Pulmonary Function Recovery After Treatment In Drug Sensitive TB: What Factors Matter?

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Abstract.

Background: Indonesia ranks second globally in tuberculosis burden, and up to 50% of treated patients develop pulmonary dysfunction. Objectives: To identify clinical and radiographic factors influencing spirometric recovery after treatment in drug-sensitive pulmonary tuberculosis. Methods: Analytical observational study with cross-sectional design. Population comprised adults (>18 years) in Medan who completed standard drug-sensitive TB therapy within six months. Sixty participants were selected by consecutive sampling. Instruments included spirometry (Global Lung Function Initiative 2022 equations) and chest radiograph scoring. A structured questionnaire captured demographics, TB history, comorbidities, and smoking. Data analysis involved bivariate tests (chi-square, Kruskal–Wallis, Fisher's exact) and multivariate logistic regression (enter method). Results: Advanced radiographic lesion extent was the only independent predictor of abnormal spirometry (Exp(B)=4.889; 95% CI 1.386–17.241; p=0.014). Other variables lost significance after adjustment. Conclusion: Initial lesion burden on chest radiograph strongly determines pulmonary function recovery post-treatment. Early stratification by lesion extent is recommended for targeted follow-up and rehabilitation.

Keywords: *Chest Radiography; Drug-Sensitive Tuberculosis; Pulmonary Function; Spirometry and Treatment Outcomes.*

I. INTRODUCTION

Pulmonary tuberculosis (TB) remains one of the world's leading infectious disease burdens, with 10 million new cases and 1.4 million deaths reported in 2021 (World Health Organization, 2022). Despite high treatment success rates of up to 85%, a substantial proportion of TB survivors experience long-term lung function impairment. Systematic reviews report that former patients exhibit mean forced expiratory volume in 1 s (FEV_1) at 76.6% of predicted and forced vital capacity (FVC) at 81.8% of predicted, with 10–15% suffering severe impairment detectable by spirometry (Ivanova et al., 2023; Johnson & Johnson, 2023). Spirometry is the cornerstone of pulmonary function testing, providing quantitative measures of airflow obstruction and restriction that guide clinical management of chronic lung diseases. Recent efforts to refine reference equations—accounting for age, sex, height, and ethnicity—have yielded more comprehensive models for interpreting flow–volume loops, yet their adoption remains inconsistent across regions (Johnson & Johnson, 2023; Choi et al., 2025).

Research Problem

First, post-TB lung disease (PTLD) lacks universally accepted diagnostic and management guidelines, resulting in underdiagnosis and suboptimal care for survivors. Although spirometry is recommended to assess airway obstruction and restriction after TB, no evidence-based international consensus exists to standardize its use in PTLD evaluation (Ivanova et al., 2023; Cupido et al., 2024). Second, heterogeneity in spirometry reference equations complicates interpretation of lung function recovery. The Global Lung Function Initiative (GLI) 2012 and 2022 race-neutral models improve comparability but may reclassify disease severity relative to legacy equations, impacting clinical decisions (Choi et al., 2025; Johnson & Johnson, 2023). Regional validation studies remain limited, particularly in Southeast Asian populations.Third, determinants of pulmonary function recovery in drug-sensitive TB are poorly characterized. While factors such as history of recurrent TB, extent of radiographic lesions, diabetes, HIV co-infection, and smoking have been implicated, existing meta-analyses often aggregate heterogeneous

cohorts and do not quantify the relative impact of each factor in controlled multivariate analyses (Ivanova et al., 2023; Ratnakumar et al., 2023).

Study Objectives, Urgency, and Novelty

This study aims to identify and quantify the key clinical and radiographic factors influencing spirometric recovery in adults with drug-sensitive pulmonary TB who have completed therapy. Addressing this gap is urgent given Indonesia's status as the country with the second-highest TB burden globally and the high prevalence of post-treatment lung dysfunction in survivors. The novelty lies in conducting a systematic, multivariate analysis focusing exclusively on drug-sensitive TB, incorporating standardized spirometry interpreted by GLI 2022 reference equations, and validating findings in an Indonesian cohort—thereby providing regionally relevant evidence to.

II. METHODS

The study employed an analytical observational design with a cross-sectional approach to assess pulmonary function in drug-sensitive tuberculosis survivors. This design allows evaluation of exposure variables and outcomes at a single point, facilitating identification of associations without manipulation of variables (Sugiyono, 2022; Creswell, 2023).Data were collected using spirometry (Global Lung Function Initiative 2022 reference equations) to measure FEV_1, FVC, and FEV_1/FVC ratios. Chest radiographs were interpreted to categorize the extent of lung lesions into minimal, moderate, and advanced stages. A structured questionnaire captured demographic data (age, gender), clinical history (previous TB treatment, diabetes mellitus, HIV status), and smoking habits. Bivariate analyses (chi-square, Kruskal–Wallis, Fisher's exact tests) identified variables associated with abnormal spirometry ($p<0.05$), followed by multivariate logistic regression (enter method) to determine independent predictors of persistent pulmonary dysfunction (Creswell, 2023; Emzir, 2021).

The study population comprised adults (>18 years) residing in Medan who had completed standard drug-sensitive TB therapy within the previous six months at H. Adam Malik and USU General Hospitals. From a sampling frame of treated cases, 60 participants were selected via consecutive sampling until the target was reached. Inclusion criteria ensured mental competence and absence of acute illness; exclusion criteria ruled out uncontrolled metabolic diseases and pregnancy (Sudaryono et al., 2024; Cresswell, 2023). The research procedure began with ethical approval and informed consent. Demographic and clinical histories were recorded, followed by chest X-ray scoring by two blinded pulmonologists. Spirometry was performed according to ATS/ERS guidelines, with three reproducible maneuvers recorded and the highest values used. Data entry and cleaning preceded statistical analyses, which were conducted using SPSS v26. Logistic regression models were built incrementally, introducing variables in order of descending p-value to isolate the variable with the greatest impact on pulmonary impairment (Sugiyono, 2022; Creswell, 2023).

III. RESULTS AND DISCUSSIONS

Results

A total of 60 samples who fulfill the criteria inclusion and exclusion criteria were included in this study. Samples were then grouped into several groups based on age, gender, BMI, history of previous tuberculosis treatment, extent of lung lesions on x-ray, history of diabetes mellitus, history of HIV, smoking habits and spirometry results (Table1). Then, those variables will be grouped based on the results of the spirometry (Table 2).

Table 1. Characteristics Patients After Completing Anti-Tuberculosis Treatment

Characteristic	Frequency (n)	Percentage (%)
Age (Year)		
18-< 35	25	41,7
35-50	14	23,3
>50	21	35
Gender		

Male	26	43,3
Female	34	56,7
Body Mass Index		
Underweight	13	21,7
Normoweight	41	68,3
Overweight	6	10
History of Tuberculosis Treatment		
Yes	8	13,3
No	52	86,6
Extent of Lung Lesion		
Normal-Minimal Lesion	21	35
Moderate Lesion	13	21,7
Advanced Lesion	26	43,3
History of Diabetes Melitus		
Yes	8	13,3
No	52	86,7
History of HIV-AIDS		
Yes	1	1,7
No	59	98,3
Spirometry Results		
Normal	20	33,3
Restriction		
Mild Restriction	15	25
Moderate Restriction	5	8,3
Severe Restriction	3	5
Obstruction		
Mild Obstruction	10	16,6
Moderate Obstruction	7	11,6
Severe-very severe obstruction	0	0

Table 2. Relationship between Independent Variables and Spirometry Examination in Patients After Completed Anti Tuberculosis Treatment

Variables	**Abnormal n = 40**	**Normal n = 20**	**P value**
Age			
18 - <35 years	15 (60)	10 (40)	0,223[a]
35 – 50 years	8 (57,1)	6 (42,9)	
> 50 years	17 (81)	4 (19)	
Gender			0,141[a]
Male	20 (76,9)	6 (23,1)	
Female	20 (58,8)	14 (41,2)	
BMI			0,295[b]
Underweight	11 (84,6)	2 (15,4)	
Normoweight	25 (61)	16 (39)	
Overweight	4 (66,7)	2 (33,3)	
History of Tuberculosis Treatment			0,043[c]
Yes	8 (100)	0	
No	32 (61,5)	20 (38,5)	
Extent the Lung Lesion			0,010[a]
Normal – minimal lesion	9 (42,9)	12 (57,1)	
Moderate lesion	9 (69,2)	4 (30,8)	
Advanced lesion	22 (84,6)	4 (15,4)	

History of Diabetes Melitus			0,836[a]
Yes	11 (68,8)	5 (31,2)	
No	29 (65,9)	15 (34,1)	
HIV-AIDS			1,000[c]
Yes	1 (100)	0	
No	39 (66,1)	20 (33,9)	
Smoking Habits			0,105[a]
Yes	14 (82,4)	3 (17,6)	
No	26 (60,5)	17	

[a]*chi square -test,* [b]*Kruskal Wallis test,* [c]*Fischer's exact test*

Table 3 . Multivariate Analysis of Factors Influencing Pulmonary Function in Patients After Completed Anti Tuberculosis Treatment

Variable	Exp(B)	95% CI for EXP(B)	
		Lower	Upper
Selection I			
Age	2,346	0,516	10,654
Gender	1,026	0,175	5,998
Tuberculosis History	5,980	0,000	,
Extent of Lung Lesions	3,141	0,821	12,023
Smoking Habits	1,608	0,171	15,139
Constant	0,748		
Selection II			
Age	2,179	0,482	9,860
Gender	1,138	0,211	6,147
Extent of Lung Lesion	4,270	1,154	15,806
Smoking Habits	1,456	0,165	12,877
Constant	0,808		
Selection III			
Age	2,151	0,479	9,656
Extent of Lung Lesions	4,340	1,192	15,809
Smoking Habits	1,623	0,310	8,493
Constant	0,827		
Selection IV			
Age	2,679	0,716	10,030
Extent of Lung Lesions	4,605	1,280	16,572
Constant			
Selection V			
Extent of Lung Lesions	4,889	1,386	17,241
Constant	1,125		

Using the enter method, which involves introducing one independent variable at a time starting from the variable with the highest p-value greater than 0.05, it was found that only one independent variable significantly affects lung function in patients with drug-sensitive pulmonary tuberculosis who have completed anti-tuberculosis treatment in this study, namely the size of the lesion (p = 0.014) with an Exp (B) value of 4.889 (95% CI = 1.386 – 17.241). This means that subjects with advanced lesion size are 4.899 times more likely to experience abnormal lung function compared to subjects with non-advanced lesions.

Discussion

In this study, age did not emerge as a significant determinant of post-treatment pulmonary dysfunction (p = 0.223). Although physiologic declines in FEV_1 accelerate with advancing age—approximately 25–30 mL/year from the fourth decade and up to 60 mL/year after age 70—compensatory mechanisms and heterogeneity in host response may obscure this effect in cross-sectional analyses (Quanjer et al., 2012; Orme, 1988). Moreover, age-related comorbidities such as malnutrition and immunosenescence contribute to TB reactivation risk but may not directly translate into measurable spirometric deficits once microbiological cure is achieved.Gender differences in pulmonary sequelae following tuberculosis have been inconsistently reported. Despite men demonstrating higher absolute FEV_1 and FVC values, the FEV_1/FVC ratio—a key marker for obstructive patterns—was comparable between sexes (Zakaria et al., 2019; Silva et

al., 2018). The lack of significant association in our cohort (p = 0.141) suggests that sex-specific hormonal or immunologic factors exert limited influence on lung function recovery once treatment is completed.Body mass index (BMI) likewise showed no significant relationship with abnormal spirometry (p = 0.295), contrasting prior reports linking adiposity to reduced pulmonary volumes (Carey et al., 1999; Gabrielsen et al., 2011).

This discrepancy may reflect the narrow BMI distribution in our sample, predominantly within the normal weight range (68.3%), and absence of extreme obesity, limiting the power to detect small decrements in FVC or FEV_1.A history of prior tuberculosis treatment demonstrated a significant bivariate association with abnormal lung function (p = 0.043). Recurrent TB episodes exacerbate parenchymal destruction, as evidenced by cumulative declines in FEV_1 up to 410 mL after three episodes (Hnizdo et al., 2000; Pasipanodya et al., 2007). However, in multivariate models, prior treatment history lost significance when adjusted for lesion extent, indicating that radiographic severity captures the downstream effect of repeated disease.The extent of lung lesions on chest radiograph was the sole independent predictor of persistent pulmonary impairment, conferring a 4.889-fold increased risk of abnormal spirometry (95% CI 1.386–17.241, p = 0.014). Extensive cavitary and fibrotic changes reflect irreversible structural damage mediated by matrix metalloproteinases and pro-fibrotic cytokines (MMP-1, MMP-9, TNF-α), which disrupt alveolar architecture and airway patency (Belton et al., 2016; Alsayed & Gunosewoyo, 2023). This finding underscores the central role of initial disease burden in shaping long-term functional outcomes and supports early radiographic assessment to stratify follow-up care.Neither diabetes mellitus (p = 0.836) nor HIV co-infection (p = 1.000) were significantly associated with lung function deficits.

Although diabetes increases TB susceptibility and mortality risk two- to three-fold, its impact on post-treatment spirometry appears mediated by glycemic control and microvascular complications rather than direct parenchymal damage (Wilkinson et al., 2022; Silva et al., 2018). Similarly, HIV-related impairment of TNF-α–mediated macrophage apoptosis may intensify acute TB pathology but does not uniquely predict long-term ventilatory patterns once effective antiretroviral therapy is in place.Smoking history showed a non-significant trend toward increased abnormal spirometry (p = 0.105). Chronic tobacco exposure induces oxidative stress and airway remodeling that predispose to obstructive patterns, yet few subjects were active smokers at study entry, limiting statistical power (Urrutia et al., 2005; Bhat et al., 2017). Future research with more detailed quantification of pack-years and integration of diffusion capacity testing may better elucidate the combined effects of TB and tobacco on residual lung injury.Overall, these results highlight radiographic lesion extent as the principal factor influencing pulmonary function recovery post-TB treatment. Strategies to minimize lesion progression—through early diagnosis, treatment adherence, and host-directed therapies—may yield the greatest benefit in preserving lung health. Systematic spirometry and radiographic monitoring should be incorporated into post-treatment care protocols to identify high-risk survivors and tailor rehabilitation interventions.

IV. CONCLUSION

This study demonstrates that the extent of radiographic lung lesions is the primary determinant of persistent pulmonary impairment among adults completing treatment for drug-sensitive tuberculosis. Patients with advanced lesion extent on chest radiograph were nearly five times more likely to exhibit abnormal spirometry results compared with those having minimal or moderate lesions. Other factors—including age, gender, body mass index, history of prior tuberculosis treatment, diabetes mellitus, HIV co-infection, and smoking habits—did not retain independent significance after adjustment for lesion severity. These findings underscore the critical role of initial disease burden in shaping long-term lung function and highlight the value of quantitative radiographic assessment alongside spirometry in post-treatment follow-up care. Despite its contributions, the study is limited by its cross-sectional design, which precludes causal inference, and by a relatively small sample drawn from two hospitals in a single geographic region, which may limit generalizability.

The exclusion of patients with uncontrolled metabolic diseases and pregnant women further narrows applicability. Future research should employ longitudinal designs with larger, multi-center cohorts to

validate these associations over time and explore the dynamic interplay between lesion progression, host immune response, and pulmonary rehabilitation interventions. Additionally, integrating advanced imaging modalities and diffusion capacity testing could enhance the characterization of structural and functional sequelae. From a practical perspective, early stratification of TB survivors by lesion extent should inform tailored rehabilitation programs, resource allocation, and monitoring protocols to optimize recovery of lung function and reduce the burden of post-tuberculosis lung disease.

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