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Tuberculosis Incidence Among Patients with Diabetes Mellitusin Indonesia

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Abstract— WHO has identified Diabetes Mellitus (DM) as a neglected, significant, and re-emerging risk of tuberculosis (TB).This study aims to analyze factors influencing the incidence of TB among Diabetes Mellitus (DM) patients in Indonesia.A quantitativecross-sectional design was used in this research with secondary data from Indonesian Basic Health Research (Riskesdas) 2018. The data analysis conducted by using univariate, bivariate and multivariate analysis. The distribution of each variable were described by univariate analysis. Bivariate and multivariate analysis showed the risk factor and the most dominant factor that significantly associated with TB incident among DM Patient in Indonesia.This study found that 0,67% (n = 247) of respondents (n= 37,460) who diagnosed with TB and respondents who diagnosed with DM are 2,8% (n=1,061). The bivariate analysis found that smoking history (p-value = 0,035), diagnosis of cancer (p-value 0,017), and poor ventilation (p-value = 0,017) are the risk factor that significantly associated with TB incident among DM Patient in Indonesia. Diagnosis of cancer is the most dominant factor that influencing incident of TB among DM Patients in Indonesia (sig 0.011 <0.05).The need for further research on cancer following TB diagnosis to maximize the effective screening and early detection strategies.

Keywords: Cancer, Diabetes Mellitus, Risk Factor, Smoking, Tuberculosis

1. Introduction

The coexistence of tuberculosis (TB) and diabetes mellitus (DM) is a significant public health concern, particularly in countries like Indonesia, where both diseases are prevalent. According to World Health Organization (WHO), Indonesia is one of the major contributors to the global increase between 2020 and 2021 alongside with India and the Philippines [1]. Out of a total of 969,000 estimated TB cases in Indonesia, only 443,235 (45.7%) cases were found, while 525,765 (54.3%) other cases had not been found and reported[1]. On the other hand, based on the International Diabetes Federation (IDF) estimates for 2021, there are approximately 11.3 million adults aged 20-79 years living with diabetes in Indonesia. This accounts for a diabetes prevalence rate of around 7.6% of the adult population [2].

DM patients have a higher susceptibility to TB infection compared to non-diabetes patients[3]. Diabetes weakens the immune system, making it harder for the body to fight off TB bacteria. Poorly controlled blood sugar levels further compromise the immune response, increasing the risk of TB infection [4]. Based on the previous study, patients with diabetes have a higher incidence of TB compared to the general population. The risk is estimated to be two to three times higher among individuals with diabetes[5]. Furthermore, studies have shown that poorly controlled diabetes can lead to multiple complications, including vascular disease and neuropathy, which further increase the risk of developing tuberculosis [6]. Diabetes also weakens the immune system, making individuals more susceptible to infections of TB leads by hyperglycemia and cellular insulinogenic, which have indirect effects on

macrophage and lymphocyte function. It is important to note that while diabetes mellitus is a risk factor for tuberculosis, the reverse is also true. Tuberculosis has been identified as a risk factor for the progression of diabetes mellitus. This bidirectional relationship between the two diseases underscores the need for comprehensive management and treatment approaches for patients who suffer from both conditions[4].

Inclusion of patients with diabetes mellitus in the target group for tuberculosis preventive treatment is crucial. The Indonesia government develop the TPT (TB Preventive Treatment) which primarily focuses on children and persons living with HIV. However, according to the previous study a greater number of TB cases can be attributed to individuals developing DM before contracting HIV rather than vice versa [7]. The expansion of scope for TPT program is needed to encompass individuals with DM would align it more accurately with epidemiological data and help address this significant risk factor for tuberculosis transmission.

Thus, this study was to investigate the factors influencing tuberculosis among patients with diabetes mellitus through an analysis of comprehensive longitudinal data obtained from Indonesia Basic Health Research. This research effort aimed to contribute towards enhancing healthcare policies by providing valuable insights into the prevention and management of tuberculosis within the diabetic population.

2. Method

2.1 Study area and setting

This research was conducted in Indonesia according to the location for data collection for the 2018 Basic Health Research (Riskesdas). Riskesdas was conducted in 34 provinces, 416 districts and 98 cities in Indonesia.

2.2 Study design and population

A quantitative study with a cross-sectional design was used in this study. Population in this study is according to the population in the Indonesia Riskesdas 2018 which all households in Indonesia the target sample visited was 300,000 households from 30,000 Census Blocks (BS) conducted by the Central Bureau of Statistics (BPS) with the PPS (probability proportional to size) method using linear systematic sampling, with Two Stage Sampling.

2.3 Sampling method and sample size

In this study, we used the secondary data from The Basic Health Research (Riskesdas) in 2018. The targeted sample aare DM patients who successfully became the respondents of The Basic Health Research (Riskesdas) in 2018 and answered the blood sugar/ HbA1c section of the questionnaire.

2.4 Operational definitions of variables

The **TB**variable : Patient who diagnosed with TB for the last 1 year by doctor/nurse/midwife categorized as "Suffering from TB" and "Not suffering from TB".
The **DM**variable : Patient who diagnosed with DM by doctor categorized as "Suffering from DM" and "No suffering from DM".
Age : The age of the respondents are calculated from the date of birth in years categorized as “12-17 years”, “17-25 years”, “25-35 years”, “35-45 years”, “45-55 years”, “55-65 years”, and “> 65 years”.
Educationlevel : Last completed education by respondents based on the last or highest educational data of the respondent in the category "Never attended school", "Not graduated from Elementary School or equivalent", "Graduated from Elementary School or equivalent ", "Graduated from Junior High School

or equivalent", "Graduated from Senior High School or equivalent", "Graduated from D1/D2/D3", and "Graduated from College".

Occupational : Based on data on the employment status of respondents in the categories "Not working", "School", "Civil/Army/Police/BUMD Servants", "Private Employees", "Self-Employed", "Farmers", "Fishermen", "Workers /Driver/Household Helper", and "Others".

The **HbA1c** variable is taken from the results of HbA1C measurements in mg/dl which are processed into fasting blood sugar and intermittent blood sugar data with the categories "Controlled" and "Uncontrolled".

SmokingHistory : Smoking behavior includes the respondent's smoking habit every day or occasionally in the last month, while never smoking, namely the respondent never tried smoking until the time of data collection.

The **alcohol**Intake : Alcohol consumption by respondents in the last 1 month

Diagnose of **cancer** : Patients diagnosed with cancer by a doctor

Diagnose of **kidney failure** : Patients diagnosed as suffering from chronic kidney failure (at least kidney disease for 3 consecutive months by doctor

Diagnose of **rheumatoid arthritis** : Patient diagnosed with joint disease/rheumatism by a doctor

The bad **ventilation** : variable was taken from several data, namely ventilation data for bedrooms, cooking rooms, and family rooms in the category "Yes, area ≥ 10% floor area", "Yes, area < 10% floor area", and "None". The variable of convenience for health facilities was taken from several questions, namely "Does [HOUSEHOLD] know where the nearest hospital is?", "Does [HOUSEHOLD] know where the nearest puskesmas is?" and "Does [HOUSEHOLD] know where the closest clinic/doctor's practice is?" with the results of the answers in the category "In the district/city", "In the nearest district/city", "none", and "don't know".

2.5 Data collection and quality control

In this study, we used the secondary data from The Basic Health Research (Riskesdas) in 2018. Riskedas is a Indonesia's community-based health survey which conducted every 5 years by the Health Research and Development Authority (Badan Penelitian dan Pengembangan Kesehatan) to assess public health progress, risk factors and the state of health development at the provincial and district level/city level. Researchers received data from the Indonesian Health Research and Development Agency and accessed thedataby submitting an applicationon https://www.litbang.kemkes.go.id/layanan-permintaan-data-riset/ website. This study is a quantitative study with a cross-sectional design.

Statistical analysis

This study was analayzed by conducting univariate, bivariate and multivariate analysis. Univariate analysis aims to describe each variable, both the dependent variable and the independent variable (host factors and environmental factors). Bivariate and multivariate analysis conducted by only using data with people with diabetes diagnosis. Bivariate analysis was carried out to see the relationship between the independent variables (host factors and environmental factors) and the incidence of TB. Furthermore, logistic regression test was used in multivariate analysis to find out the relationship between the independent variables (host factors and environmental factors) and the dominants variables of risk factor of Tuberculosis among Diabetes Mellitus patients.

3. Results and Discussion

Thereare0,67% (n = 247) of respondents (n= 37,460) who diagnosed with TB and respondents who

diagnosed with DM are 2,8% (n=1,061).The majority patients DM who experience TB are female (63.4%),aged from 55-65 years old (19,4%), graduated from elementary school (55%), for the occupational the majority are from patients who are not working (48,6%), patients with no smoking history (12,3%).

Tabel 1. Univariate Analysis

Univariate Analysis All Data	
Variable	**Frequency (%) (n = 37,460)**
Tuberculosis (TB)	
Yes, in the last ≤ 6 months	0.3
Yes, >6 months	0.4
No	97.6
Diabetes mellitus (DM)	
Yes	2.8
No	95.4
Univariate Analysis of DM Patients	
Variable	**Frequency (%) (n = 1,061)**
Tuberculosis (TB)	
Yes, in the last ≤ 6 months	0.5
Yes, >6 months	1.1
No	98.4
Gender	
Male	36.6
Female	63.4
Age	
12 – 17 years old	0.1
25 – 35 years old	1.5
35 – 45 years old	9.8
45 – 55 years old	32.6
55 – 65 years old	36.6
>65 years old	19.4
Education	
Never attended school	9.8
Not graduated from Elementary School/MI	17.8
Graduated from Elementary School/MI	27.3
Graduated from Junior High School/MTS	13.9
Graduated from Senior High School/MA	20.7
Graduated from D1/D2/D3	3.9
Graduated from College	6.5
Occupational	
Not working	48.6
School	0.7
Civil /Army /Police /BUMD Servants	3.3
Private employees	5.8
Self-employed	18

Farmers	11.2
Fisherman	0.4
Workers /Driver /Household helper	4.9
Others	7.1
Smoking History	
Yes, everyday	12.1
Yes, not everyday	2.8
Never smoked	12.3
Alcohol	
Yes	0.9
No	99.1
Cancer	
Yes	0.8
No	99.2
Kidney Failure	
Yes	1.2
No	98.8
Rheumatoid Arthritis	
Yes	20.9
No	79.1
Bedroom Ventilation	
Yes, area ≥ 10% floor area	51.8
Yes, area < 10% floor area	34.1
None	12.8
Cooking Room Ventilation	
Yes, area ≥ 10% floor area	45.7
Yes, area < 10% floor area	31.9
None	20.5
Family Room Ventilation	
Yes, area ≥ 10% floor area	59.5
Yes, area < 10% floor area	28.4
None	7.9
Health Facilities	
a. Hospitals	
In the district/city	84.7
In the nearest district/city	9.9
None	1.2
Don't know	41
b. Puskesmas	
In the district/city	93.2
In the nearest district/city	5.6
None	0.2
Don't know	1
c. Clinic or Doctor Practice	
In the district/city	84.5
In the nearest district/city	4.2

None	2.1
Don't know	9.1
Fasting blood sugar	
Controlled	66.7
Uncontrolled	33.3
Intermittent blood sugar	
Controlled	99.3
Uncontrolled	0.7

Table 2. Bivariate Analysis

Variabels	
Socio-Demographics	**Pvalue**
Gender	0.120
Age	0.479
Family History of TB	0.921
Host Factor	
Smoking History	**0.035**
Smoking History for the last 1 month	0,450
Alcohol Intake History	0.921
Diagnosis of Cancer	**0.017**
Diagnosis of Chronic Kidney Failure	0.898
Diagnosis of Rheumatoid arthritis	0.102
Intermittent blood sugar	0.861
Fasting Blood Sugar	0.700
Environmental Factor	
Poor Ventilation	0,017
Access of Hospital	0,960
Access of Primary Healthcare	0,883

Table 3. Multivariate Analysis

	B	**SE**	**Wald**	**Df**	**Sig**	**Exp. (B)**	**95% CI**	
							Low	**Up**
Cancer	3,742	1,473	6,450	1	0,011	42,167	2,349	756,914
Constant	-3,742	2,858	1,713	1	0,191	0,024		

According to Table 2, the chi-square test showed that smoking history, diagnosis of cancer, and poor ventilation are the risk factor that significantly associated with TB incident among DM Patient in

Indonesia. Furthermore, the logistic regression test in Table 3 was used to explore the dominant factor that effecting incident of TB among DM Patients in Indonesia. Table 3 shows that diagnosis of cancer were the most dominant factor to influence the incident of TB. This shows that DM patient who has cancer were 42 times more likely to experience pulmonary TB than DM patient without cancer diagnosis(sig 0.011 <0.05).

The study aims to analyze the risk factors (gender, age family history, smoking habits, alcohol intake, diagnosis of cancer, diagnosis of chronic kidney failure, diagnosis of Rheumatoid arthritis, Intermittent blood sugar, Fasting Blood Sugar, poor ventilation, access of hospital and primary healthcare) that affect the incident of TB among DM patients in Indonesia. Based on the findings, smoking history (p-value = 0,035), diagnosis of cancer (p-value 0,017), and poor ventilation (p-value = 0,017) have significantly associated with incident of TB among DM patients in Indonesia.

This study found that smoking history had significant association with incident of TB among of DM Patient (p-value = 0,035). In the previous study, smoking showed significant association with TB(P < 0.0001) [8]. Numerous research studies point out that both active and passive exposure to tobacco smoke increases the likelihood of acquiring latent tuberculosis infection as well as exacerbating the progression from LTBI to active TB. Furthermore, smoking has been linked with the development of cavitary lesions, higher bacillary load, slower conversion of sputum smears, and a greater risk of reactivating TB or experiencing death during or after treatment. Importantly, smokers face a similar level of risk for TB reactivation compared to patients with end-stage renal disease or individuals receiving anti-Tumor Necrosis Factor-alpha (α) therapy[9]–[12].

Other studyreveal disparities in how tuberculosis manifests clinically between individuals who smoke and non-smoker. It is evident that TB patients who smoked had a greater prevalence of pulmonary forms (50%), cavitary lesions (90%), and positive sputum smear results (40%), irrespective of factors like age, gender, and alcohol consumption[11]. Smoking habits can further compound the risk of tuberculosis (TB) among patients with diabetes mellitus (DM). When patients with diabetes smoke, it exacerbates the negative effects on their respiratory health and immune system, increasing the susceptibility to TB infection and worsening the outcomes.

This study found that cancer had significant association with incident of TB among of DM Patient (p-value = 0,017).The connection between tuberculosis and cancer is intricate and potentially hazardous[13]. In patients with cancer, the immune system might be compromised due to prolonged chemotherapy, radiotherapy, or surgery, thereby heightening the vulnerability to tuberculosis infection[14], [15]. Conversely, a cohort study revealed that pulmonary tuberculosis is linked to an elevated likelihood of developing lung cancers[16]. This poses a challenge in clinical settings as misdiagnosis can occur when patients have a previous history of either cancer or tuberculosis but lack specific information for accurate identification[17], [18].

The previous research indicates that certain cancer types specifically lung cancer (without histopathological confirmation), lymphoma, hematopoietic cancers, digestive organ cancers, urinary tract cancers and lung cancer (with histopathological confirmation) have significantly higher adjusted incidence rate ratios compared to the general population[19]. Cancer patients are increased risk of developing TB especially systemic diseases can be a risk when the host resistant reactions fail to uncontrolled bacterial replication and active disease occurs[20].

This research found that poor ventilation had significant association with incident of TB among of DM

Patient (p-value = 0,017). TB is a communicable illness that is transmitted through the air via infectious aerosol particles produced when infected individuals cough [21].Within indoor settings, these contagious aerosols tend to accumulate over time, posing a risk to all occupants unless there is a continuous influx of fresh outdoor air through ventilation systems[22]. Inadequate ventilation has been linked to an increased likelihood of tuberculin skin test conversion, indicating potential exposure and infection[23].

In theory, enhancing the rate of ventilation has a significant impact on reducing the risk of tuberculosis transmission yet it is important to note that achieving complete elimination of transmission may not be feasible[24]. Nonetheless, in order to effectively tackle the TB epidemic, it is only necessary to decrease the effective reproductive ratio (the ratio between new secondary infectious cases and source cases) below one rather than reaching zero[25]. Modelling studies conducted using data from high schools in South Africa have indicated that this threshold can be achieved by maintaining an airflow rate of 8.6 L/s per person or an indoor carbon dioxide concentration level of around 1000 parts per million (ppm). Despite these theoretical findings, there remains a lack of empirical evidence validating this threshold under real-world conditions[26].

4. Conclusion

The study showed that risk factors of incidence of TB among DM patients are smoking history, diagnosis of cancer, and poor ventilation. The result also demonstrated that diagnosis of cancer is the most dominant factor that influence TB among DM patients. The need of further research on cancer following TB diagnosis to maximize the effective screening and early detection strategies. Healthcare facilities should have a high index of suspicion for cancer in people with TB, particularly in the first year following TB diagnosis.

Abbreviations

Consist of abbreviations mentioned in the article (from Abstract to Conclusion).

Competing Interest

The authors declare that there are no competing financial, professional, or personal interests that might have affected the research in this manuscript.

Ethical approval

Ethical approval was obtained from The Research and Community Engagement Ethical Committee (Komisi Etik Riset dan Pengabdian Kesehatan Masyarakat) of Faculty of Public Health Universitas Indonesia (Reference 46/UN2.F10.D11/PPM.00.02/2023 dated 03.03.2023).

Availability of Data and Materials

As a source of data and information from ProQuest, Scopus, and Science Direct databases.

Authors' Contribution

MRB and AB contributed substantially to the concept and work design. CC conducted data analysis and data interpretation. SNH drafting of the manuscript. MRB and AB revised critically for the content and final approval of the version to be published.

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