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Risk Factors of Pulmonary Tuberculosis in Type 2 Diabetes Mellitus in Yogyakarta

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ABSTRACT

Background: The prevalence of pulmonary tuberculosis (TB) increases along with the increasing prevalence of Type 2 Diabetes Mellitus (T2DM) patients. The frequency of TB in type 2 DM patients (10 to 15%) and the prevalence of this infectious disease is 2 to 5 times higher in DM patients compared to non-diabetics. This study aimed to analyze the risk factors for pulmonary TB in T2DM patients in Yogyakarta.
Subjects and Method: This study uses a case-control study design conducted at RESPIRA Lung Hospital Yogyakarta from January 16 to February 20, 2023. The number of samples was 52 people with a total of 26 people in the case and control groups. Samples were taken by consecutive sampling technique. The independent variables were age, gender, employment, education, BMI, smoking status, clinical symptoms, family history of TB, previous history of TB, and income level). The dependent variable is the incidence of TB in DM patients. Control groups are respondents without a diagnosis of DM and TB patients. Conversely, the cases are personal with diagnosis TB and DM patient Data were collected using a questionnaire. Data analysis was carried out descriptively, bivariate with Chi-square, and multivariate with multiple logistic regression.
Results: The demonstrated research that the risk factors that influence the incidence of TB in T2DM patients are gender (aOR = 9.60; 95% CI: 0.14 to 55.96; p=0.012), Age (aOR=0.24; 95% CI: 0.07 to 0.76; p=0.015).
Conclusion: The female sex has a 9.60 times higher risk of experiencing TB compared to men in T2DM patients.

Keywords: Diabetes Mellitus; pulmonary tuberculosis; risk factors

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BACKGROUND

The number of Diabetes Mellitus (DM) cases worldwide was recorded at around 415 million people with a percentage of 91% of them suffering from type 2 DM (IDF, 2015). Meanwhile, the prevalence of pulmonary

tuberculosis (TB) accompanied by DM globally in 2016 ranged from 0.38% to 14% with an average global prevalence of 4.1% (WHO, 2020b). An estimated 40% of total cases of pulmonary TB accompanied by DM globally are found to originate in India and China (Zheng et al., 2021). Of the approximately 350 million people suffering from DM worldwide, approximately 9.4 million new cases of TB and 1.7 million TB deaths per year are found, this prevalence is comparable in low- and middle-income countries (Khalil and Ramadan, 2016; Gotera et al., 2021). An increase in the prevalence of DM, as a risk factor for TB, is also accompanied by an increase in TB prevalence. There are about 1.3 million DM sufferers with and who die before the age of 70 years as much as 4% (Nasution et al., 2021; Savitri, 2021).

Indonesia currently ranks seventh in the highest prevalence of DM in the world after China, India, USA, Brazil, Russia and Mexico. Indonesia is also the country with the number of new TB cases and the second total TB in the world after India (Risna Dewi et al., 2017). Indonesia has a high TB caseload with an incidence of 1,000,000, a prevalence of 1,600,000, and a death toll of 100,000 out of a total population of 254 million in 2014 (WHO, 2020a). Meanwhile, based on the results of Basic Health Research (Riskesdas), the prevalence of DM in Yogyakarta ranks third highest, in Indonesia, which is 3.1% in 2018 (Kemenkes RI, 2018).

Several studies in the world show that 5-30% of TB patients have DM (TBDM). The prevalence of pulmonary TB increases along with the increase in the prevalence of DM. The frequency of DM in TB patients is reported to be around 10-15% and the prevalence of this infectious disease is 2-5 times higher in DM patients compared to non-DM patients (Yanti, 2017; Rohman, 2018). Research in Indonesia in 2001-2005 conducted on 454 DM sufferers reported that 60 of them were also diagnosed with pulmonary TB (Einarson et al., 2018). The risk of DM sufferers experiencing pulmonary TB is 4.7 times, while the risk of experiencing TB in general is 1.5-8.8 times. The relative risk of active TB infection in DM patients increased by 2.44 to 8.33 times (Baghaei et al., 2013; Mihardja et al., 2015; Savitri, 2021).

Gender is related to the incidence of TBDM (Risna Dewi et al., 2017; Savitri, 2021; Yosephine et al., 2021). Men are shown to be more at risk of suffering from TBDM than women (Gotera et al., 2021). While other studies show that older age increases the risk of TBDM (Khalil and Ramadan, 2016; Dewi et al., 2017; Nasution et al., 2021; Yosephine et al., 2021).

Other studies have shown that significant factors for the occurrence of Pulmonary TB in type 2 DM patients are contact with TB patients, long suffering from DM and HbA1c levels (Alisjahbana et al., 2020; Gotera et al., 2021). The prevalence of pulmonary TB and DM is 16.7% and DM is associated with the incidence of pulmonary TB (Kottarath et al., 2015). Living in urban areas, having low levels of education, place of birth, ethnicity, economic status and employment are also associated risk factors for TBDM (Gotera et al., 2021). Room activity was reported as a low risk factor for TBDM comorbidities. Gender, old age, urban residence, smoking, sedentary lifestyle, poor glycemic control, family history of DM and TB, contact with TB sufferers, and long suffering from DM, proved to be risk factors for TBDM (Wulandari and Sugiri, 2013; Girardi et al., 2017; Workneh et al., 2017; Rohman, 2018).

Based on this background, it is important to conduct a study to explore the risk factors for TBDM in Yogyakarta. Therefore,

this study was conducted with the aim of determining the risk factors for the incidence of Pulmonary TB in DM patients in Yogyakarta, based on: age, gender, status of residence, type of occupation, type of DM therapy, blood sugar levels, smoking history, history of close contact with TB patients, income level, body mass index (BMI), long suffering from DM, and home environmental conditions. With the knowledge of these risk factors, it is hoped that efforts can be made to prevent the occurrence of Pulmonary TB in DM sufferers so that the degree of public health can be improved.

SUBJECTS AND METHOD

1. Study Design

The research was carried out at Panembahan Senopati Hospital and Yogyakarta Respira Lung Hospital in January-March 2023. These two hospitals were chosen because the number of TBDM cases is the highest in Yogyakarta.

2. Population and Sample

The dependent variable of this study is the incidence of Pulmonary TB in patients with DM, while the independent variables: include age, sex, employment status, educational status, BMI status, smoking status, clinical symptoms, family TB history, and previous TB history, as well as income level.

3. Study Variables

The independent variables were age, gender, employment, education, BMI, smoking status, clinical symptoms, family history of TB, previous history of TB, and income level). The dependent variable is the incidence of TB in DM patients.

4. Conceptual Definition

Incidence of Pulmonary TB in patients with DM: a subject diagnosed by health workers with DM and has been diagnosed with TB by health workers and has undergone sputum or Mantoux examination and chest photo examination.

Age: is the age of the respondent at the time of the interview.

Sex: is a gender status that is physically and biologically differentiated based on external genital organs.

Employment Status: is the respondent's employment status at the time of TB diagnosis.

Education Status: is the last educational status taken by respondents.

BMI status: is a tool to measure nutritional status based on respondents' weight and height.

Smoking Status: is an activity carried out by the hospital based on whether or not they have smoked within three months before being diagnosed with TB by health workers.

Clinical Symptoms: are symptoms experienced by respondents when diagnosed with TB based on respondents' Medical Record data.

Previous TB history: are respondents who have previously been diagnosed with TB, recovered, and then diagnosed with TB again by health workers.

Family TB symptoms: are respondents who have family members (father, mother, or child) who have experienced TB.

Income Level: is the income level of respondents at the time of diagnosis of TB.

5. Study Instruments

Primary data were collected by interview method using questionnaires to determine the characteristics of respondents, while secondary data were obtained from the results of searching the subject's medical records. Patients who were declared TB based on rongent results and DM patients were diagnosed using cut-of-point blood sugar levels (fasting blood glucose ≥ 126 mg/dl or postprandial ≥ 200 mg/dl) (IDF Diabetes Atlas 2021, 2021).

6. Data Analysis

Data analysis was carried out descriptively and analytically, namely: bivariate with Chi-

square ($\chi 2$) and multivariate using multiple logistic regression tests.

7. Research Ethics

This research has been licensed with EC number: 00221/KT.7.4/VIII/2022.

RESULTS

1. Sample Characteristic

The results of the study were obtained from 52 participating respondents and presented in the form of descriptive, bivariate, and multivariate analysis as follows. Descriptive analysis, to describe the characteristics of the research subject according to the independent variable studied. The size used is the amount and proportion. The results of this analysis will be presented in tabular form. Bivariate analysis was conducted to see the relationship between both independent and dependent variables and multivariate analysis was to determine the dominant risk factors associated with the incidence of Pulmonary TB in patients with DM: The frequency distribution based on respondent characteristics in Table 1 shows that most respondents were aged >60 years (53.8%), with female gender (69.2%), had low education status (≤equivalent junior high school) (57.7%), employment status i.e. not working (69.2%), low monthly income (<2,066,438) (76.9%), married (84.6%), normal nutritional status with BMI results between 18.5-25.0 (46.2%), and had no family history of TB (96.2%) and no previous history of TB (100%).

Table 1. Frequency Distribution on responden characteristics

Variable	Case		Control	
	n	%	n	%
TB				
Yes	9	34.6	25	96.2
No	17	65	1	3.8
Age				
<50 years	5	19.2	11	42.3
50-60 years	7	26.9	9	34.6
>60 years	14	53.8	6	23.1
Gender				
Male	8	30.8	15	57.7
Female	18	69.2	11	42.3
Education Status				
High (≥ Senior High School)	11	42.3	13	50.0
Low (≤Junior High School)	15	57.7	13	50.0
Employment Status				
Work	8	30.8	14	53.8
Not Working	18	69.2	12	46.2
Monthly Income				
High (≥2.066.438)	6	23.1	0	0
Low (<2.066.438)	20	76.9	26	100
Marital Status				
Marry	22	84.6	20	76.9
Divorce	3	11.5	1	3.8
Unmarried	1	5.8	5	19.2
IMT Status				
Overweight	8	30.8	1	3.8
Underweight	6	23.1	13	50.0
Normal	12	46.2	12	46.2

Variable	Case		Control	
	n	%	n	%
Family TB History				
Yes	1	3.8	2	7.7
Not	25	96.2	24	92.3
Previous TB History				
Yes	0	0	3	11.5
Not	26	100	23	88.5

Table 2 obtained the results that the clinical symptoms of the case group were cough >2 weeks (31%), cough with phlegm (40%), cough with phlegm with blood (25%), chest pain (36.8%), shortness of breath (34.5%), weakness (37.9%), fever (33.3%), chills (30%), night sweating (43.5%), decreased appetite (33.3%), weight loss (34.3%).

Table 2. Frequency distribution based on clinical symptoms

Clinical symptomp	Case		Control	
	n	%	n	%
Cough >2 Weeks				
Yes	9	31	20	69
No	17	73.9	6	26.1
Coughing with phlegm				
Yes	8	40	12	60
No	18	56.3	14	43.8
Coughing with Blood				
Yes	1	25	3	75
No	25	52.1	23	47.9
Chest pain				
Yes	7	36.8	12	63.2
No	19	57.6	14	42.4
Shortness of breath				
Yes	10	34.5	19	65.5
No	16	69.6	7	30.4
Weakness				
Yes	11	37.9	18	62.1
No	15	65.2	8	34.6
Fever				
Yes	7	33.3	14	66.7
No	19	61.3	12	38.7
shivering pain				
Yes	3	30	7	70
No	23	54.8	19	45.2
Drying at Night				
Yes	10	43.5	13	56.5
No	16	55.2	13	44,8
decreased appetite				
Yes	9	33.3	18	66.7
No	17	68	8	32
weight loss				
Yes	12	34.3	23	65.7
No	14	82.4	3	17.6

2. Bivariate Analysis

Table 3 showed that from 52 responses there was no relationship between age, sex, educational status, employment status, marital status, family TB history, and previous history of Pulmonary TB with the incidence of Pulmonary TB in patients with DM (p >0.050). The variable monthly income (OR= 0.43; CI 95%= 0.31 to 0.60). That is, DM sufferers with low monthly income have a 0.43 times higher risk of developing Pulmonary TB. There is an association between BMI status and TB incidence (p<0.050), and clinical symptoms also have an association with TB incidence in DM patients (OR= 0.43; CI 95%= 0.13 to 0.60) and an association with the incidence of Pulmonary TB in people with DM. That is, DM sufferers with clinical symptoms have a 0.43 times higher risk of developing pulmonary TB.

Based on the analysis alcohol consumption and smoking are not associated with the incidence of TB in patients with DM. Family support reminds us that taking medication and delivering it to health services have no relationship with the incidence of TB in people with DM. Based on home conditions: lighting and ventilation have no relationship with the incidence of TB in patients with DM (p > 0.050).

Table 3. Bivariate analysis of respondents with the incidence of pulmonary tuberculosis in Diabetics Mellitus

Independent Variables	Case		Control		OR	95% CI		p
	n	%	n	%		Lower Limit	Upper Limit	
TB								
Yes	9	34.6	25	96.2	0.02	0.00	0.18	0.001
No	17	65	1	3.8				
Age								
<50 years	5	19.2	11	42.3				
50-60 years	7	26.9	9	34.6				0.050
>60 years	14	53.8	6	23.1				
Gender								
Male	8	30.8	15	57.7	0.32	0.10	1.01	0.090
Female	18	69.2	11	42.3				
Education Status								
High (≥ Senior High School)	11	42.3	13	50.0	1.34	0.45	4.07	0.780
Low (≤Junior High School)	15	57.7	13	50.0				
Employment Status								
Work	8	30.8	14	53.8	0.38	0.12	1.18	0.160
Not Working	18	69.2	12	46.2				
Monthly Income								
High (≥2.066.438)	6	23.1	0	0	0.43	0.31	0.60	
Low (<2.066.438)	20	76.9	26	100				0.020
Marital Status								
Marry	22	84.6	20	76.9				
Divorce	3	11.5	1	3.8				0.150
Unmarried	1	5.8	5	19.2				

Variabel	Kasus		Kontrol		OR	95% CI		p
	n	%	n	%		Lower Limit	Upper Limit	
IMT Status								
Overweight	8	30.8	1	3.8				
Underweight	6	23.1	13	50.0				0.01
Normal	12	46.2	12	46.2				
Alcohol Consumption	2	7.7	1	3.8				1.000
Yes	24	92.3	25	96.2	2.08	0.17	24.50	
No								
Smoking Status								
Yes	2	7.7	4	15.4	0.45	0.07	2.75	0.660
Not	24	92.3	22	84.6				
Clinical symptoms	20	76.9	26	100		0.31	0.60	0.020
Yes	6	23.1	0	0	0.43			
Not								
Family TB History	1	3.8	2	7.7	0.48	0.04	5.64	1.000
Yes	25	96.2	24	92.3				
Not								
The family reminds to take medicine	22	84.6	24	92.3		0.36	13.11	0.660
Yes	4	15.4	2	7.7	2.18			
Not								
Family escort to health facility						0.18	5.48	
Yes	23	88.5	23	88.5	1.00			
Not	3	11.5	2	11.5				1.000
Home Ventilation	24	92.3	23	88.5		0.09	4.18	1.000
Adequate	2	7.7	3	11.5	0.63			
Inadequate								
Home Lighting								
Adequate	24	92.3	24	92.3	1.00	0.13	7.69	1.000
Inadequate	2	7.7	2	7.7				
Previous TB History	0	0	3	11.5	2.13	1.58	2.86	0.230
Yes	26	100	23	88.5				
Not								

* sig <0.250

3. Multivariate Analysis

Based on Table 4, it can be known that the final model in multivariate analysis shows that risk factors in patients with DM associated with the incidence of pulmonary TB are BMI status, age, sex and clinical symptoms. The risk factor that has the greatest influence on the incidence of TB is gender. DM patients with female sex have a 9.60 times higher risk of experiencing TB compared to men (aOR= 0.32; 95% CI= 0.10 to 1.01).

Table 4. Results of multivariate analysis of risk factors for TB incidence in patients DM

Variabel	B	Sig	Exp (B)	95% CI	
				Lower	Upper
IMT Status	1.50	0.098	4.51	0.75	26.92
Age	-1.41	0.015	0.24	0.07	0.76
Gender	2.26	0.012	9.60	1.64	55.96
Clinical Symtomps	21.90	0.999	3.24	0.01	10.76

DISCUSSION

This study shows that age and sex risk factors have a relationship with the incidence of TB in patients with type 2 DM based on a multivariate analysis where the value of p<0.050, and obtained sex as the risk factor that has the greatest influence on the incidence of TB in patients with type 2 DM. While risk factors for BMI status and clinical symptoms with the incidence of TB in patients with type 2 DM have a value of p >0.050 so there is no meaningful relationship.

The results are in line with research by Yosephine et al, (2021) which shows that age and gender risk factors are associated with the incidence of TB in people with DM. However, in the study conducted (Lusiani, 2019) different results were obtained where gender and age risk factors were not associated with the incidence of TB in patients with type 2 DM. TB is most commonly found at a young age or productive age, which is 15 to 50 years. Therefore, getting older will cause a person to be more susceptible to various kinds of health problems or diseases, one of which is TB caused by a decrease in the immunological system (ADA, 2018; Suprapto et al., 2022).

Gender is also a risk factor that can increase the occurrence of TB, where TB is more often found in the male sex because men can carry the influence of cigarettes and alcohol drinks which can cause a decrease in the body's defense system so that it is easy to infect or get disease compared to women (Suprapto et al., 2022). But in this study women with DM are more common, this can happen because the research samples found in the field are predominantly female. According to Ridwan, (2020) TB also has a tendency to often occur in women and lead to death. So this shows that men and women with DM have the same risk of getting TB. TB disease can attack humans of all ages with almost the same ratio between male and female sex (Somantri, 2007; Anwar et al., 2022).

BMI status with TB incidence in DM patients shows no significant relationship. Different results are aimed at studies (Lusiani, 2019) where on the contrary BMI status has a relationship with the incidence of TB in DM patients. This can be different because in this study many patients are already in the recovery period, so that weight and body condition have returned to normal. Nutritional deficiencies in a person will certainly affect the strength of the immune system and immunological response to diseases such as TB (Suryo, 2010).

This study showed that there was no association between clinical symptoms and the incidence of TB in patients with type 2 diabetes in the results of a multivariate analysis. Diabetes Mellitus (DM) is one of the risk factors for triggering TB, so that every DM patient will be advised to do TB screening by examining TB symptoms and thoracic photos (Lawrence and Moore, 2021). People with clinical symptoms will be considered as suspected TB first, then proceed with an examination that must be done to confirm

the diagnosis, namely by conducting direct microscopic sputum examination (Alisjahbana et al., 2020).

The weakness in this study is that the size of the sample obtained is still very small so that it is likely to affect the results of the analysis. Therefore, it can still be improved in future research and also the process in administration is still inefficient. While the advantage in research is that the results of the study can be a reference in managing type 2 DM patients with a good TB diagnosis to suppress complications of other comorbidities.

AUTHOR CONTRIBUTION

FN: Designing proposals, data analysis, research instruments, research methods; NJ: data analysis; DA: Collecting data; NK: collecting data; DMFAF: Technical field, research relations; SKD: Analyzing data and interpreting data; S and TM: designing proposals.

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CONFLICT OF INTEREST

Nill.

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