



ANALYSIS OF COMORBIDITIES AND SMOKING HISTORY WITH THE INCIDENCE OF PULMONARY TUBERCULOSIS AT SURAKARTA GENERAL HOSPITAL

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ABSTRACT

Background: Tuberculosis (TB) is an infectious disease that is the top cause of death worldwide. Indonesia has the second-highest tuberculosis incidence in the world after India. One of the risk factors for tuberculosis that is difficult to avoid is smoking and comorbidities associated with decreased body resistance. Surakarta Central General Hospital has excellent pulmonary disease services. The healthcare facility treated the highest number of registered and treated pulmonary Tuberculosis patients in Surakarta City in 2019-2021. **Objective:** This study aims to determine whether there is a relationship between comorbidities and smoking history and the incidence of Pulmonary Tuberculosis at the Surakarta Central General Hospital. **Methods:** This research was conducted at the Surakarta Central General Hospital in March 2022. Sample withdrawal was carried out using nonprobability sampling with a purposive sampling technique. The data sources used in this study include secondary data from medical records confirmed by primary data by interviewing and distributing questionnaires. This study is an observational quantitative study with a case-control research design. The sample of this study amounted to 96 people (48 case groups and 48 control groups). Data analysis using the chi-square test. **Results:** The results showed that there was an association between comorbidities ($p=0.040$; $OR=3.541$; $95\%CI=1,160-10,808$) and smoking history ($p=0.048$; $OR=3.182$; $95\%CI=1,113-9,100$) with the incidence of pulmonary tuberculosis. Most patients were male, with the highest age range of 45-54, as many as 24 people, and 55-64 years, as many as 24. Most patients did not have a job (24 people) and had an income \geq UMR (56 people). Patients' highest level of education was primary education (37 people). **Conclusion:** This study concludes an association between comorbidities and smoking history with the incidence of pulmonary tuberculosis in Surakarta General Hospital.

Keywords: Tuberculosis, Smoking, HIV, DM, Hypertension.

INTRODUCTION

Tuberculosis (TB) is an infectious disease that is the top cause of death worldwide, making it one of the Sustainable Health Development Goals (SDGs). An estimated 10 million people had tuberculosis, and 1.4 million died in 2019. Mycobacterium tuberculosis bacillus is the causative agent of tuberculosis, which can be transmitted when a person with tuberculosis releases bacteria into the air, for example, by coughing. Tuberculosis can affect anyone and anywhere.¹

Indonesia has the second highest tuberculosis disease rate in the world after India. In 2020, the highest number of tuberculosis cases were reported in provinces with the largest population, namely West Java, East Java, and Central Java. The number of cases in these three provinces is almost half of Indonesia's total tuberculosis cases, namely 46%.² Surakarta Central General Hospital, which is a transformation of the Surakarta Community Lung Health Center (BBKPM), which has excellence in pulmonary disease services, is a health service facility that handles the highest number of registered

and treated pulmonary tuberculosis patients in Surakarta City each year, in 2021 the number of pulmonary tuberculosis cases at the Surakarta General Hospital was recorded at 254 cases³, the number of cases increased when compared to the previous two years, namely in 2019 with 98 patients and in 2020 with 202 cases.⁴

Several risk factors can affect a person's susceptibility to pulmonary tuberculosis, such as low immunity (immunosuppression), comorbidities such as HIV and diabetes mellitus, chemicals (alcohol, cigarettes, and illegal drugs) and poverty, direct contact with patients with pulmonary tuberculosis, poor nutrition (malnutrition) and housing conditions. Patients with chronic tuberculosis disease have a greater risk of non-communicable comorbidities. Comorbid conditions may increase the risk of reactivation of latent tuberculosis infection (LTBI) and the risk of tuberculosis directly after infection.⁵

Another research in Indonesia with the study Prevalence of Diabetes Mellitus and Pulmonary Tuberculosis showed an association between a history of diabetes mellitus and pulmonary tuberculosis



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(26.7%), p-value = 0.038, OR = 5.092; 95% CI = 0.981- 26.430.⁶ Tuberculosis and HIV/AIDS infection have a strong relationship, with HIV infection increasing the incidence of tuberculosis disease. HIV patients have a 20-fold increased risk of developing tuberculosis. One of the risk factors for tuberculosis that is difficult to avoid is smoking.⁷ Another study in Kupang with research on the Relationship between Smoking Habits in Active and Passive Smokers with the Incidence of Pulmonary Tuberculosis at Sikumana Health Center, Kupang City showed that there was a significant relationship between smoking status (P = 0.037; OR = 10.889), age of smoking (P = 0.040; OR = 21.000), and length of smoking (P = 0.035, OR 20.000), so it can be concluded that there is a significant relationship between smoking habits in active and passive smokers with the incidence of pulmonary TB at Sikumana Health Center, Kupang City.⁸

The author chose "Analysis of Comorbidities and Smoking History with the Incidence of Pulmonary Tuberculosis in Surakarta Central General Hospital" from the description above. Surakarta Central General Hospital became the place of research based on data on the highest incidence of pulmonary tuberculosis in Surakarta City. Smoking history and comorbidities were the variables in this study.

METHODS

This study is an observational quantitative study with a case-control research design. The case group population in this study were people suffering from pulmonary tuberculosis at the Surakarta General Hospital, namely 280 people registered in January 2021 - March 2022. The control group population in this study were patients who were not confirmed with pulmonary tuberculosis at Surakarta General Hospital and were registered and recorded in January 2021 - March 2022. This research was conducted at the Surakarta Central General Hospital in March 2022. Sample withdrawal was carried out using nonprobability sampling with a purposive sampling technique. The data sources used in this study include secondary data from medical records confirmed by primary data by interviewing and distributing questionnaires.

The inclusion and exclusion criteria are as follows:

- a. Case group inclusion criteria
 1. Pulmonary TB registered from 2021 to March 2022
 2. Aged 15-65 years
- b. Case group exclusion criteria
 1. Not willing to sign informed consent
- c. Control group inclusion criteria
 1. Patients with treatment recorded in the patient register book at Surakarta General Hospital in 2021-2022
 2. Aged 15-65 years
 3. Not currently confirmed pulmonary TB
- d. Control group exclusion criteria
 1. Not willing to sign informed consent
 2. Have been confirmed/have recovered from pulmonary TB disease

Sample size was calculated using the Lemeshow formula:

$$n_1=n_2=\frac{(Z_{1-\frac{\alpha}{2}}\sqrt{2p(1-p)}+Z_{1-\beta}\sqrt{p_1(1-p_1)+p_2(1-p_2)})^2}{(p_1-p_2)^2}$$

Description :

$n_1=n_2$ = sample size

$Z_{1-\frac{\alpha}{2}}$ = Standard deviation of alpha, value 1.96 (Z_{α} value at 95% CI, $\alpha = 0.05$)

$Z_{1-\beta}$ = Standard deviation of beta, value 0.842 (power 80%)

P_1 = Proportion in the case group

$$P_1 = \frac{(OR)P_2}{(OR)P_2+(1-P_2)}$$

P_2 = proportion in the control group

$$P = \frac{P_1+P_2}{2}$$

Independent variable	OR	P1	P2	P	n
Smoking history	3,701 ⁹	0,787	0,5	0,643	43
Comorbidities	5,091 ⁶	0,835	0,5	0,667	30

The results of the minimum sample calculation in this study were 43 respondents. To anticipate the effect of non-response, it is calculated by the formula:

$$q = \frac{1}{1-f}$$

Description:

q = Non-response factor

f = percentage of estimated non-response effect 10% percent (0.1)



$$q = \frac{1}{1-f}$$

q = 1,11

n = q x minimum sample size

n = 1.11 x 43

n = 47,73 ≈ 48

The ratio of case and control groups is 1:1, so 48 respondents in the case group and 48 respondents in the control group are obtained, so the total sample is 96 respondents.

Operational Definition of Variables

a. Comorbidities

Definition: Comorbidities are diseases that accompany patients other than pulmonary TB disease, such as DM, HIV/AIDS, and hypertension, where the condition is still present during the TB treatment and is related to immune suppression.

Measuring instrument: Medical records confirmed by questionnaire

Outcome measure:

1. Yes (Comorbidities)
2. No (Without comorbidities)

Data scale: Nominal

b. Smoking History

Definition: A person who has smoked at least 100 cigarettes and is still smoking in the past year.¹⁰

Measurement instrument: Questionnaire

Outcome Measures:

1. Yes (Smoking)
2. No (No smoking)

Data scale: Nominal

c. Pulmonary Tuberculosis

Definition: A condition in which a person suffers from an infectious lung disease caused by mycobacterium tuberculosis bacteria.¹¹ Cases of the disease are known based on medical record data from Surakarta General Hospital in 2021-march 2022.

Measurement instrument: Medical records confirmed by questionnaire

Outcome Measures:

1. Case (Pulmonary tuberculosis)
2. Control (No pulmonary tuberculosis)

Data scale: Nominal

RESULTS

Characteristics of respondents

Table 1 shows that most patients in the case and control groups were male, namely 58 people; the highest age range was 45-54 and 55-64 years, which amounted to 24 people. Most of the patients did not have a job, namely 24 people. Patients' highest level of education was elementary level, namely 37 people, and as many as 56 patients had an income ≥ minimum wage.

Comorbidities

Table 2 shows that most patients had comorbid diabetes mellitus, namely 12 people (Nine people in the case group (suffering from pulmonary tuberculosis) and three people in the control group (not suffering from pulmonary tuberculosis)). Besides that, there were also patients with comorbid hypertension, as many as six people, and one patient was found to have HIV disease in the control group (no pulmonary tuberculosis).

Smoking History

Based on Table 3, it can be seen that most patients in the case and control groups were non-smokers, namely 75 people, and as many as 19 people had the habit of smoking clove/filter types. Patients with a smoking history of > 20 years were 13 people, and most patients had a history of cigarette consumption of 1-10 and 11-20 cigarettes per day, each of which was eight people. Most patients had a history of being moderate smokers, as many as eight people for tobacco cigarettes, while for vape smokers, one person was a light smoker (3-11 dripping / day), and one other person was a heavy smoker (12-20 dripping/day). Based on the status of passive smokers or patients who are exposed to cigarette smoke from other people, it was found that 49 patients were passive smokers, with 32 of them suffering from pulmonary tuberculosis.



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Table 1. Frequency distribution of respondent characteristics based on gender, age, and occupation, education and income

Variable	Case		Control	
	n	%	n	%
Gender				
Male	25	52,1	33	68,7
Female	23	47,9	15	31,3
Age				
15-24	4	8,3	4	8,3
25-34	3	6,3	7	14,6
35-44	11	22,9	11	22,9
45-54	15	31,3	9	18,8
55-64	12	25,0	12	25
≥ 65	3	6,3	5	10,4
Occupation				
Not working	12	25,0	12	25,0
Farmer	3	6,3	3	6,3
Laborer	11	22,9	5	10,4
Trader	6	12,5	0	0,0
Self employed	11	22,9	10	20,8
Civil Cervant	2	4,2	0	0,0
Student	0	0,0	4	8,3
Other	3	6,3	14	29,2
Education				
Did not finish elementary school	2	4,2	2	4,2
Elementary school	23	47,9	14	38,5
Secondary school	14	29,2	20	35,4
High school	9	18,8	12	21,9
Income				
No income	12	25,0	16	33,3
< minimum wage	9	18,8	3	6,3
≥ minimum wage	27	56,3	29	60,4

Source: (Primary Data, 2022)

Table 2. Frequency distribution of respondent characteristics based on comorbidities

Variable	Case		Control	
	(n)	%	(n)	%
DM	9	18,7	3	6,3
Not DM	39	81,3	45	93,7
HIV	0	0,0	1	2,1
Not HIV	48	100,0	47	97,9
Hipertensi	5	10,4	1	2,1
Not Hipertensi	43	89,6	47	97,9

Source: (Primary Data, 2022)

Table 3. Frequency distribution of respondents' characteristics based on type of cigarette, length of smoking, and number of cigarettes consumed in one day and degree of smoking.

Variable	Case		Control	
	(n)	%	(n)	%
Type of cigarette				
No smoking	33	68,7	42	87,5
Kretek/ filter	13	27,1	6	12,5
Kretek/ filter and Vape	2	4,2	0	0,0
Length of smoking				
No smoking	33	68,7	42	87,5
≤ 10 years	3	6,3	0	0,0

11-20 years	1	2,1	4	8,3
>20 years	11	22,9	2	4,2
Number of cigarettes (days)				
No smoking	33	68,8	42	87,5
1-10 cigarettes	5	10,4	3	6,3
11-20 cigarettes	6	12,5	2	4,2
>20 cigarettes	4	8,3	1	2,1
Degree of smoking Tobacco)				
No smoking	33	68,8	42	87,5
≤ 199 (mild)	4	8,3	3	6,3
200-599 (moderate)	6	12,5	2	4,2
≥ 600 (heavy)	5	10,4	1	2,1
Passive Smokers				
Passive	32	66,7	17	35,4
Not affected	16	33,3	31	64,6

Source: (Primary Data, 2022)

The Relationship Between Comorbidities and the Incidence of Pulmonary Tuberculosis

Based on Table 4, 19 patients were found to suffer from pulmonary tuberculosis with comorbidities; the results of the bivariate analysis with the chi-square test of the relationship between comorbidities and the incidence of pulmonary tuberculosis showed a p-value = 0.040 <0.05; OR value = 3.51; 95% CI = 1,160-10,808. So, it is known that there is a relationship between comorbidities and the incidence of pulmonary tuberculosis in Surakarta General Hospital.

The Relationship Between Smoking History and the Incidence of Pulmonary Tuberculosis

Based on Table 5, 21 patients were found to suffer from pulmonary tuberculosis with a history of smoking; the results of the bivariate analysis with the chi-square test of the relationship between smoking history and the incidence of pulmonary tuberculosis obtained a p-value = 0.048 <0.05; OR = 3.182; 95% CI = 1,160-10,808 which means there is a relationship between smoking history and the incidence of pulmonary tuberculosis at Surakarta General Hospital.

Table 4. Cross tabulation of the association between comorbidities and the incidence of pulmonary tuberculosis

Comorbidities	Tuberculosis (TBC)				P-Value	OR	95% CI
	Case		control				
	n	%	n	%			
Yes	14	29,2	5	10,4		3,541	1,160-10,808
No	34	70,8	43	89,6	0,040		
Total	48	100	48	100			

Source: (Primary Data, 2022)



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Table 5. Cross tabulation of the association between smoking history and the incidence of pulmonary tuberculosis

Smoking History	Tuberculosis (TBC)				P-Value	OR	95%CI
	Case		Control				
	n	%	n	%			
Yes	15	31,3	6	12,5	0,048	3,182	1,113-9,100
No	33	68,7	42	87,5			
Total	48	100	48	100			

Source: (Primary Data, 2022)

DISCUSSIONS

Univariate analysis described several variables studied, namely comorbidities and smoking history. In contrast, bivariate analysis determined the relationship between independent variables (smoking history and comorbidities) and dependent variables (pulmonary tuberculosis).

The results of the bivariate analysis with the chi-square test of the relationship between comorbidities and the incidence of pulmonary TB obtained a p-value = 0.040 < 0.05; OR value = 3.51; 95%CI=1,160-10,808, which means that there is a significant relationship between comorbidities and the incidence of pulmonary TB at the Surakarta Central General Hospital. In this study, it is known that people with comorbidities have a risk of developing pulmonary TB 3.51 times greater than people who do not have comorbidities.

Similar research in Aceh with research Risk factors for pulmonary tuberculosis transmission in families living in the same house in East Aceh district states the results of the relationship between comorbidities (p=0.0001) and pulmonary TB transmission in families living in the same place in East Aceh District.¹² Other research in Palembang from the study of the characteristics of Tuberculosis patients at Public Health Center Seberang Ulu 1 Palembang found 13.2% of TB patients with DM, 45% of TB patients with hypertension, 47.5% of TB patients with anaemia, 55% of TB patients with malnutrition.¹³ Non-communicable comorbidities such as hypertension and diabetes mellitus arise from a combination of non-modifiable and modifiable risk factors. The risk factors that individuals cannot modify are age, gender, and genetics. While modifiable risk factors include smoking behaviour, alcohol consumption, and poor diet, as well as insufficient physical activity.¹⁴ Surakarta General Hospital has been relatively routine in making efforts to prevent the risk of non-communicable diseases and pulmonary tuberculosis by interacting directly

through health counselling to patients and indirectly by providing leaflets and putting up posters around the registration counter. However, the number is still limited to the clinic's waiting room.

Comorbidities are one of the things that complicate the treatment of pulmonary tuberculosis. The presence of comorbidities can increase the risk of negligence in seeking treatment. Patients with comorbidities other than tuberculosis have a double disease burden that is likely to be less focused on undergoing tuberculosis treatment, which impacts the level of treatment compliance of pulmonary tuberculosis patients. Diabetes mellitus (DM) is one of the non-communicable chronic diseases that can lead to a decrease in the function of the body's immune cells, which function as the body's defence mechanism and disrupt the process of the respiratory epithelium and cilia movement so that patients are susceptible to infection, one of which is pulmonary tuberculosis infection. Metformin is the recommended first-choice glucose-lowering agent in type 2 DM, and there is no reason why this should be different for patients with active tuberculosis disease. Treatment adjustments according to patient characteristics, disease severity of TB and DM, timing, and dose of glucose-lowering drugs.¹⁵ Efavirenz is a known inducer of enzyme metabolism; therefore, there is a risk of drug-drug interactions affecting the pharmacokinetics of rifampicin during co-administration when treating TB and HIV concurrently, so appropriate management and monitoring is needed to treat both diseases.¹⁶ Tuberculosis, as a trigger for immunologic response, may cause impaired endothelial function and lead to an increased risk of heart disease and possibly hypertension, and vice versa. Hypertension may have subtle effects on the immune system that may increase the risk of tuberculosis.¹⁷ There is a steady trend for an increasing proportion of people in the structure of hypertension in combination with tuberculosis. The prevalence of hypertension among people over 30 varies from 3.4% to 40.7%.¹⁸

The results of the bivariate analysis with the chi-square test of the relationship between smoking history and the incidence of pulmonary tuberculosis obtained a p-value = 0.048 < 0.05; OR = 3.182; 95%CI= 1,113-9,100, so it can be interpreted that there is a significant relationship between smoking history and the incidence of pulmonary tuberculosis



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at the Surakarta Central General Hospital and people who smoke have a risk of developing pulmonary tuberculosis 3.182 times greater than people who do not smoke. In this study, based on the analysis of gender and the incidence of pulmonary tuberculosis, it can be seen that 25 people (52.1%) of men suffered from pulmonary tuberculosis and 23 people (47.9%) of women suffered from pulmonary tuberculosis. In comparison, the results of the analysis between smoking and the incidence of pulmonary tuberculosis show that 15 people who smoke (31.3%) suffered from pulmonary tuberculosis. Of the number of patients who smoked, as many as 21 people (100%) were male. The incidence of tuberculosis is more prevalent in men; this can be caused by several things, such as the level of mobility and workload of men who are higher than women, lack of rest, and men having unhealthy lifestyles such as smoking and drinking alcohol, which can reduce the body's immune system.¹⁹

Similar research studies in Bitung with research on Risk Factor Analysis of Pulmonary TB incidence in the Working Area of Puskesmas Girian Weru Bitung City state that there is an association between smoking habits and the incidence of pulmonary tuberculosis with a p-value = 0.047 <0.05; OR = 2.727; CI = 0,992- 7,499 Where respondents who smoke have a 2.727 times risk of developing pulmonary TB compared to those who do not smoke.²⁰ Tobacco smoking increases the risk of progression of Latent Tuberculosis Infection (LTBI) to TB. Active smoking increases the severity of pulmonary TB (clinical: cough, dyspnea, fatigue with longer recovery time; chest x-ray; higher sputum positivity after two months of treatment). Tobacco smoke impairs the lungs' defence mechanisms against infection, making patients more susceptible to infection and prone to disease progression after latent infection.²¹

This study has several limitations, including this study uses a case-control study research design so that the possibility of recall bias is very high due to the limited memory of respondents, this study uses bivariate analysis so that it does not consider confounding variables and the long latency period of tuberculosis can cause ambiguity in the relationship between comorbidities and smoking history with the incidence of pulmonary tuberculosis.

CONCLUSION

There was a significant relationship between comorbidities and the incidence of pulmonary tuberculosis with a value of $p=0.040 <0.05$, and there was a significant relationship between smoking history and the incidence of pulmonary tuberculosis with a value of $p=0.048 <0.05$.

ETHICAL APPROVAL

This research obtained a research permit from the Health Research Ethics Commission (KEPK) at the Faculty of Medicine, Universitas Muhammadiyah Surakarta number 4118/B.1/KEPK-FKUMS/II/2022.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization and methodology, writing—original draft preparation, Irlisa Rahma Warasti; validation, formal analysis, data curation, writing—review and editing, Windi Wulandari

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