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Factors Affecting Lung Function in Patients with Drug-Sensitive Tuberculosis after Treatment.

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ABSTRACT

Introduction: Some studies show restrictive and obstruction disorders but still rarely describe factors such as the extent of lung lesions and the history of recurrent tuberculosis to pulmonary physology. To identify the factors affecting the lung function of patients suffering from tuberculosis sensitive to drug post-treatment in patients treated in Outpatient clinic USU Hospital and Adam Malik Hospital.

Method: Data that has been collected and then processed and analyzed descriptively to see to see the frequency distribution of the subject of the study based on characteristics. Data in a categorical scale is displayed in percentages while data in a numerical is shown in ratio values and standard deviations. The data will be processed through bivariate analysis using a chi-sqaure test with a degree of fertility p< 0.05 and be continued by multivariate analyses to find out which factor has the greatest role against the independent variable.

Results: Using the enter method, it was found that only one significant independent variable influenced the lung function in patients with drug-sensitive pulmonary tuberculosis in this study is the area of the lesion (p = 0,014) with an Exp (B) value of 4,889 (95% IK = 1,386 – 17,241) which means that subjects with an advanced area of lesion would tend to be at a 4.899 times greater risk of developing an abnormal area of lung function than those with an unadvanced area.

Conclusion: The extent of the lung lesion is the variable that most affects the lung function of patients with post-treatment tuberculosis in this study.

Keywords

Tuberculosis, Post treatment, Pulmonary physiology, Spirometry

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INTRODUCTION

Spirometry is a common test for lung function. Spirometry is widely used to assess lung function in order to obtain information about lung function and monitor lung health. Through spirometry examination, one can determine the effects of diseases on lung function, assess airway responsiveness, and monitor the progression of diseases or the outcomes of interventions in treatment. This spirometry can be used alongside other physical examination findings, symptoms, and medical history to determine a diagnosis.[1]

Spirometry can generally be performed on all patients who can inhale and exhale while conscious; however, there are several conditions that serve as relative contraindications for spirometry, such as conditions caused by increased myocardial demand or changes in blood pressure, increased intracranial/intraocular pressure, increased sinus and middle ear pressure, and increased intrathoracic and intra-abdominal pressure.[1,2]

Normal spirometry is indicated by normal values of FVC, FEV1, and FEV1/FVC. If abnormalities are found in these values, it may indicate the presence of obstructive and restrictive disorders. Obstructive disorders are characterized by a FEV1/FVC value below the lower limit of normal, while restrictive disorders are identified by FVC and FEV1 values below the lower limit of normal, accompanied by a FEV1/FVC value greater than the lower limit.[3-9]

Tuberculosis is a chronic and contagious disease caused by the bacteria Mycobacterium tuberculosis. This bacterium is rod-shaped and acid-resistant, which is why it is known as Acid-Resistant Bacteria. (BTA). Most TB germs infect the lung parenchyma and cause pulmonary TB; however, these bacteria can also infect other organs, known as extrapulmonary TB, such as the pleura, lymph nodes, bones, and other extrapulmonary organs. Tuberculosis is usually transmitted from one person to another through airborne droplets (< 5 microns) that are released when a person with pulmonary TB coughs, sneezes, or talks. Droplets can also be released by patients during procedures that generate aerosols, such as sputum induction and bronchoscopy.[10-15]

The treatment of tuberculosis with anti-tuberculosis drugs has an effectiveness of up to 85%. However, up to half of tuberculosis survivors experience some pulmonary dysfunction even after microbiological cure. Pulmonary disorders range from minor abnormalities to shortness of breath. Lung involvement is heterogeneous. Patients may present with manifestations of cavities, bronchiectasis, fibrosis, or nodular infiltrates, or may have a combination of several pulmonary pathologies. This incident is closely related to host-pathogen interactions and immunological events. The heterogeneity of lung damage is also related to genetic variations that code for or regulate the host's immune response.The PIAT (Pulmonary Impairment after TB) can indicate airway obstruction and restrictive ventilation disorders. Respiratory disturbances can be detected with spirometry, which quantitatively measures the flow and volume of air inhaled and exhaled. Airway obstruction is related to a decrease in the capacity to expel air from the lungs and may be associated with inflammation. On the other hand, the restriction is related to the inability to achieve maximal inhalation due to fibrosis and stiffness in the lung parenchyma.[6-25]

METHOD

This research design is an analytical observational study with a cross-sectional design. The research was carried out at H. Adam Malik General Hospital and USU General Hospital Medan. The inclusion criteria for this patient are as follows: Patients with drug-sensitive tuberculosis who have completed tuberculosis treatment and reside in Medan within 6 months after being declared cured, aged over 18 years, no history of mental disorders or mental retardation and no history of acute illness at the time of examination. while the exclusion criteria are as follows: patients with uncontrolled metabolic diseases, pregnant women and. Based on these criteria, a total of 43 patients were obtained using a consecutive nonrandom sampling method.

Based on the sample calculation, the number of samples in this study is 60 people. Subsequently, these samples will be classified based on independent and dependent variables. All samples will undergo spirometry examination and will be grouped based on research variables (age, gender, BMI, history of previous tuberculosis treatment, extent of lung lesions on X-ray, history of diabetes mellitus, history of HIV, and smoking habits).

RESULTS

Table 1. The Relationship Between Age and Spirometry Examination in Patients with Drug-Sensitive Pulmonary Tuberculosis Who Have Completed Anti-Tuberculosis Treatment.

Ages	Abnormal; n = 40	Normal; n = 20	p
18 - <35 years	15 (60)	10 (40)	0,223*
35 – 50 years	8 (57,1)	6 (42,9)	
> 50 years	17 (81)	4 (19)	

Data presented with frequency (%) *Chi Square

Using the Chi Square test, it was shown that there is no significant relationship between age and abnormal spirometry result (p=0.223).

Table 2. The Relationship Between Gender and Spirometry Examination in Patients with Drug-Sensitive Pulmonary Tuberculosis Who Have Completed Anti-Tuberculosis Treatment.

Gender	Abnormal; n = 40	Normal; n = 20	p
Male	20 (76,9)	6 (23,1)	0,141*
Female	20 (58,8)	14 (41,2)	

Data presented with frequency (%) *Chi Square

Using the Chi Square test, it was shown that there is no significant relationship between gender and abnormal spirometry result (p=0.141).

Table 3. The Relationship Between Body Mass Index and Spirometry Examination in Patients with Drug-Sensitive Pulmonary Tuberculosis Who Have Completed Anti-Tuberculosis Treatment.

BMI	Abnormal; n = 40	Normal; n = 20	P
Underweight	11 (84,6)	2 (15,4)	0,295*
Normoweight	25 (61)	16 (39)	
Overweight	4 (66,7)	2 (33,3)	

Data presented with frequency (%) *Kruskal Wallis

Using the Kruskal Wallis test, it was shown that there is no significant relationship between gender and abnormal spirometry result (p=0.295).

Table 4. The Relationship Between Tuberculosis Treatment History and Spirometry Examination in Patients with Drug-Sensitive Pulmonary Tuberculosis Who Have Completed Anti-Tuberculosis Treatment.

History of Tuberculosis Treatment	Abnormal; n = 40	Normal; n = 20	p
Yes	8 (100)	0	0,043*
No	32 (61,5)	20 (38,5)	

Data presented with frequency (%) *Fischer's Exact

Using the Fischer's Exact test, it was shown that there is significant relationship between history of Tuberculosis treatment and abnormal spirometry result (p=0.043).

Table 5. The Relationship Between the Extent of Lung Lesions and Lung Function in Patients with Drug-Sensitive Pulmonary Tuberculosis Who Have Completed Anti-Tuberculosis Treatment.

Extent of Lung Lesions	Abnormal; n = 40	Normal; n = 20	p
Normal – minimal lesion	9 (42,9)	12 (57,1)	0,010*
Moderate lesion	9 (69,2)	4 (30,8)	
Advanced lesion	22 (84,6)	4 (15,4)	

Data presented with frequency (%) *Chi Square

Using the Chi Square test, it was shown that there is significant relationship between the extent of lung lesion and abnormal spirometry result (p=0.010).

Table 6. The Relationship Between Diabetes Melitus History and Lung Function in Patients with Drug-Sensitive Pulmonary Tuberculosis Who Have Completed Anti-Tuberculosis Treatment.

History Of Diabetes Melitus	Abnormal; n = 40	Normal; n = 20	p
Ya	11 (68,8)	5 (31,2)	0,836
Tidak	29 (65,9)	15 (34,1)	

*Data presented with frequency (%) *Chi Square*

Using the Chi Square test, it was shown that there is no significant relationship between the Diabetes Melitus History and abnormal spirometry result (p=0.836).

Table 7. The Relationship Between HIV History and Lung Function in Patients with Drug-Sensitive Pulmonary Tuberculosis Who Have Completed Anti-Tuberculosis Treatment.

HIV-AIDS	Abnormal; n = 40	Normal; n = 20	p
Yes	1 (100)	0	1,000[c]
No	39 (66,1)	20 (33,9)	

Data presented with frequency (%) *Chi Square

Using the Chi Square test, it was shown that there is no significant relationship between the HIV history and abnormal spirometry result (p=1.000).

Table 8. The Relationship Between Smoking Habits and Lung Function in Patients with Drug-Sensitive Pulmonary Tuberculosis Who Have Completed Anti-Tuberculosis Treatment.

Smoking Habits	Abnormal; n = 40	Normal; n = 20	p
Yes	14 (82,4)	3 (17,6)	0,105[a]
No	26 (60,5)	17 (39,5)	

Data presented with frequency (%) *Chi Square

Using the Chi Square test, it was shown that there is no significant relationship between the HIV history and abnormal spirometry result (p=1.000).

Table 9. Multivariate Analysis of Factors Influencing Pulmonary Function in Patients with Drug-Sensitive Pulmonary Tuberculosis Who Have Completed Anti-Tuberculosis Treatment.

Variabel	B	p	Exp(B)	95% CI for EXP(B)	
				Lower	Upper
Selection I					
Age	0,853	0,270	2,346	0,516	10,654
Gender	0,025	0,978	1,026	0,175	5,998
Tuberculosis History	20,210	0,999	5,98E+9	0,000	
Extent of Lung Lesions	1,145	0,095	3,141	0,821	12,023
Smoking Habits	0,475	0,678	1,608	0,171	15,139
Constant	0,290	0,508	0,748		
Selection II					
Age	0,779	0,312	2,179	0,482	9,860
Gender	0,130	0,880	1,138	0,211	6,147
Extent of Lung Lesion	1,452	0,030	4,270	1,154	15,806
Smoking Habits	0,376	0,736	1,456	0,165	12,877
Constant	0,213	0,617	0,808		
Selection III					
Age	0,766	0,317	2,151	0,479	9,656
Extent of Lung Lesions	1,468	0,026	4,340	1,192	15,809
Smoking Habits	0,484	0,566	1,623	0,310	8,493
Constant	0,190	0,632	0,827		
Selection IV					
Age	0,985	0,143	2,679	0,716	10,030
Extent of Lung Lesions	1,527	0,019	4,605	1,280	16,572
Constant	0,160	0,685			
Selection V					
Extent of Lung Lesions	1,587	0,014	4,889	1,386	17,241
Constant	.0,18	0,732	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 lesion.

DISCUSSION

Several other cross-sectional studies have shown a linear decrease in FEV1 with increasing age. Longitudinal studies indicate a nonlinear decline with age. The rate of decline in FEV1 is estimated to be 25-30 ml per year, starting at ages 34-40, and it can increase to up to 60 ml per year after the age of 70. Additionally, in older age, the risk of infections, particularly serious infections, increases with age and the predisposition to the reactivation of tuberculosis. The factors influencing this risk are related to anatomical and physiological changes, as well as malnutrition and comorbidities. Research conducted by Meiyan et al. concluded that being over 60 years old is one of the factors that exacerbates lung function. However, this study did not show a significant relationship between age and abnormal pulmonary function (p= 0.223).[26-41]

Men have a larger lung volume than women. Research by Rahamiah et al. shows that FEV1%, predicted FVC, and peak expiratory flow are significantly higher in men; however, there are no significant differences in the FEV1/FVC ratio and BMI. Men are at a higher risk of developing lung infections compared to women. Men tend to have habits of smoking and alcohol consumption. Smoking is closely related to ciliary dysfunction, which can lower immune responses and macrophage resistance, with or without a decrease in CD4 counts. Smoking promotes a decrease in the production of IL-12 and TNF alpha, which increases the risk of granuloma formation, subsequently raising the risk of developing active tuberculosis.[16] Research conducted by Zakaeria et al. also concluded that gender contributes to the decline in lung function. Though, Using the Chi-Square test, this study found no significant relationship between gender and abnormal pulmonary function (p=0.141).

Research conducted by Ghobain concluded that obesity has no effect on spirometry tests. However, research shows different results, such as the study conducted by Carey, which found that obesity is related to a decrease in FEV1. Carey concluded that every 10 kg increase in weight induces a decrease in FEV1 of 96 ml in men and 51 ml in women. During the same period, a body mass index (BMI) of < 21.3 kg/m² showed an increase in FVC of 60 ml until the age of 38. Other research indicates an inverse relationship between body mass index and FVC. Participants with a BMI > 26.4 kg/m² showed a decrease in FVC of 185 ml, while participants with a BMI < 21.3 kg/m² showed an increase in FVC of 71 ml.[42-44] Using the Kruskal Wallis test, this study found no significant relationship between BMI in tuberculosis patients who completed treatment and abnormal lung function (p=0.295).

Research conducted by Hnizdo concluded that there is a decrease in FEV1 and FVC values during recurrent Tuberculosis events. There was a decrease in FEV1 of 153 ml during the first episode of TB, 326 ml during the second episode, and 410 ml during the third episode of Tuberculosis treatment, while the decrease in FVC was 96 ml during the first episode, 286 ml during the second episode, and 345 ml during the third episode of Tuberculosis treatment.[45-46] FEV1/FVC % significantly decreased in subjects with a history of pulmonary tuberculosis compared to those without a previous history of pulmonary tuberculosis ($p < 0.001$). Additionally, FEV6, FEF25-75%, and PEF were lower in subjects with a history of pulmonary tuberculosis ($p < 0.001$). Subjects with a history of pulmonary tuberculosis showed a higher proportion of COPD than those without a history of pulmonary tuberculosis ($p < 0.001$). When examining each stage of COPD, subjects with a history of pulmonary tuberculosis exhibited a higher proportion than those without a history of pulmonary tuberculosis at each stage ($p < 0.001$ for each).[47] In line with this research, the Fischer's Exact test showed a significant relationship between the history of previous Tuberculosis treatment and abnormal lung function (p=0.043).

The presence of tuberculosis infection triggers a hypersensitivity reaction and releases inflammatory mediators. Mediators matrix metalloproteinase-1 and 9 play a role in granuloma formation, while matrix metalloproteinase 8, 3, and 12 trigger cavitation formation, and TNF-α and interferon induce fibrosis formation.[13,14,18] In this study, the Chi Square test showed a significant relationship between the size of lung lesions and abnormal lung function (p=0.010).

Diabetes is one of the factors that exacerbates the severity of tuberculosis. The prevalence of diabetes affects the incidence and mortality of TB. Diabetes Mellitus increases the risk of tuberculosis infection two to three times, the risk of death during treatment two times, the risk of relapse four times, and the occurrence of drug resistance two times.[11] Active tuberculosis tends to occur more frequently when there is poor glycemic control. According to the meta-analysis by Wilkinson et al., about 4% of people with type 2 diabetes develop tuberculosis. Since the number of individuals with undiagnosed diabetes worldwide is estimated to be over 50%, the proportion of tuberculosis among those with diabetes should also be much higher. Analytical models attempting to project the future burden of tuberculosis in diabetes predict that the increase in diabetes will respond to a decrease in tuberculosis incidence of at least 3% over the next 15 years. There is a two to four times higher risk of active TB in individuals with diabetes compared to non-diabetic individuals. In this study, pulmonary function tests were conducted on tuberculosis patients who had completed treatment, with comorbid diabetes, without assessing HbA1c levels or the regularity of diabetes medication use.Using the Chi Square test, this study shows that no significant relationship was found between the history of diabetes mellitus and abnormal lung function (p=0.836).

HIV co-infection is a risk factor for decreased lung function. Several studies indicate that HIV patients have a higher risk of gas exchange disorders. TB co-infection is the most significant risk factor for the development of active TB, whether it be new infections, reinfections, or the activation of latent TB into active TB.[15] An increase in TNF α production is believed to elevate the incidence of active TB. HIV infection disrupts TNFα-mediated macrophage apoptosis alongside M. Tuberculosis infection. The decrease in apoptosis and the increase in necrosis of infected macrophages assist the infection process and delay the specific antigen response. [48-51] In this study, the Fisher's Exact test showed that no significant relationship was found between HIV-AIDS and abnormal pulmonary function.

Exposure to cigarette smoke can disrupt the balance of immune cells in the lungs, leading to chronic inflammation and impaired immune responses. The substances known in cigarettes cause oxidative stress, inflammation, apoptosis, and senescence due to their exposure to environmental pollutants and the presence of oxidation enzymes. The lungs are very vulnerable to oxidative stress. Persistent oxidative stress caused by chronic exposure to cigarettes can lead to respiratory diseases such as chronic obstructive pulmonary disease (COPD), pulmonary fibrosis, and lung cancer.[52-56] The analysis shows the relationship between tuberculosis and the amount of smoking exposure. Those who smoke more than 10 cigarettes a day (or more than 3 days a week) have a higher risk of pulmonary tuberculosis compared to non-smokers. Passive smokers exposed to tobacco smoke more than 3 times a week outdoors have a higher risk of pulmonary tuberculosis than those with exposure of 3 times a week or less. [57,58] In this study, statistically, no relationship was found between the smoking history and lung function post-tuberculosis treatment, although there is a significant clinical relationship.

CONCLUSION

Using the enter method, it was found that subjects with advanced lesion area are likely to have a risk of experiencing abnormal pulmonary function 4.899 times greater compared to subjects with non-advanced lesion area.

DECLARATIONS

Ethics approval and consent to participate. Per,ission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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All authors significantly contribute to the work reported execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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