Original Article

Comparison of baseline pulmonary function, dyspnea severity, and exercise capacity among active TB and TB-negative cases seen in a TB referral clinic

Kento Takahashi, MD,[1] Andre Angelo Tanque, MD,[1] Samuel Duran, MD[2]

AFFILIATIONS
[1]Section of Pulmonary Medicine, Department of Internal Medicine, East Avenue Medical Center, Quezon City
[2]TB DOTS, Department of Internal Medicine, East Avenue Medical Center, Quezon City

CORRESPONDING AUTHOR
Kento Takahashi, MD
Section of Pulmonary Medicine, Department of Internal Medicine, East Avenue Medical Center, Quezon City, Manila; doc.kento@gmail.com

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ABSTRACT

Background: Tuberculosis (TB) remains a major health concern in high-burden countries like the Philippines. While post-TB lung disease is well documented, baseline pulmonary function and exercise capacity at the time of TB diagnosis are less studied.

Objective: To compare baseline pulmonary function, dyspnea severity, and exercise capacity between active TB and TB-negative individuals, and to identify clinical factors associated with impairment.

Methodology: A cross-sectional study among 290 adults with presumptive pulmonary TB was conducted. After initiating treatment and confirming sputum negativity, participants underwent spirometry, mMRC dyspnea grading, and the six-minute walk test (6MWT). Patients were categorized as active TB (bacteriologically-confirmed or clinically-diagnosed) or TB-negative. Group comparisons and multivariable regression analyses were performed.

Results: Of 290 participants, 139 had active TB and 151 were TB-negative. Active TB patients were younger and had fewer comorbidities. Nearly one-third of active TB patients had abnormal spirometry at baseline. Compared to TB-negative controls, active TB patients had higher mean forced expiratory volume in 1 second (FEV_1) (2.26 ± 0.74 L vs 1.80 ± 0.75 L), forced vital capacity (FVC) (2.97 ± 1.11 L vs. 2.31 ± 0.86 L), and 6MWT distance (539.3 ± 120.5 m vs 488.6 ± 157.3 m) (all p <0.01). Chronic lung diseases were more prevalent among TB-negative individuals. After adjustment, previous TB treatment was the clinical factor most strongly associated with impaired spirometry (aOR 5.02, 95% CI 2.42 to 10.40), moderate-to-severe dyspnea at presentation (aOR 2.06, 95% CI 1.26 to 3.35), and reduced 6MWT distance (β -48.5 m, 95% CI -71.2 to -25.8).

Conclusions: Many patients with active TB exhibit lung impairment even at diagnosis. Nevertheless, active TB patients had surprisingly better lung function in this study which may be attributed to the higher prevalence of asthma and chronic obstructive pulmonary disease in the TB-negative group. Prior TB treatment is independently associated with spirometric and functional decline. Early pulmonary assessment should be integrated into TB care to inform rehabilitation strategies.

Keywords: tuberculosis, spirometry, six-minute walk test, mMRC

INTRODUCTION

Tuberculosis (TB) continues to have a high disease burden globally, affecting an estimated 10.6 million people worldwide in 2022. The Philippines is among the countries with the highest TB burden, ranking fourth, with approximately 7% of global cases.[1] Beyond its mortality and microbiological aspects, TB can cause long-term pulmonary sequelae even after successful treatment. Post-TB chronic lung disease—including airway obstruction, restrictive deficits, and destroyed lung parenchyma–contribute to significant morbidity and reduced quality of life, yet is often under-assessed in clinical practice. Studies report that roughly 20% to more than 80% of TB survivors sustain some permanent lung impairment, indicating a wide spectrum of post-TB lung damage.[2] Pulmonary function tests (PFTs) such as spirometry, along with functional measures like the six-minute walk test (6MWT) and the modified Medical Research Council (mMRC) dyspnea scale, are critical tools to objectively assess respiratory function and its impact on daily life. TB-related lung injury often manifests as irreversible airflow limitation and loss of lung volume (sometimes a mixed obstructive–restrictive pattern),[3] which can lead to exercise intolerance and chronic respiratory symptoms. Early detection and management are important for better outcomes in patients with chronic respiratory diseases.

Therefore, we aimed to compare the baseline pulmonary function, dyspnea severity, and exercise capacity in individuals with active TB disease with TB-negative controls, and to evaluate clinical factors of impairment in terms of lung function, dyspnea during daily activities, and exercise capacity.

METHODOLOGY

Study design and setting

We conducted a cross-sectional study at a TB referral clinic in the Philippines in 2024.

Study participants

All adult presumptive pulmonary TB patients seen in the TB referral clinic in Quezon City for diagnostic evaluation and who underwent testing with smear microscopy, TB LAMP, and/or Xpert MTB/RIF following the National Tuberculosis Control Program Manual of Procedures[4] from August 2024 to February 2025 were included.

Ethical considerations

All participants provided informed consent which was discussed prior to the conduct of the study and once the patient was deemed eligible to be included. The study was done in adherence to the Declaration of Helsinki and was approved by

the East Avenue Medical Center Institutional Ethics Review Board (EAMC IERB 2024-44). Safety of participants was ensured prior to, during, and at the end of the procedures.

Study procedures

Based on the diagnostic workup, patients were classified into two groups: active TB (patients diagnosed with pulmonary TB, either bacteriologically-confirmed through positive sputum tests or clinically-diagnosed by a physician based on clinical and radiographic findings despite negative microbiologic results) and TB-negative (those in whom TB was ruled out and for whom an alternative diagnosis was made).

Baseline demographic and clinical data (including smoking status, symptoms, comorbidities, and previous TB treatment [i.e., retreatment case]) were recorded.

Pulmonary function was assessed using a calibrated portable spirometer. For infection control, spirometry in active TB patients was performed one month after initiating treatment and only after a repeat negative sputum microscopy confirmed reduced infectivity. The technician conducting the test utilized proper personal protective equipment, and institutional infection control protocols were strictly followed. While there was a delay in the timing of the performance of pulmonary function test with respect to diagnosis, we believe that pulmonary function is unlikely to change within one month of initiating treatment. All testing followed American Thoracic Society/European Respiratory Society 2019 standards.[5] Key spirometric measures were: forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) expressed in liters (L) and as percentages of predicted normal values (FEV_1 %predicted, FVC %predicted); and the FEV_1/FVC ratio. We defined impaired lung function based on standard criteria: FEV_1 <80% predicted, FVC <80% predicted, or FEV_1/FVC <70%. Fixed cut-off values were used for consistency with commonly applied clinical definitions and prior studies, allowing easier interpretation and comparison of results, and with reference standard derived from Global Lung Initiative. If any of these values fell below the threshold, the patient was considered to have an abnormal PFT (suggesting an obstructive or restrictive defect). Other spirometric parameters that were measured were: peak expiratory flow (PEF; in liters per second), forced expiratory time (FET; in seconds); and maximal voluntary ventilation (MVV; in liters per minute).

Dyspnea was assessed using the modified Medical Research Council (mMRC) scale; we considered mMRC grade ≥ 2 as having moderate-to-severe baseline dyspnea.

Exercise capacity was evaluated using the six-minute walk test (6MWT), following a standard ATS protocol to measure the distance walked in six minutes on a flat course.[6] Additionally, overall fatigue or breathlessness was graded using the modified Borg rating of perceived exertion, from 0 (none) to 10 (maximum).

Sample size and sampling

Sample size was calculated based on 2023 clinic records of approximately 924 TB patients. Using a 95% confidence level and 5% margin of error, at least 272 participants were required. Consecutive sampling was done.

Statistical analysis

For analysis, continuous variables were reported as mean ± standard deviation (SD) or median (interquartile range [IQR]) as appropriate, and categorical variables as number (percentage). Group comparisons between active TB and TB-negative groups were performed using independent Student's t -tests for approximately normally distributed continuous variables (or Mann–Whitney U tests if the distributions were non-normal), and chi-square tests (or Fisher's exact tests) for categorical variables. Key results were summarized in tables. Within the active TB cohort, subgroup comparisons between bacteriologically-confirmed versus clinically-diagnosed groups were done. For each comparison, we calculated absolute differences in means or odds ratios (ORs) for proportions, with 95% confidence intervals (CIs), to quantify effect sizes. To identify independent factors of impairment, we performed multivariable regression analyses. A logistic regression model was constructed for the binary outcome of impaired lung function (as defined above), including TB status (active vs negative), age, sex, body mass index, smoking status, and—for TB patients—retreatment status and bacteriologic confirmation as covariates. Adjusted ORs with 95% CIs and p-values were reported for each factor. A second logistic model was ran for moderate-to-severe dyspnea (mMRC ≥2 vs <2) using the same independent variables. Lastly, a linear regression model was applied to the 6MWT distance (in meters) using the same factors; β coefficients (mean differences) with 95% CIs and p-values were obtained. A two-tailed $p < 0.05$ was considered statistically significant for all analyses. Data were analyzed using SPSS version 25.0 (IBM Corp) and R 4.0 software. The study was reported in accordance with the STROBE guidelines for observational studies.

RESULTS

A total of 290 participants met the inclusion criteria, with 139 classified as having active pulmonary TB and 151 as TB-negative. As seen in Table 1, the active TB group was significantly younger than the TB-negative group (mean age 42.0 ± 17.7 vs 48.5 ± 15.6 years, $p = 0.001$). Sex distribution and marital status were similar between groups (both $p > 0.1$). Educational attainment differed markedly: active TB patients were more likely to have attended or completed college (50.4% vs 16.6%) whereas TB-negative individuals more commonly had only elementary or high school education (both $p \leq 0.001$). Full-time employment was more frequent in the active TB group (65.5% vs 39.7%, $p < 0.001$) while unemployment was higher in the TB-negative group (54.3% vs 30.2%, $p < 0.001$).

Regarding presenting symptoms, classical constitutional symptoms were more common in active TB (some data not shown in table). In particular, unintentional weight loss was reported in 13.7% of active TB patients versus 4.0% of TB-negative patients ($p = 0.006$), and the combination of cough, fever, weight loss, and night sweats was also more frequent in the active TB group. Conversely, dyspnea (either alone or with cough) was more often reported by TB-negative individuals: for example, 13.2% of TB-negative patients had both dyspnea and cough at presentation, compared to none of the active TB patients ($p < 0.001$). The TB-negative group also had significantly higher rates of chronic respiratory comorbidities, notably asthma (6.6% vs 0%, $p = 0.002$) and chronic obstructive pulmonary disease (COPD, 13.2% vs 0%, $p < 0.001$), and hypertension (13.2% vs 4.3%, $p = 0.014$). In contrast, diabetes mellitus was more frequent among those with active TB (7.9% vs 0%, $p < 0.001$). Overall, two-thirds of active TB patients had no comorbid conditions, significantly more than the TB-negative group (66.9% vs 35.1%, $p < 0.001$).

Baseline functional assessments showed better mean pulmonary function and exercise capacity in the active TB group. Active TB patients walked farther on the 6MWT (mean 539.3 ± 120.5 m vs 488.6 ± 157.3 m, p = 0.002), and had higher mean FEV_1 (2.26 ± 0.74 L vs 1.80 ± 0.75 L, p <0.001) and FVC (2.97 ± 1.11 L vs 2.31 ± 0.86 L, p <0.001) than TB-negative individuals. There were no significant differences between groups in the FEV_1/FVC ratio, mMRC dyspnea scores, Borg exertional score, smoking history, or alcohol use (all p >0.1). Nevertheless, nearly one-third of active TB patients had abnormal spirometry at baseline.

In Table 2, we performed a subgroup analysis of the 139 active TB cases to explore differences by diagnostic classification.

Table 1. Baseline characteristics of study participants according to TB status (N = 290)

	Active TB (n = 139)	TB-negative (n = 151)	p-value
Age, years (mean ± SD)	42.00 ± 17.73	48.52 ± 15.57	0.001
Sex			
Female	61 (43.9)	81 (53.6)	0.123
Male	78 (56.1)	70 (46.4)	0.123
Marital status			
Married	87 (62.6)	106 (70.2)	0.212
Single	52 (37.4)	45 (29.8)	0.212
Educational attainment			
College	70 (50.4)	25 (16.6)	<0.001
Elementary	8 (5.8)	32 (21.2)	<0.001
High School	53 (38.1)	87 (57.6)	0.001
Vocational	8 (5.8)	7 (4.6)	0.869
Employment status			
Full-time	91 (65.5)	60 (39.7)	<0.001
Not working	42 (30.2)	82 (54.3)	<0.001
Part-time	6 (4.3)	9 (6.0)	0.714
Symptoms			
Asymptomatic	38 (27.3)	49 (32.5)	0.412
Cough	33 (23.7)	42 (27.8)	0.511
Dyspnea	8 (5.8)	25 (16.6)	0.005
Fever	13 (9.4)	6 (4.0)	0.094
Weight loss	19 (13.7)	6 (4.0)	0.006
Night sweats	7 (5.0)	0 (0)	0.005
Comorbidity			
Asthma	0 (0)	10 (6.6)	0.002
COPD	0 (0)	20 (13.2)	<0.001
Hypertension	6 (4.3)	20 (13.2)	0.014
Diabetes	11 (7.9)	0 (0)	<0.001
Cancer	3 (2.2)	2 (1.3)	0.667
6MWT distance, m (mean ± SD)	540 ± 120	489 ± 157	0.002
FEV_1, L (mean ± SD)	2.26 ± 0.74	1.80 ± 0.75	<0.001
FEV_1, %predicted (mean ± SD)	73.0 ± 22.5	59.7 ± 21.7	<0.001
FVC, L	2.97 ± 1.11	2.31 ± 0.86	<0.001
FVC, %predicted (mean ± SD)	68.6 ± 21.0	60.5 ± 18.6	<0.001
FEV_1/FVC, ratio (mean ± SD)	80.7 ± 12.5	78.4 ± 13.2	0.113
PEF, L/s (mean ± SD)	5.0 ± 3.5	4.5 ± 3.8	0.130
FET, s (mean ± SD)	4.0 ± 3.0	4.8 ± 3.5	0.020
MVV, L/min (mean ± SD)	90 ± 50	80 ± 45	0.050
6MWT Borg score ≥1	20 (14.4)	23 (15.2)	0.852
6MWT Borg score ≥4	4 (2.9)	0 (0)	0.049

Data presented as n (%) unless otherwise stated.
TB: tuberculosis; COPD: chronic obstructive pulmonary disease; 6MWT: six-minute walk test; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; PEF: peak expiratory flow; FET: forced expiratory time; MVV : maximal voluntary ventilation

Among active TB patients, those who were bacteriologically-confirmed (n = 72) were significantly younger than those who were clinically diagnosed (n = 67) (median age 28 years vs 53 years, p = 0.002). The bacteriologically-confirmed group also had a higher proportion of males, although the sex difference was not significant (58% vs 54% male, p = 0.585). Educational attainment differed: none of the bacteriologically-confirmed cases had only elementary education, compared to 12% of the clinically-diagnosed group (p <0.001). Conversely, the clinically-diagnosed group had no individuals with vocational education compared to the bacteriologically-confirmed group (0% vs 11%). Employment status was slightly different, with full-time employment more common in bacteriologically-confirmed patients (68.1% vs 62.7%, p = 0.019).

Clinically, there was heterogeneity in symptom profiles (some data not shown in table). Bacteriologically-confirmed TB patients were more likely to have classic TB symptoms: more than half in the bacteriologically-confirmed group reported significant weight loss at diagnosis (56.9% vs 26.9% in the clinically-diagnosed group, p <0.001), and night sweats were reported by 9.7% of bacteriologically-confirmed cases compared to none of the clinically-diagnosed cases (p = 0.009). In contrast, clinically-diagnosed TB patients tended to have fewer typical symptoms but a higher burden of certain comorbidities. Notably, 17.9% of clinically-diagnosed patients had a history of cancer (vs 0% of the bacteriologically-confirmed, p <0.001). While none in the clinically-diagnosed group had hypertension or diabetes, these conditions were present in 19.4% and 5.6% of the bacteriologically-confirmed group, respectively (for hypertension, p <0.001; for diabetes, p = 0.043). Prior TB was much more prevalent in the clinically-diagnosed group: 50.8% of clinically-diagnosed patients were retreatment cases (having had prior TB treatment) compared to only 15.3% of the bacteriologically-confirmed group (p <0.001).

In terms of lung function, patients with clinically-diagnosed TB achieved a significantly greater distance on the 6MWT (median 611 m vs 485 m, p <0.001), and had higher baseline FEV_1 and FVC values. Specifically, mean FEV_1 %predicted was 76% in the clinically-diagnosed group versus 63% in the bacteriologically-confirmed group (p = 0.001), and mean FVC %predicted was 71% vs 65.5% (p = 0.047). Clinically-diagnosed patients also had higher maximal voluntary ventilation (MVV) and longer forced expiratory time (FET) on spirometry than bacteriologically-confirmed patients (median MVV 107 L/min vs 77 L/min, p = 0.009; median FET 4.82 s vs 3.51 s, p = 0.004). Patients in the clinically-diagnosed group reported lower exertional symptoms during the 6MWT–only 9.0% had significant post-walk dyspnea versus 29.2% in the bacteriologically-confirmed group (p = 0.003)—and none experienced angina after the walk (no difference between groups). However, ratings on the Borg scale of perceived exertion were higher in the bacteriologically-confirmed group. Specifically, 18.1% of bacteriologically-confirmed patients reported a Borg score of 4 (severe breathlessness) after the 6MWT, compared to 0% in the clinically-diagnosed group (overall p <0.001).

In multivariable analyses (Table 3), a history of prior TB treatment (retreatment case) emerged as the strongest independent factor associated with baseline pulmonary impairment. After adjusting for age, sex, BMI, smoking status, and TB confirmation status, patients with previous TB treatment had significantly higher odds of having abnormal

Table 2. Subgroup analysis of active TB patients according to diagnostic classification (n = 139)

	Bacteriologically confirmed (n = 72)	Clinically diagnosed (n = 67)	p-value
Age, years (median [IQR])	28 [23]	53 [23]	0.002
Sex			
Female	30 (41.7)	31 (46.3)	0.585
Male	42 (58.3)	36 (53.7)	0.585
Marital status			
Married	41 (56.9)	46 (68.7)	0.154
Single	31 (43.1)	21 (31.3)	0.154
Educational attainment			
Elementary	0 (0)	8 (11.9)	<0.001
High School	31 (43.1)	22 (32.8)	…
College	33 (45.8)	37 (55.2)	…
Vocational	8 (11.1)	0 (0)	...
Employment status			
Full-time	49 (68.1)	42 (62.7)	0.019
Not working	20 (27.8)	20 (29.9)	0.781
Part-time	3 (4.2)	5 (7.5)	0.480
Weight loss at diagnosis	41 (56.9)	18 (26.9)	<0.001
Night sweats	7 (9.7)	0 (0)	0.009
Any classic TB symptoms[1]	65 (90.3)	43 (64.2)	<0.001
Comorbidity			
Cancer	0 (0)	12 (17.9)	<0.001
Hypertension	14 (19.4)	0 (0)	<0.001
Diabetes	4 (5.6)	0 (0)	0.043
Prior TB (retreatment)	11 (15.3)	34 (50.8)	<0.001
6MWT distance, m (median [IQR])	485 [100]	611 [125]	<0.001
FEV_1 %predicted (mean ± SD)	63.0 ± 19.2	76.0 ± 18.7	0.001
FVC %predicted (mean ± SD)	65.5 ± 17.5	71.0 ± 16.3	0.047
MVV, L/min (median [IQR])	77 [34]	107 [59.5]	0.009
FET, s (median [IQR])	3.51 [4.64]	4.82 [1.11]	0.004
Borg score = 1 after 6MWT	7 (9.7)	12 (17.9)	0.157
Borg score = 4 after 6MWT	13 (18.1)	0 (0)	<0.001

Data presented as n (%) unless otherwise stated.
[1]Any of the following symptoms at presentation: cough, fever, weight loss, or night sweats.
TB: tuberculosis; 6MWT: six-minute walk test; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MVV: maximal voluntary ventilation; FET: forced expiratory time

spirometry at diagnosis (adjusted OR 5.02, 95% CI 2.42 to 10.40; p <0.001). Previous TB treatment was also associated with greater odds of moderate-to-severe dyspnea (mMRC ≥2) at presentation (adjusted OR ~3, p <0.01) and with a shorter 6MWT distance (adjusted β -48.5 m, 95% CI -71.2 to -25.8; p <0.001) in the regression models. By contrast, factors such as patient sex, age, and whether TB case was bacteriologically-confirmed or not did not independently identify impaired lung function in the adjusted model once TB history was accounted for.

In the multivariable model incorporating continuous pulmonary function and exercise capacity measures (Table 4), only a history of previous TB treatment remained significantly associated with moderate-to-severe dyspnea or mMRC ≥2 (aOR 2.06, 95% CI 1.26 to 3.35; p = 0.004). None of the spirometric or functional parameters were independently associated with dyspnea severity after adjustment.

Table 3. Multivariable regression analysis of factors associated with impaired spirometry and 6MWT

	aOR for impaired spirometry (95% CI)	p-value	β for 6MWT distance (95% CI)	p-value (β)
Previous TB treatment	5.02 (2.42 to 10.40)	<0.001	-48.5 (-71.2 to -25.8)	<0.001
Bacteriologically confirmed	1.32 (0.65 to 2.70)	0.430	-12.3 (-33.8 to 9.2)	0.260
Age (per year)	1.01 (0.99 to 1.04)	0.250	-0.60 (-1.52 to 0.32)	0.200
Sex (male)	0.98 (0.60 to 1.61)	0.920	2.10 (-5.7 to 9.9)	0.590
BMI (per kg/m²)	1.03 (0.98 to 1.08)	0.140	1.20 (-0.4 to 2.8)	0.120
Smoking (current/ former)	1.10 (0.85 to 1.41)	0.450	-5.80 (-20.1 to 8.5)	0.420

TB: tuberculosis; BMI: body mass index; aOR: adjusted odds ratio; 6MWT: six-minute walk test

Table 4. Multivariate regression analysis of factors associated with moderate-to-severe dyspnea (mMRC ≥2)

	aOR (95% CI)	p-value
Intercept	1.72 (0.2 to 15.12)	0.625
Age (per year)	0.99 (0.98 to 1.01)	0.499
Male (vs Female)	1.36 (0.83 to 2.21)	0.223
BMI (per kg/m²)	0.97 (0.93 to 1.01)	0.146
Ever smoker (pack-years >0)	1.16 (0.71 to 1.88)	0.560
Active TB (vs TB-negative)	0.98 (0.56 to 1.71)	0.939
Previous TB treatment	2.06 (1.26 to 3.35)	0.004
Bacteriologically-confirmed (vs others)	1.48 (0.7 to 3.11)	0.304
FEV_1 (%predicted)	1.0 (0.99 to 1.01)	0.392
FVC (%predicted)	1.0 (0.99 to 1.01)	0.890
FEV_1/FVC ratio	1.0 (0.98 to 1.01)	0.619
6MWT distance (per meter)	1.0 (1.0 to 1.0)	0.405

BMI: body mass index; TB: tuberculosis; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; 6MWT: six-minute walk test; aOR: adjusted odds ratio

DISCUSSION

While it may appear paradoxical that TB-negative individuals in this study demonstrated lower mean FEV_1 and FVC values compared to patients with active TB disease, this counterintuitive finding may be explained by differences between the populations. The TB-negative group in our study had a higher prevalence of chronic respiratory disorders (asthma, COPD) and other comorbidities that likely contributed to diminished lung function. Our multivariable analysis confirmed that these underlying factors (especially prior TB) outweighed the effect of active TB itself on baseline impairment. Essentially, many "TB-negative" participants had chronic lung disease unrelated to TB, leading to worse pulmonary metrics at diagnosis, whereas active TB patients, despite having an active infection, often lacked significant chronic lung injury at baseline.

This study provides novel insights into the functional respiratory status of patients newly diagnosed with active pulmonary TB. Surprisingly, individuals with active TB had, on average, better spirometric values and 6MWT performance relative to TB-negative controls. This does not imply that TB infection improves lung function; rather, it may reflect a selection phenomenon. Those who were ultimately confirmed to have TB tended to be younger and without chronic lung conditions, whereas many TB suspects who turned out to be TB -negative had pre-existing lung problems that likely prompted

their initial evaluation. Nevertheless, a substantial proportion of patients with active TB did show evidence of early functional compromise. Approximately 30% of the active TB cohort already met criteria for abnormal spirometry at the time of diagnosis, underscoring that early lung impairment is present in a significant subset of cases even at baseline.

Our subgroup analysis revealed considerable heterogeneity within the active TB population. Patients with bacteriologically-confirmed TB were younger and had fewer comorbidities specifically cancer than those with clinically-diagnosed TB, yet paradoxically showed worse lung function on average. This aligns with the idea that patients in the clinically-diagnosed group (often retreatment cases) may have adapted to chronic lung changes over time or had milder acute disease, whereas new TB cases with heavy bacterial burden experienced more acute loss of lung capacity. Additionally, clinically-diagnosed patients—by virtue of previous TB episodes—have already undergone interventions that preserved their functional status. Prior TB was notably more common in the clinically-diagnosed group, and our regression results identified it as a key independent associated factor for impairment. These findings reinforce the notion that cumulative lung damage from past TB can significantly impair present lung function—a conclusion supported by a recent systematic review that found that a history of TB is associated with significantly decreased lung function compared to no history.[3]

In the Philippine context, our study adds to the limited literature on pulmonary function during active TB disease. A local study by Masumoto et al found that Filipino TB patients in Manila experienced significantly impaired health-related quality of life, especially those with low education, positive sputum smears, and multiple symptoms.[7] Our findings complement this by focusing on physiologic function: even when lung volumes are relatively preserved on average, many patients have underlying impairment that might later manifest as reduced quality of life.

Another key finding is the impact of prior TB on current function. Patients with a history of prior TB (retreatment cases) consistently showed worse lung metrics at baseline, underscoring the cumulative damage from repeated episodes on respiratory health despite treatment. This suggests that clinicians should be particularly vigilant in evaluating lung function in retreatment TB cases, as they are at higher risk of baseline pulmonary impairment.

The finding that previous TB treatment was associated with moderate-to-severe dyspnea highlights the lasting functional impact of post-TB lung disease. Studies have shown that breathlessness and exercise limitation may persist despite normalized lung volumes and treatment completion, reflecting residual airway and parenchymal damage or deconditioning not captured by routine pulmonary function tests.[8-9]

Early initiation of pulmonary rehabilitation and breathing exercises during TB treatment may help improve outcomes for such high-risk patients. Supervised exercise programs lead to improvements in exercise capacity, lung function, and quality of life, supported by findings from a recent review on pulmonary rehabilitation in TB survivors. This is supported by emerging evidence: a recent review documented that pulmonary rehabilitation in TB survivors can significantly improve exercise capacity, lung function, and quality of life.[10] These considerations highlight the need to integrate functional assessment and rehabilitation into TB care, not only after cure but even during treatment, to mitigate long-term disability.

To our knowledge, this study is among the first studies in the Philippines to rigorously characterize baseline lung function in active TB patients and compare it with appropriate controls. Strengths include the relatively large sample size and comprehensive data collection including spirometry, exercise testing, and symptom scores for all participants at diagnosis. We adhered to international standards for pulmonary function testing and conducted subgroup and multivariate analyses to explore underlying factors.[5] However, several limitations should be noted. The study's cross-sectional design precludes assessment of causality or long-term outcomes—we cannot determine how pulmonary function trajectories evolve after TB treatment completion based on this baseline-only analysis. Another limitation is the inability to adjust for baseline imbalances in COPD and asthma prevalence between groups, which may have confounded the observed associations with the outcomes studied. We also did not incorporate chest imaging findings in our analysis; the extent of radiographic disease (e.g., cavitation or fibrosis) may explain some of the functional differences and would strengthen interpretations if included. Misclassification is another concern; the "clinically-diagnosed" TB group might have included some patients who in fact had non-TB disease (given the lack of microbiological confirmation), although all were treated as TB by experienced physicians. We attempted to minimize this by only including clinically-diagnosed cases with consistent clinical and radiologic evidence and having an alternative diagnosis for the TB-negative group. Additionally, we did not formally assess adherence to or the quality of pulmonary function maneuvers beyond adhering to ATS criteria; however, all patients were well coached, and poor effort tests were repeated to ensure valid results. Finally, our study was conducted at a single tertiary referral center which may limit generalizability. Patients seen at specialized clinics could differ from those managed in primary care–for example, more severe or complex cases might be overrepresented. Nonetheless, the referral-center context also enhanced the internal validity of measurements. Lastly, the study may be underpowered for the subgroup comparisons of bacteriologically-confirmed and clinically-diagnosed TB.

CONCLUSIONS

Our findings indicate that a substantial proportion of patients with active tuberculosis already exhibit lung impairment at the time of diagnosis. While active TB disease was associated with generally better lung function compared to TB-negative individuals, this paradox is likely attributable to a higher burden of chronic respiratory comorbidities (such as asthma and COPD) in the TB-negative group. Patients with history of previous TB treatment demonstrate worse functional outcomes, underscoring the cumulative impact of repeated disease episodes on respiratory health.

These findings emphasize the importance of comprehensive respiratory assessment including spirometry and 6MWT in at-risk patients. Routine evaluation of lung function may aid in identifying patients at risk for long-term pulmonary sequelae and enable early referral to pulmonary rehabilitation. Future studies should incorporate more detailed phenotyping and longitudinal follow-up to better understand the trajectory of TB -related lung impairment and to disentangle the overlapping effects of infectious and chronic pulmonary diseases.

Data Availability Statement
Datasets are not publicly available because participants in the study did not give written consent for their data to be shared.

Statement of Authorship
All authors certified fulfillment of ICMJE authorship criteria.

Authors' Disclosure
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