

# Risk factors of pulmonary tuberculosis among diabetes mellitus patients in Denpasar City

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## Abstract

**Background and Purpose:** Tuberculosis (TB) is more common in developing countries, including Indonesia. Denpasar City contributes the most on the total number of TB patients in Bali Province. There is evidence on increased burden of diabetes mellitus (DM) patients with TB comorbidity. This study aims to examine risk factors of TB among DM patients.

**Method:** A case control study was conducted in Denpasar City. A total of 135 samples, 45 cases and 90 controls, were recruited to participate in the study. Cases were DM patients with TB comorbidity and were taken from patients register between 2013 to 2015. Controls were DM patients without TB comorbidity and were taken from Bali Province screening operational study. Data were collected using interviews, observations, measurements and document review. Data were analysed using bivariate analysis and multivariate with logistic regression model.

**Results:** Demographic characteristics between cases and controls were comparable in sex and family income but not comparable in age groups, education, domicile, and employment. Risk factors of TB among DM patients were house density (AOR=36.11; 95%CI: 5.0-259.9), undernutrition (AOR=24.76; 95%CI: 3.7-162.3), inadequate glycemic control (AOR=12.64; 95%CI: 2.4-66.2), and being employed (AOR=10.55; 95%CI: 1.2-92.7). TB infection among DM patients was associated with aged<60 years (AOR=7.47; 95%CI: 1.2-44.3) and being male (AOR=5.42 ;95%CI: 1.2-24.0). TB co-infection among DM patients was also associated with low education level (AOR=6.96; 95%CI: 1.0-48.6), contact with TB patients (AOR=5.84; 95%CI: 0.7-46.6) and inadequate house ventilation (AOR=2.92; 95%CI: 0.6-13.1).

**Conclusion:** Socio-demographic characteristics, physical environments of the house and clinical conditions are risk factors of TB among DM patients.

**Keywords:** diabetes mellitus, pulmonary tuberculosis, case-control, Denpasar City

## Introduction

There are 285 million people currently living with DM globally. International Diabetes Foundation reported that a total of 9.1 million people in Indonesia are living with DM. It is predicted that by 2013 the figure will reach 21.3 million people.<sup>3</sup> World Health Organisation (WHO) suggests that the rising of DM problem in TB endemic areas including Indonesia<sup>2</sup> will put the TB control program in more difficult situation.<sup>1</sup>

Denpasar City is the highest contributor for DM and TB patients in Bali Province. Data from Denpasar City Health Office showed that between January and August 2015, a total of 2496 DM patients were reported from community health centres and 1896 were reported from hospitals.<sup>4</sup> Meanwhile, Denpasar Health Office reported TB prevalence in 2014 was 121.47 per 100,000 population with the mortality rate of 2.5 per 100,000 population.<sup>4</sup> This study aims to examine risk factors of TB among DM patients in Denpasar City.

## Methods

A case control study was conducted in Denpasar City between November 2015 and May 2016. A total of 135 samples were selected to participate in the study, involving 45 cases and 90 controls. Cases were DM patients with TB co-morbidity taken from patients register book covering 11 community health centres in Denpasar City between 2013 and 2015. Controls were DM patients who underwent TB screening with negative result in 11 community health centres in Denpasar City based on screening operational study of Bali Province Health Office.<sup>5</sup> Both cases and controls were approached by first author during home visit and who wished to participate in the study were recruited until the sample requirement was achieved.

Independent variables were socio-demographic characteristics included age, sex, address, education, employment, and family income; clinical conditions; physical conditions of the house; and social environments. Clinical data were obtained from medical record which consisted of glycemic control, DM medication, duration of having DM and nutritional status. Glycemic control was defined as the fasting blood sugar measured three times in years before the TB diagnosis for cases and three times during the first year of DM diagnosis for controls. A good glycemic control was defined at 72-126 mg/dl and above 126 mg/dl was considered as a poor glycemic control.<sup>6</sup> The duration of having DM was the period between diagnosis of DM and the time when TB diagnosis was confirmed for cases, while among controls was defined as the period of having DM from the diagnosis and the time of interview. DM medication was type of medicine used before they were diagnosed with TB for cases and among controls was defined as type of medicine used when the interview was conducted. Nutritional status was measured by the body mass index (BMI) formula and

classified into underweight (BMI between 17.0-18.4 kg/m<sup>2</sup>) and normoweight (BMI between 18.5-25.0 kg/m<sup>2</sup>).<sup>7</sup>

Data on physical environments of the house included house density, ventilation, and lighting were obtained through interview and observation. House density was measured based on total bedrooms in the house, total people living in the house and total people living in a bedroom. High density was defined if more than two people staying in one bedroom.<sup>8</sup> House ventilation was measured based on total window in the house, if the window is frequently opened up, or availability of ventilation holes at the house. Composite score of 0-3 was categorized as inadequate ventilation while score of 4-6 was defined as having adequate ventilation. House lighting was measured based on several criteria included the brightness during the day, availability of glass based roof at the house, and the position of windows at the house. Composite score of 0-3 was defined as having inadequate house lighting.

Social environments included contact history with TB patients and smoking exposure were obtained through interview. Contact history with TB patients was defined as interaction between respondent and TB patient inside or outside the house. Smoking exposure was defined as self-exposure through active smoking or being passively exposed by other smokers.

Data were analysed using bivariate and multivariate techniques in STATA SE 12. All variables with p-value <0.25 in bivariate analysis were included in the multivariate analysis to calculate the adjusted odd ratio (AOR). This study protocol has been approved by the Human Research Ethics Committee of Faculty of Medicine Udayana University and Sanglah General Hospital Denpasar.

## Results

Socio-demographic characteristics of respondents are shown in Table 1. Cases and controls are not comparable in terms of age, domicile, education and employment status.

Findings from bivariate analysis are shown in Table 2. Several variables were found to have significant association with TB comorbidity among DM patients that include poor glycemic control, had been diagnosed with DM for less than 5 years, malnutrition, inadequate house ventilation, high house density, smoke exposure and contact history with TB patient.

Multivariate analysis with a backward logistic regression technique is presented in Table 3. A total of nine variables were included in the model, six variables were found to increase the risk of TB comorbidity among DM patients that were high house density (AOR=36.11; 95%CI: 5.0-259.9), malnutrition (AOR=24.76; 95%CI: 3.7-162.3), poor glycemic control (AOR=12.64; 95%CI: 2.4-66.2), being employed (AOR=10.55; 95%CI: 1.2-92.7), aged<60 years (AOR=7.47; 95%CI: 1.2-44.3) and being male (AOR=5.42; 95%CI: 1.2-24.0).

## Discussion

This study showed that several clinical conditions (glycemic control, nutritional status), physical environments of the house (density, ventilation), social environments (contact history with TB patient) and socio-demographic characteristics (age, sex) were risk factors of TB comorbidity among DM patients.

Poor glycemic control is a risk factor of TB comorbidity among DM patients. A study in Persahabatan Hospital, Jakarta found that a high level of HbA1c (>8%) was found in 68 subjects (39.1%) with TB comorbidity among DM patients.<sup>9</sup> Similar finding was found in Hongkong where DM patients with poor glycemic control (HbA1c >7%) were more likely to have TB than those with good glycemic control.<sup>10</sup> In addition, high level of HbA1c induces deterioration of TB patients leading to increased mortality.<sup>11,12</sup>

This study suggests that screening TB among DM patients should be performed regularly especially among those who have poor glycemic control.

**Table 1. Socio-demographic characteristics comparison between cases and control**

Variables		Cases		Control		p value
		n	%	n	%	
Age	<60 years	35	77.78	22	24.44	<0.001
	≥60 years	10	22.22	68	75.56	
Sex	Male	30	66.67	45	50.00	0.066
	Female	15	33.33	45	50.00	
Domicile	North Denpasar	10	22.22	36	40.00	0.001
	West Denpasar	25	55.56	20	22.22	
	South Denpasar	8	17.78	17	18.89	
	East Denpasar	2	4.44	17	18.89	
Education	High (≥senior high school)	14	31.11	57	63.33	<0.001
	Low (≤junior high school)	31	68.89	33	36.67	
Employment	Active	42	93.33	36	40.00	<0.001
	Retired	3	6.67	54	60.00	
Family income	High (≥Rp. 2,007,000)*	39	86.67	84	93.33	0.199
	Low (<Rp. 2,007,000)	6	13.33	6	6.67	

\*) Based on minimum salary requirement of Denpasar City

**Table 2. Bivariate analysis of risk factors of TB comorbidity among DM patients**

Variables		Cases		Controls		OR	p value
		n	%	n	%		
Glycemic control	Poor	42	93.33	31	34.44	26.64	<0.001
	Good	3	6.67	59	65.56		
Duration of having DM	<5years	33	73.33	36	40.00	4.12	<0.001
	≥5years	12	26.67	54	60.00		
Types of medication	OHD*& insulin	8	17.78	19	21.11	0.80	0.648
	Insulin	37	82.22	71	78.89		
Nutritional status	Undernutrition	10	22.22	2	2.22	12.57	0.002
	Normal	35	77.78	88	97.78		
House ventilation	Inadequate	25	55.56	15	16.67	6.25	<0.001
	Adequate	20	44.44	75	83.33		
House lighting	Inadequate	27	60.00	32	35.56	2.71	0.008
	Adequate	18	40.00	58	64.44		
House density	High	14	31.11	2	2.22	19.87	<0.001
	Low	31	68.89	88	97.78		
Smoke exposure	Yes	35	77.78	50	55.56	2.80	0.013
	No	10	22.22	40	44.44		
Contact history	Yes	14	31.11	10	11.11	3.61	0.006
	No	31	68.89	80	88.89		

\*) Oral hypoglycemic drugs

**Table 3. Multivariate analysis of risk factors of TB comorbidity among DM patients**

Variables	Adjusted OR	95%CI	p value
Poor glycemic control	12.64	2.4-66.2	0.003
Undernutrition	24.76	3.7-162.3	0.001
High house density	36.11	5.0-259.9	<0.001
Inadequate house ventilation	2.92	0.6-13.1	0.161
Positive contact history	5.84	0.7-46.6	0.096
Age <60 years	7.47	1.2-44.3	0.027
Male	5.42	1.2-24.0	0.026
Low education level	6.96	1.0-48.6	0.050
Employed	10.55	1.2-92.7	0.033

This study also revealed that malnutrition is a risk factor of TB comorbidity among DM patients. Other studies in Asia, especially in Korea and China also found similar findings. DM patients with BMI of <18.5 kg/m<sup>2</sup> were more likely to acquire TB infection than those with BMI of 18.5-25.0 kg/m<sup>2</sup>.<sup>13,14</sup> This present study suggests that TB screening among malnourished DM patients is essential to improve case detection rate for TB. Furthermore, this routine screening will also reduce the overall TB prevalence and mortality rate associated with pulmonary TB.

This study also found significant association between physical conditions of the house and TB and DM comorbidity. High house density is a risk factor for DM and TB comorbidity. Houses with high density are generally a risk factor for disease transmission, mental health and general health status.<sup>15</sup> A study conducted by Ministry of Health of Indonesia in 2000 found that: (1) under-five children who sleep in the same bedroom with TB patients were 2.8 times more likely to acquire TB infection; (2) the risk for TB transmission increased four times when more than one TB patients stay in the same house;

(3) the transmission rate within family members was high and one TB patient can transmit the disease to 2-3 family members.<sup>15</sup> A study conducted in 2013 in Padang City, Sumatra Island also showed similar finding. A high house density increased the risk for TB transmission by 1.6 times.<sup>16</sup> Promotion to avoid house contact with TB patient should be conducted to prevent DM and TB comorbidity. Similarly, DM patients who had been diagnosed with TB should be encouraged to avoid house contact to prevent TB transmission to the rest of family members.

Socio-demographic conditions which included age, sex, education and employment status are also risk factors of DM and TB comorbidity. Age <60 years and being employed increase risk of DM and TB comorbidity. People are more likely to work when they are still within the productive age category.<sup>17</sup> High density working environment increases probability to meet more people, leading to an increased risk for TB infection among productive age people.<sup>18</sup> This finding is consistent with the 2007 Basic Health Survey which found that 75% of TB patients in Indonesia were among people who are economically productive (aged of 15-49 years).<sup>19</sup> Furthermore, reports from TB Program, Ministry of Health of Indonesia between 2000 and 2010 revealed that the majority of BTA positive TB patients were found among productive aged people (15-50 years).<sup>20</sup> Our study found that males DM patients were more likely to experience TB than females.

This study has several limitations. In our study, the glycemic control was measured using fasting blood sugar level which may not accurately predict the poor glycemic control. Therefore, comparison with other studies must be interpreted with caution. Several variables such as house density, lighting and ventilation were obtained from interview and observation which is a subjective measurement. Sample was

taken only from the community health centres, meanwhile there are significant number of DM patients utilize other health services facilities. Therefore, the generalization of the findings must be taken cautiously.

## Conclusion

Risk factors of TB comorbidity among DM patients are poor glycemic control, malnourished, high house density, age <60 years, being male and employed.

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