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Airflow obstruction and small airway dysfunction following pulmonary tuberculosis: a cross-sectional survey

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ABSTRACT

Objectives Pulmonary function impairment and chronic respiratory symptoms after tuberculosis are relatively common in low-income and middle-income countries. We aimed to estimate the impact of post-tuberculosis (post-TB) on pulmonary function.

Methods This large cross-sectional, population-based study included subjects aged 15 years or older with technically acceptable postbronchodilator spirometry measurements. Post-TB was diagnosed on the basis of radiological evidence and/or medical history. Airflow obstruction was defined as a postbronchodilator forced expiratory volume in 1 s/forced vital capacity ratio below the lower limit of normal of Global Lung Function Initiative (GLI) lung function equations. Small airway dysfunction was diagnosed if at least two of the following indicators were less than 65% of predicted: maximal mid-expiratory flow, forced expiratory flow (FEF) 50% or FEF 75%.

Results In this population sample (N=8680, mean age: 40.1 years), 610 (7.0% (95% CI 6.5 to 7.6) participants were post-TB. Post-TB subjects had more frequent respiratory symptoms (46.8% vs 28.3%). Among post-TB subjects, 130 (21.3% (95% CI 18.1 to 24.8)) had airflow obstruction; OR of airflow obstruction was significantly associated with post-TB after adjustment for other confounding factors (OR 1.31, 95% CI 1.05 to 1.62). Post-TB was also associated with small airway dysfunction (OR 1.28, 95% CI1.07 to 1.53), which was present in 297 (48.9% (95% CI 33.9 to 53.0)) post-TB subjects.

Conclusions Our findings support existing knowledge that post-TB is positively associated with pulmonary function impairment and make for frequent respiratory symptoms. Post-TB should be considered as a potentially important cause of airflow obstruction and respiratory symptoms in patients originating from countries with a high burden of tuberculosis.

Key messages

What is already known on this topic

⇒ Several publications have reported the prevalence of post-tuberculosis (post-TB) sequelae, but the definition of post-TB and studied population are inconsistent. We wished estimate the prevalence of post-TB in low-income areas in China and identify the impact of post-TB on pulmonary function.

What this study adds

⇒ Our findings confirmed that post-TB is highly prevalent, is positively associated with airflow obstruction and associated with a high frequency of respiratory symptoms.

How this study might affect research, practice or policy

⇒ Better understanding and addressing airflow obstruction and respiratory symptoms after TB is needed; this is most relevant in low-resource, high-burden settings, where healthcare resources and diagnostics means are limited.

INTRODUCTION

Tuberculosis (TB) is a major global health problem especially in low-income and middle-income countries; it is among the top 10 causes of death and the leading cause from a single infectious agent. An estimated 10.0 million people developed TB worldwide, leading to an estimated 1.3 million TB deaths among HIV-negative people in 2020.[1] China is the third contributor to this worldwide epidemic and accounts for 8.4% of all cases, after India (26%) and Indonesia (8.5%).[2] While treatment is available and efficient in non-multidrug-resistant/extensively drug-resistant (MDR/XDR) cases, microbiological cure may not prevent long-term pulmonary complications of TB.

While smoking remains the key risk factor for chronic obstructive pulmonary disease (COPD), a considerable burden of the disease in low-income and middle-income countries cannot be explained by smoking alone. TB and other non-smoking risk factors of COPD such as domestic pollution are of increasing importance.[3–6] An association between past TB and airflow obstruction, characteristic of COPD, has been reported in large population-based epidemiological studies.[7–10] However, most of these studies included subjects above 40 years of age and are limited to low TB burden regions. There is also some evidence that pulmonary TB is related to persistent symptoms and has a substantial adverse impact on quality of life. A high burden of self-reported symptoms after TB treatment completion has been reported.[11–13] Better understanding

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and addressing of airflow obstruction and respiratory symptoms after TB is needed: this is most relevant in low-resource, high-burden settings, where healthcare resources and diagnostic modalities are limited.

In this study, we aimed to describe the general characteristics, pulmonary function parameters and chronic respiratory symptoms of people with post-TB. We also quantified the association between post-TB status and chronic respiratory symptoms and further characterised the relationship between post-TB and pulmonary function impairment.

METHODS

Study design and participants

The present study, conducted in Tibet and Xinjiang Uygur Autonomous Regions, analysed pulmonary health in long-term residents of these areas aged 15 years or older, details of which have been reported elsewhere.[14] A multistage stratified sampling procedure was used to select subjects from 13 local regions between June 2015 and August 2016. The proportion of samples from each gender and age group was based on the 2010 census of the Chinese population. A standardised questionnaire covering sociodemographic status, living conditions, respiratory symptoms, history of respiratory diseases and comorbidities, environmental and occupational factors was administered by experienced interviewers at local community health centres. Furthermore, a range of physical measurements were undertaken using a standard protocol, including anthropometry, blood pressure, oxygen saturation by pulse oximetry (SpO_2) and lung function. A posterior–anterior chest radiograph was obtained during deep inspiration in a standing position using a radiography unit.

Procedures

Pulmonary function tests were measured by trained technicians in all qualified study participants (spirometry) with a MasterScreenTM Pneumo PC spirometer (CareFusion, Yorba Linda, California) according to the American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations by trained technicians.[15] The spirometer was calibrated daily using a 3-litre syringe to ensure measured volumes within 3% of syringe volume, before data collection; ambient temperature, humidity and altitude were also recorded daily. Each participant underwent the same procedure two times, before and after receiving a bronchodilator (BD) (400 ug of salbutamol through a 500 mL spacer). The forced expiratory manoeuvres were performed 3–8 times until the forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) were reproducible within 150 mL.[16] Acceptability of FVC and FEV_1 was scored using an A to F grading system. Performing three acceptable manoeuvres with an FVC variability of 100 mL or less was rated 'A', a variability of 100–150 mL was rated 'B'; variability between 150 and 200 mL was scored 'C'. A, B or C grades were considered acceptable for analysis. Data were uploaded daily to a database, examined for incoherent data by the study supervisors and by the principal investigator. Quality control, based on the American Thoracic Society/European Respiratory Society criteria, was performed by a field supervisor at the filing centre, and included analysis of flow volume curves for artefacts and appropriate technique. Airflow obstruction was defined as a post-BD FEV_1/FVC ratio below the lower limit of normal (LLN) for height, age and sex, based on the reference values from the Global Lung Function Initiative (GLI) lung function equations for a North East Asian population.[17] A post-BD FEV_1/FVC ratio of <0.70 was also used to define airflow obstruction in a sensitivity analysis based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.[18] Spirometric restriction was defined as a post-BD FVC ratio below the LLN for the height, age and sex based on the same reference population with a normal FEV_1/FVC ratio. We used three indicators of lung function to assess small airway dysfunction, namely, maximal mid-expiratory flow (MMEF), forced expiratory flow (FEF) at 50% of vital capacity and FEF at 75% of vital capacity. Small airway dysfunction was diagnosed when at least two of these three indicators were below 65% of predicted values.[19]

Post-TB was defined as having highly suggestive images of pulmonary TB sequalae on chest radiographs and/or a positive medical history of TB.[7–9] The diagnosis of post-TB lesions was considered in the presence of discrete linear or reticular fibrotic scars or dense nodules with distinct margins, with or without calcifications, within the upper lobes.[20] The radiographs were reviewed by two experienced radiologists who were blinded to the details of the participants, using standard criteria for reporting radiologic abnormalities.[21] Discordant findings were resolved by discussion and consensus. A medical history of tuberculosis was defined as a positive answer to the question 'Has a doctor or other healthcare provider ever told you that you had tuberculosis?'.

Definitions of ever smoker, never smoker, household air pollution (HAP), occupational exposure have been previously reported.[14] Self-reported history of physician-diagnosed hypertension, chronic cardiovascular disease of any cause, diabetes mellitus, dyslipidaemia and asthma was also obtained. We defined the chronic respiratory symptoms by their persistence for at least 3 consecutive months during a year based on questionnaires.

Statistical analysis

All analyses were performed with R statistical programme V.4.0.3 (www.r-project. org/). The analyses included a description of the sample, evaluation of mean spirometric results, calculation of the prevalence of airflow obstruction and small airway dysfunction according to history of post-TB. Statistical significance of differences was tested by analysis of variance (ANOVA) or Student's t test for continuous variables and by $\chi 2$ test for categorical variables. Logistic regression models were built to quantify the relationship between post-TB and airflow obstruction. Potential confounders considered were: age, sex, region, educational level, smoking history and pack-years, HAP, occupational exposure and history of asthma. ORs with 95% CIs were determined for three models. Differences with two-sided $p<0.05$ were considered statistically significant.

RESULTS

Of the 12 991 subjects invited to participate, 11 747 completed the survey questionnaire and performed chest X-rays. Among them, 2503 participants were excluded from this analysis because they could not complete post-BD testing. After excluding 564 participants without reliable spirometric data, the final study sample included 8680 participants (4407 (50.8%) women, 4273 (49.2%) men), with an overall mean age of 40.1 (SD 15.3) years (online supplemental figure E1).

Among the 8680 participants, 610 (7.0%) had evidence of post-TB (table 1). Number of post-TB subjects, as defined by evidence of post-TB on chest radiographs only, was 463 (5.3% (95% CI 4.9% to 5.8%)), while that based on self-reported history of TB only was 98 (1.1% (95% CI 0.9% to 1.4%)). There were 49 (0.6% (95% CI 0.4 to 0.7%)) subjects for whom there was both evidence of post-TB on chest radiographs and a history

Table 1 Characteristics of participants according to history of post-TB

Variables	Post-TB (n=610)	Non post-TB (n=8070)	P value
Male	328 (53.8%)	3945 (48.9%)	0.022
Age, years	49.31 (15.21)	39.49 (15.17)	<0.001
City dweller	256 (42.1%)	2580 (32.1%)	<0.001
Education level			
Primary school and lower	362 (59.4%)	3512 (43.5%)	<0.001
Middle and high school	180 (29.5%)	3225 (40.0%)	
College and higher	68 (11.1%)	1333 (16.5%)	
Smoking status			
Never smoker	405 (66.4%)	5866 (72.7%)	<0.001
Ever smoker	205 (33.6%)	2201 (27.3%)	
Comorbidities			
Hypertension	97 (16.3%)	636 (8.0%)	<0.001
Chronic cardiovascular disease	11 (1.8%)	66 (0.8%)	0.022
Diabetes mellitus	14 (2.7%)	128 (2.1%)	0.303
Dyslipidaemia	70 (13.4%)	478 (7.9%)	<0.001
History of asthma	32 (5.3%)	118 (1.5%)	<0.001
Respiratory symptoms			
Frequent cough	109 (18.0%)	757 (9.5%)	<0.001
Sputum	110 (18.2%)	750 (9.4%)	<0.001
Recurrent wheezing	54 (8.9%)	310 (3.9%)	<0.001
Dyspnoea in daily life	198 (32.7%)	1570 (19.6%)	<0.001
At least one of the symptoms	284 (46.8%)	2259 (28.3%)	<0.001
Lung function parameters			
FVC post-BD, L	3.57 (1.02)	3.73 (0.96)	<0.001
FVC post-BD % pred	106.20 (25.55)	104.19 (22.33)	0.060
FEV_1 post-BD, L	2.80 (0.91)	3.07 (0.85)	<0.001
FEV_1 post-BD % pred	100.55 (28.49)	101.47 (23.60)	0.437
FEV_1/FVC post-BD, %	78.40 (12.18)	82.38 (10.72)	<0.001
MMEF post-BD % pred	68.95 (35.07)	78.90 (57.69)	<0.001
$FEF_{50\%}$ post-BD % pred	83.52 (36.17)	88.48 (31.06)	0.001
$FEF_{75\%}$ post-BD % pred	85.01 (58.02)	92.33 (47.12)	0.003
Oxyhemoglobin saturation (SpO_2), %	91.39 (6.39)	93.45 (5.25)	<0.0001

Data are expressed as number (%) or mean (SD).
FEF, forced expiratory flow; FEV_1, forced expiratory volume in the first second; FVC, forced vital capacity; MMEF, maximum mid-expiratory flow; post-BD, post-bronchodilator.

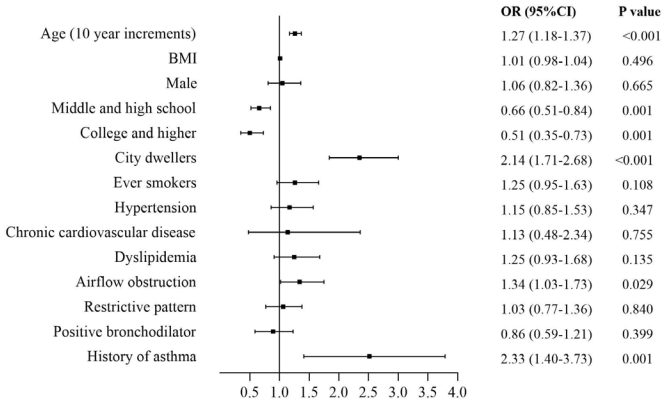

Figure 1 Forest plot showing OR for post-TB participants. Each square represents an OR. The horizontal lines indicate 95% CIs. BMI, body mass index; TB, tuberculosis.

of TB. Post-TB individuals were more likely to be men, older, ever smokers, city dwellers and have a lower educational level. They reported more comorbidities and had lower oxygen saturation (SpO_2). They had a higher frequency of chronic cough, sputum, recurrent wheezing and dyspnoea in daily life when compared with those without 'post-TB'. Also, they reported a higher rate of at least one of the listed respiratory symptoms (46.8% vs 28.3%). Spirometric indices: when compared with subjects without 'post-TB', post-TB participants had lower post-BD values for FEV_1/FVC% (mean (SD): 78.4 (12.2) vs 82.4 (10.7), p<0.001), FVC (3.57 (1.02) vs 3.73 (0.96), p<0.001) and FEV_1 (2.80 (0.91) vs 3.07 (0.85), p<0.001) and lower MMEF, FEF_{50} and FEF_{75} values as % of predicted. Older age, being a city dweller, having a history of asthma and suffering from airflow obstruction significantly increased probability of having a post-TB status, while higher educational level was related with a lower risk (figure 1).

Overall prevalence of airflow obstruction in post-TB subjects (21.3% (95% CI 18.1% to 24.8%) was significantly higher than in 'non-post-TB' subjects (15.2% (95% CI 14.5% to 16.0%)). This was also the case for small airway dysfunction (48.9% (297 of 607) vs 37.5% (2993 of 7987)). Standardised prevalence of these conditions increased steadily with age (p<0.001 for airflow obstruction and small airway dysfunction) (figure 2). Using the GOLD threshold of a fixed FEV_1/FVC ratio <0.7, prevalence of airflow obstruction in post-TB subjects (all: 19.3% (95% CI 16.2 to 22.4); men: 22.3% (95% CI 17.8 to 26.8); women: 16.0% (95% CI 11.7 to 20.3)) was also significantly higher than in 'non-post-TB' participants (all: 10.9% (95% CI 10.2 to 11.6); men: 12.2% (95% CI 11.2 to 13.2); women: 9.6% (95% CI 8.7 to 10.5)) (figure 3).

Table 2 presents the characteristics and spirometric results of participants according to post-TB and airflow obstruction status. Subjects with airflow obstruction and a history of post-TB had lower post-BD spirometric values, a higher proportion of GOLD III-IV stages (online supplemental figure E2), more respiratory symptoms, a more frequent history of asthma, a lower SpO_2 and a higher percentage of subjects with a chronic obstructive pulmonary disease assessment test (CAT) score ≥10 compared with 'non-post-TB' participants. Importantly, post-TB subjects without airflow obstruction actually reported more respiratory symptoms (46.0% vs 29.5%, p<0.001) and had a lower SpO_2 (91.0% (0.2) vs 94.4% (0.1), p<0.001) and a lower FVC (absolute value and % predicted) than 'non-post-TB' subjects with airflow obstruction.

Subjects with a restrictive pattern: online supplemental table E1 shows the demographic characteristics of participants according to their lung function (presence of a restrictive pattern vs normal) and post-TB status. Post-TB participants with normal spirometry had nearly two times as much respiratory symptoms as those without a history of post-TB and had lower pre-BD and post-BD (% predicted) FEV_1/FVC% and MMEF. Post-TB subjects with a restrictive pattern had more respiratory symptoms, lower SpO_2 and more severe lung function indices. Prevalence of airflow obstruction, restrictive pattern and small airway dysfunction according to post-TB status is shown in online supplemental figure E3.

When compared with 'non-post-TB' participants, having a post-TB status was associated with an OR (95% CI) of 1.31

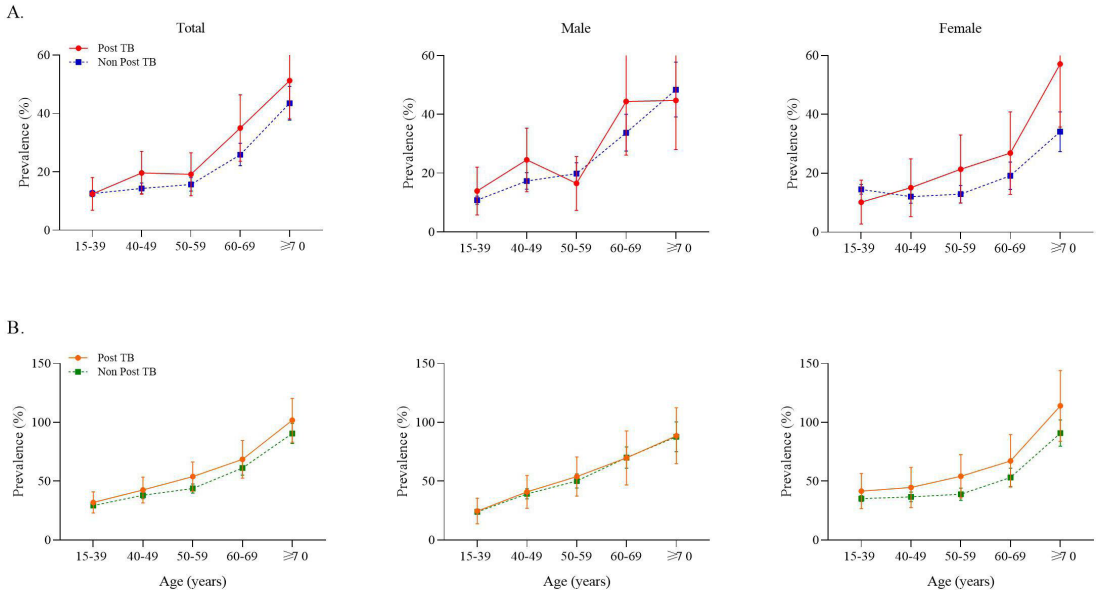

Figure 2 Standardised prevalence of airflow obstruction and small airway dysfunction in subjects based on history of post-TB. (A) Standardised prevalence of airflow obstruction. (B) Standardised prevalence of small airway dysfunction. Dots represent mean prevalence and error bars represent 95% CI. TB, tuberculosis.

(1.05 to 1.62) for airflow obstruction and of 1.28 (1.07 to 1.53) for small airway dysfunction after adjusting for gender, age, region, education, smoking status, exposure to HAP, occupation and history of asthma. In a subgroup analysis, being a post-TB never smoker was independently associated with airflow obstruction (1.37 (1.04 to 1.78], p=0.023) and (1.47 (1.18 to 1.83), p<0.001) small airway dysfunction after adjusting for above-mentioned variables (table 3). The effect sizes for potential confounders are provided in online supplemental tables E2 and E3. Post-TB was significantly associated with respiratory symptoms after adjusting for gender, age, region and education, smoking status, exposure to HAP and occupation (online supplemental table E4).

DISCUSSION

To the best of our knowledge, this is the first study with a rigorous sampling design to estimate the burden of post-TB and assess the association with chronic airflow obstruction and respiratory symptoms in China. Our findings suggest that socioeconomic status, respiratory symptoms, comorbidities and lung function parameters were worse in participants who had post-TB compared with 'non post-TB' participants, and even worse in those with post-TB and airflow obstruction. Our data show that 7.0% of residents had post-TB: in this group, 21.3% had airflow obstruction and 48.9% small airway dysfunction. Post-TB was associated with an increased odds of airflow obstruction and small airway dysfunction after adjustment for confounding factors. The magnitude of the OR between TB and airflow obstruction was much higher among never smokers, which suggests that post-TB may be a major risk factor per se especially among never smokers. We also filled in the age gap by providing data for subjects aged below 40 years old, since most previous reports of an association between airflow obstruction and post-TB included subjects aged over 40.[6 8–10]

Prior publications have reported the prevalence of post-TB sequelae, but the related burden remains undetermined.[8–10 22 23] The reasons may be inconsistency in definition, heterogeneity of populations studied and a lack of adequate control for confounders. The findings from our study indicate that the burden of post-TB among residents aged over 15 years is substantial. In our study, the proportion of chronic respiratory symptoms in post-TB cases was nearly two times that of non-affected individuals: this can have a negative impact on quality of life. Subjects with Post-TB also had more chronic comorbidities. Also, all lung parameters were significantly decreased in Post-TB subjects, even when a BD was used. We confirm that up to half of Post-TB people suffer from chronic and clinically relevant pulmonary function impairment and, in a majority of patients with airflow obstruction, obstruction was moderate to severe.[24–27] In most cases, pulmonary function impairment remains undiagnosed and

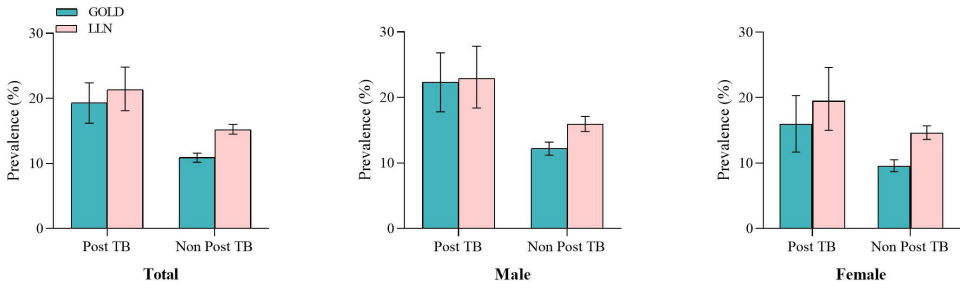

Figure 3 Prevalence of airflow obstruction based on two different diagnostic criteria for airway obstruction (GOLD and LLN) according to history of post-TB. Bars represent mean prevalence and error bars represent 95% CI. TB, tuberculosis.

Table 2 Characteristics of participants according to AO and post-TB status

Variables	P-TB (+)/AO (+) (n=130)	P-TB (–)/AO (+) (n=1230)	P-TB (+)/AO (–) (n=480)	P-TB (–)/AO (–) (n=6840)	P value*	P value†
Male	75 (57.7%)	627 (51.0%)	253 (52.7%)	3318 (48.5%)	0.519	0.075
Age group, years	53.90 (14.66)	42.34 (16.74)	48.07 (15.13)	38.98 (14.81)	<0.001	<0.001
City dwellers	53 (40.8%)	280 (22.8%)	203 (42.5%)	2300 (33.8%)	<0.001	<0.001
Education level						
Primary school and lower	93 (71.5%)	576 (46.8%)	269 (56.0%)	2936 (42.9%)	<0.001	<0.001
Middle and high school	30 (23.1%)	517 (42.0%)	150 (31.3%)	2708 (39.6%)		
College and higher	7 (5.4%)	137 (11.2%)	61 (12.7%)	1196 (17.5%)		
Smoking status						
Never smoker	85 (65.4%)	857 (69.7%)	320 (66.7%)	5009 (73.3%)	0.595	0.002
Ever smoker	45 (34.6%)	373 (30.3%)	160 (33.3%)	1828 (26.7%)		
History of asthma	16 (12.3%)	28 (2.3%)	16 (3.3%)	90 (1.3%)	0.428	0.005
Respiratory symptoms						
Frequent cough	30 (23.3%)	131 (10.7%)	79 (16.5%)	626 (9.3%)	0.001	<0.001
Sputum	31 (24.0%)	125 (10.2%)	79 (16.6%)	625 (9.2%)	<0.001	<0.001
Recurrent wheezing	18 (14.0%)	65 (5.3%)	36 (7.5%)	245 (3.6%)	0.079	<0.001
Dyspnoea in daily life	48 (37.2%)	257 (20.9%)	150 (31.4%)	1313 (19.4%)	<0.001	<0.001
At least one of the symptoms	64 (49.6%)	362 (29.5%)	220 (46.0%)	1897 (28.1%)	<0.001	<0.001
CAT score‡						
<10	22 (17.1%)	322 (26.3%)				
≥10	107 (82.9%)	904 (73.7%)				
Lung function parameters						
FVC post-BD, L	3.53 (1.11)	3.85 (1.02)	3.58 (0.99)	3.71 (0.94)	<0.001	0.004
FVC post-BD % pred	106.52 (28.16)	108.47 (24.20)	106.11 (24.83)	103.42 (21.89)	0.052	0.012
FEV_1 post-BD, L	2.17 (0.85)	2.48 (0.79)	2.98 (0.85)	3.17 (0.82)	<0.001	<0.001
FEV_1 post-BD % pred	79.41 (26.39)	83.14 (21.53)	106.28 (26.27)	104.77 (22.42)	<0.001	0.157
FEV_1/FVC post-BD, %	60.60 (10.44)	64.15 (9.99)	83.22 (7.08)	85.66 (6.86)	<0.001	<0.001
MMEF post-BD % pred	34.59 (17.63)	45.21 (73.41)	77.95 (32.87)	84.60 (52.50)	<0.001	0.013
$FEF_{50\%}$ post-BD % pred	40.74 (18.44)	47.01 (17.64)	94.84 (30.86)	95.53 (27.09)	<0.001	0.587
$FEF_{75\%}$ post-BD % pred	41.87 (34.86)	48.82 (25.95)	96.58 (57.56)	99.72 (45.9)	<0.001	0.147
SpO_2, %	92.24 (6.60)	94.58 (4.68)	91.17 (6.32)	93.25 (5.31)	<0.001	<0.001

Data are expressed as number (%) or mean (SD).
*P value difference between post-TB without airflow obstruction and airflow obstruction without post-TB.
†P value difference between normal population and post-TB without airflow obstruction.
‡CAT score difference for p<0.001.
AO, airflow obstruction; CAT, chronic obstruction pulmonary disease assessment test; FEF, forced expiratory flow; FEV_1, forced expiratory volume in the first second; FVC, forced vital capacity; MMEF, maximum mid-expiratory flow; post-BD, post-bronchodilator; P-TB, post-tuberculosis; P-TB(–)/AO(+), airflow obstruction without post-TB; P-TB(–)/AO(–), normal population without airflow obstruction and post-TB; P-TB(+)/AO(–), post-TB without airflow obstruction; P-TB(+)/AO(+), airflow obstruction with post-TB; SpO_2, oxyhemoglobin saturation.

untreated, possibly resulting in an increased mortality compared with the standard population.[28 29] Currently, there is much to do regarding the long-term medical and socioeconomic consequences of chronic lung function abnormalities after post-TB.[30]

There were also few studies reported post-TB was associated with a higher risk of airflow obstruction. The study from 13 geographically diverse, low-resource settings recruiting participants reported the adjusted odds of 3.78 times higher among those with previous tuberculosis disease than those without a history of tuberculosis disease.[6] Data from Korea National Health and Nutrition Examination Survey reported that airflow obstruction was associated with both a history and TB lesions on chest X-ray (OR 4.47, 95% CI 3.07 to 6.51) after adjustment for some confounders.[7] The finding from Burden of Obstructive Lung Disease (BOLD) results showed that a self-reported history of tuberculosis was associated with airflow obstruction (adjusted OR 2.51, 95% CI 1.83 to 3.42).[8] A cross-sectional analysis of the Guangzhou Biobank Cohort Study reported prior TB remained independently associated with an increased risk of airflow obstruction (OR: 1.37; 95% CI 1.13 to 1.67).[9] TheLatin American Project for the Investigation of Obstructive Lung Disease (PLATINO) study found participants with a medical history of tuberculosis were 2.3 times more likely to present airflow obstruction than those without such a diagnosis.[10] However, these studies included participants aged over 35 years old, incorporated no post-BD testing, used different definitions of post-TB. In the present study with a rigorous sampling design and strictly quality control, we found a nearly 1.31 time increase in risk of airflow obstruction in post-TB subjects after adjusting for confounders, and a stronger association in never smokers

Table 3 Adjusted associations for airflow obstruction according to history of post-TB in participants aged ≥15 years

	Non-post-TB	Post-TB	P value
Overall subjects			
Airflow obstruction	1230	130	
Crude OR (95% CI)	1.00 (ref)	1.50 (1.22 to 1.83)	<0.001
Adjusted OR (95% CI)*	1.00 (ref)	1.31 (1.05 to 1.62)	0.013
Restrictive pattern	1374	99	
Crude OR (95% CI)	1.00 (ref)	0.94 (0.75 to 1.17)	0.613
Adjusted OR (95% CI)*	1.00 (ref)	1.02 (0.80 to 1.28)	0.865
Small airway dysfunction†	2993	297	
Crude OR (95% CI)	1.00 (ref)	1.59 (1.35 to 1.88)	<0.001
Adjusted OR (95% CI)*	1.00 (ref)	1.28 (1.07 to 1.53)	0.006
Never smokers			
Airflow obstruction	857	85	
Crude OR (95% CI)	1.00 (ref)	1.55 (1.20 to 1.98)	<0.001
Adjusted OR (95% CI)‡	1.00 (ref)	1.37 (1.04 to 1.78)	0.023
Restrictive pattern	1005	65	
Crude OR (95% CI)	1.00 (ref)	0.92 (0.69 to 1.20)	0.575
Adjusted OR (95% CI)‡	1.00 (ref)	0.98 (0.73 to 1.30)	0.904
Small airway dysfunction	2143	205	
Crude OR (95% CI)	1.00 (ref)	1.78 (1.45 to 2.18)	<0.001
Adjusted OR (95% CI)‡	1.00 (ref)	1.47 (1.18 to 1.83)	0.001

*Adjusted OR: adjustments for age, sex, region and education plus history of asthma, and exposure to HAP and occupation and smoking status.
†Adjusted OR: adjusted OR except for smoking status.
‡Assessed in small airway dysfunction with data missing for 86 participants.
HAP, household air pollution; TB, tuberculosis.

(OR: 1.37; 95% CI 1.04 to 1.78). Besides, airflow obstruction was present in 21.3% of post-TB cases, which are consistent with a recent meta-analysis reporting a pooled prevalence of COPD in patients with post pulmonary TB of 21% (95% CI: 16% to 25%)[5] and another study from low- income and middle- income countries reporting COPD was more common (25.7%) among those with previous tuberculosis than those without a history of tuberculosis.[6] Therefore, for vast majority of patients after TB, the development of adjuvant interventions to prevent or to suspend further deterioration of lung function in individuals with post-TB could be an essential tool.

Small airway dysfunction is characterised by premature airway closure and air trapping, regional heterogeneity and exaggerated volume dependence of airflow limitation. A study emphasised that small airway dysfunction preceded both the spirometric evidence of COPD and detection of emphysema by CT and considered as a precursor of COPD and asthma.[31] The mechanisms are potential involvement of vasculature within the bronchovascular bundle in and around small airways after TB.[32] Health professionals should possibly play a more active role in the detection of small airway dysfunction after pulmonary TB. We still found that post-TB subjects with a spirometric restrictive pattern had frequent sputum, recurrent wheezing, lower oxygen saturation and severe pulmonary lung function indices. It is proposed that a chronic inflammatory response and long-term anatomic alterations induced by pulmonary tuberculosis are the main pathological basis for airflow obstruction and restriction pattern.[33–35] Chronic residual or recurrent inflammation-induced narrowing of airways, peribronchial fibrosis, extensive fibrosis and stiffening of the lung parenchyma after tuberculosis contribute to the functional findings reported.[36 37] Indeed, there was an increased odds for small airway dysfunction in post-TB subjects studied.

Our study has important public health implications. Improving detection and treatment of TB should be implemented in China, particularly in areas with poor economic and health conditions. The objectives are not only effectively controlling of TB per se but also decreasing its long-term impacts on lung function, respiratory symptoms and quality of life through professional management, early pulmonary function and chest imaging. The importance of the interrelationship between post-TB and chronic airflow obstruction has been clearly illustrated in our study, especially among never smokers. Further studies are required to better determine the role of inhaled or even systemic steroids in patients with TB in whom airway obstruction is detected.

There are some limitations to our study. First, the cross-sectional design of this study cannot formally establish the temporal sequence and causal relationship between post-TB and airflow obstruction. Longitudinal studies are needed in order to determine for how long and how often lung function impairment persists after TB. Second, ATS/ERS recommendations define the presence of a restrictive pulmonary disorder as having a total lung capacity (TLC) below the fifth percentile of predicted value. However, performing plethysmography or helium dilution measurements in a large study population such as ours is unrealistic. Using FVC as a surrogate for TLC is most often accepted in studies on restrictive pulmonary disorders. Third, the FEF50% predicted value was automatically reported from our spirometer and derived from the European Community for Steel and Coal report in 1993.[38] The equation is more appropriate for adults aged 18–70 years, so there may be a bias for older or younger people. Fourth, bronchiectasis has been shown to be associated with a history of TB and may be associated with small airway dysfunction.[39] However, chest CT was rarely available because of our resource-limited setting. Furthermore, a history of bronchiectasis was self-reported by only 14 participants precluding any further analysis. Finally, it is important to note that our findings relate to post-TB defined by self-reported history and radiological changes on chest radiographs. The extent of TB lesions on chest radiographs could not be evaluated due to limited availability of CT scans, and the definition of radiologic evidence may lack sensitivity and underestimate post-TB status. However, in a TB-prevalent region, presence of fibrotic scars or calcified nodules in the upper lobes is usually secondary to healed TB and is, thus, considered as specific.

In conclusion, post-TB status was associated with pulmonary function impairment, including airflow obstruction and small airway dysfunction, as well as with chronic respiratory symptoms. We also found that association between post-TB and pulmonary impairment was stronger among never smokers. Strategies must be developed in terms of research, prevention, earlier detection of functional impairment and management of post-TB patients as a way of preventing chronic pulmonary sequelae and disability.

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