed at determining whether airway obstruction due to PTB is a different entity from COPD due to exposure to cigarette smoke or smoke from wood-burning stoves, silicosis, etc.[38] In addition, further studies could assess responses to treatments such as the use of specific inhaled medication and pulmonary rehabilitation to improve patient quality of life.

In conclusion, impaired pulmonary function is common after treatment for PTB, regardless of the history of smoking or lung disease. Spirometry should be suggested for patients who develop mMRC grade 2-4 dyspnea or relevant radiological changes after treatment for PTB.

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Table 5. Clinical, demographic, and radiological characteristics of patients treated for pulmonary tuberculosis who had no history of lung disease or smoking (n = 204), by spirometry classification; 2014-2015.

Characteristic	No disease or mild disease		Moderate or severe disease		p
	n	%	n	%	
Gender					
Male	66	36.9	16	64.0	0.10
Female	113	63.1	9	36.0	
Age, years					
18-29	52	29.0	2	8.0	0.03
30-49	78	43.6	11	44.0	
> 49	49	27.4	12	48.0	
Skin color					
White	28	15.8	5	20.0	0.60
Non-White	149	84.2	20	80.0	
Marital status					
Married/living as married	86	50.0	14	58.3	0.24
Other[a]	86	50.0	10	41.7	
Level of education					
≤ 9 years of schooling	82	58.6	14	70.0	0.33
> 9 years of schooling	58	41.4	6	30.0	
Alcoholism					
Yes	32	18.5	4	17.4	0.90
No	141	81.5	19	82.6	
HIV/AIDS					
Yes	4	3.0	1	6.3	0.49
No	130	97.0	15	93.8	
Systemic arterial hypertension					
Yes	28	15.6	6	24.0	0.29
No	151	84.4	19	76.0	
Heart disease					
Yes	3	1.7	0		0.51
No	176	98.3	25		
Diabetes mellitus					
Yes	12	6.9	3	12.5	0.34
No	161	93.1	21	87.5	
Chronic kidney disease					
Yes	11	6.1	0	0.0	0.20
No	168	93.9	25	100.0	
Cancer					
Yes	2	1.1	1	4.0	0.26
No	177	98.9	24	96.0	
Dyspnea, mMRC					
0-1	162	94.7	19	82.6	0.03
2-4	9	5.3	4	17.4	
Cough					
Yes	42	24.3	8	34.8	0.28
No	131	75.7	15	65.2	
Expectoration					
Yes	26	15.0	6	26.1	0.18
No	147	85.0	17	73.9	
Wheezing					
Yes	7	4.0	3	13.0	0.07
No	166	96.0	20	87.0	
Chest X-ray					
Normal/NTA-I	128	82.1	12	57.1	0.01
NTA-II/III	28	17.9	9	42.9	
Disease duration to diagnosis					
< 30 days	34	24.3	3	17.7	0.54
≥ 30 days	106	75.7	14	82.4	

mMRC: modified Medical Research Council (scale); and NTA: National Tuberculosis Association (classification system). [a]Widowed, separated/divorced, or single.

AUTHOR CONTRIBUTIONS

All authors contributed to all stages of this study, including study conception and design, data acquisition and analysis, data interpretation, preparation and revision of the manuscript, and approval of the final manuscript.

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