

UNIVERSITI PUTRA MALAYSIA

RISK FACTORS OF TUBERCULOSIS AMONG DIABETES MELLITUS PATIENTS IN HOSPITAL SULTANAH BAHIYAH, ALOR SETAR 2015-2016

FARAH FATIN BINTI FAUZI

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By

FARAH FATIN BINTI FAUZI

Dissertation Submitted to the Department of Community Health, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia in Fulfilment of the Requirements for the Degree of Master of Public Health

August 2017

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By

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August 2017

Chairperson : Associate Prof. Dr. Hejar Binti Abdul Rahman Faculty : Medicine and Health Sciences

Introduction: Tuberculosis (TB) and diabetes mellitus (DM) is a double-burden disease where person with diabetes have triple risk of developing tuberculosis later in their life in view of their weak immune system. In view of both TB and DM is one of the major global health problem, combating both diseases will indirectly reduce its burden.

Objective: The aim of this study is to determine risk factors of tuberculosis (TB) among diabetes mellitus (DM) patients in Chest Clinic of Hospital Sultanah Bahiyah, Alor Setar.

Methodology: This study was conducted in Chest Clinic, Respiratory Unit of Medical Department, Hospital Sultanah Bahiyah, Alor Setar Kedah. It is an unmatched hospital based case-control study design where the study population consist of records of patients from the chest clinic HSB and diabetic clinic registry of primary care settings for both case and control. Simple random sampling method were used for this study. The case and control were randomly selected from the list of *e-Respiratory* registry of Hospital Sultanah Bahiyah.

Result: The final model has a good fit (p>0.05). Male patients who have diabetes mellitus (DM) were two times at risk of having tuberculosis as compared to female patients with DM (aOR=2.25, 95% CI=1.18, 4.30). Non-malays ethnicity who have diabetes mellitus (DM) were three times at risk of having tuberculosis as compared to Malay ethnic patients with DM (aOR=3.35, 95% CI=1.43, 7.86). Patients age of more than 50 years old at DM diagnosis two times more likely to have tuberculosis compared to patients age of less than 50 years old at DM diagnosis (aOR=2.21, 95% CI=1.18, 4.16). DM patients who smokes cigarette

were two times more likely to develop TB as compared to non-smokers DM patient (aOR=2.22, 95% CI=1.19, 4.14). DM patients who have history of contact with TB patients have 11 times odds of developing TB as compared with those who never have history of contact with TB patients (aOR=11.07, 95% CI=5.47, 22.40).

Conclusion: The important risk factors associated with tuberculosis among diabetics are gender, ethnicity, age at DM diagnosis, smoking status and history of contact with TB patient.

Keywords: tuberculosis, diabetes mellitus, tuberculosis-diabetes, risk factors



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FAKTOR RISIKO JANGKITAN TUBERKULOSIS DIKALANGAN PESAKIT DIABETES MELLITUS DI HOSPITAL SULTANAH BAHIYAH, ALOR SETAR 2015-2016

Oleh

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Pengerusi : Professor Madya Dr. Hejar Binti Abdul Rahman Fakulti : Perubatan dan Sains Kesihatan

Pendahuluan: Tuberkulosis (TB) dan diabetes mellitus (DM; kencing manis) merupakan dua penyakit yang memberi impak negatif antara satu sama lain. Pesakit yang mempunyai DM mengahadapi risiko tiga kali ganda untuk mendapat penyakit TB memandangkan sistem imunisasinya yang lemah. Oleh kerana kedua-dua penyakit ini merupakan penyakit yang sedang meningkat dikalangan rakyat Malaysia, dengan mengawal keduanya secara tidak langsung dapat menurunkan kadar beban penyakit tersebut.

Objektif: Menentukan faktor risiko jangkitan penyakit TB dikalangan pesakit DM di Klinik Dada, Unit Respiratori Hospital Sultanah Bahiyah Alor Setar bagi tahun 2015 hingga 2016.

Metodologi: Kajian ini adalah kajian *'unmatched case control'* yang dijalankan di Klinik Dada, Unit Respiratori, Hospital Sultanah Bahiyah dimana populasi kajian merupakan rekod pesakit dari senarai berdaftar di Klinik Dada Bagi keduadua *'case'* dan *'control'* dan juga rekod pesakit dari senarai berdaftar di Klinik Diabetes dari klinik kesihatan daerah Kota Setar. Persampelan secara rawak dilakukan bagi kajian ini. *'Case'* dan *'control'* dipilih secara rawak dari senarai *e-Respiratory* Hospital Sultanah Bahiyah.

Keputusan: Pesakit DM lelaki mempunyai risiko sebanyak dua kali ganda mendapat penyakit TB jika dibandingkan dengan pesakit DM wanita (aOR=2.25, 95% CI=1.18, 4.30). Pesakit DM dari etnik bukan Melayu mempunyai risiko sebanyak tiga kali ganda mendapat penyakit TB jika dibandingkan dengan pesakit DM etnik Melayu (aOR=3.35, 95% CI=1.43, 7.86). Pesakit DM yang

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berumur lebih 50 tahun ketika diagnosis DM dilakukan mempunyai risiko dua kali ganda mendapat penyakit TB jika dibandingkan dengan pesakit DM berumur kurang 50 tahun semasa diagnosis DM dilakukan (aOR=2.21, 95% CI=1.18, 4.16). Pesakit DM yang merokok mempunyai risiko sebanyak dua kali ganda mendapat penyakit TB jika dibandingkan dengan pesakit DM bukan perokok (aOR=2.22, 95% CI=1.19, 4.14). Pesakit DM yang mempunyai sejarah kontak dengan pesakit TB mempunyai risiko sebanyak 11 kali ganda dalam mendapat penyakit TB jika dibandingkan dengan pesakit DM yang tidak mempunyai sejarah kontak dengan pesakit TB (aOR=11.07, 95% CI=5.47, 22.40).

Kesimpulan: Faktor risiko penting yang berkait rapat dalam jangkitan TB dikalangan pesakit DM adalah jantina, etnik, umur ketika diagnose DM dilakukan, merokok dan sejarah kontak dengan pesakit TB yang lain.

Kata kunci: tuberkulosis, diabetes mellitus, kencing manis, tuberkulosisdiabetes, faktor risiko

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I certify that a Dissertation Examination Committee has met on 1st August 2017 to conduct the final examination of Farah Fatin Binti Fauzi on her dissertation entitled "Risk Factors Of Tuberculosis Among Diabetes Mellitus Patients In Hospital Sultanah Bahiyah, Alor Setar 2015-2016" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Public Health.

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Signature: Name of Member of Supervisory Committee: <u>Dr. Sri Ganesh A/L Muthiah</u>

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LIST OF ABBREVIATIONS

ТВ	Tuberculosis
DM	Diabetes Mellitus
TB-DM	Tuberculosis-Diabetes Mellitus Comorbidities
T2DM	Type 2 Diabetes Mellitus
T1DM	Type 1 Diabetes Mellitus
FPG	Fasting Plasma Glucose
RPG	Random Plasma Glucose
OGTT	Oral Glucose Tolerance Test
IGT	Impaired Glucose Tolerance
IFG	Impaired Fasting Glucose
BMI	Body Mass Index
МОН	Ministry of Health, Malaysia
WHO	World Health Organization
<	Lesser than
2	Greater than and equal to

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CHAPTER 1

INTRODUCTION

1.1 Background

Tuberculosis (TB) is one of the contagious airborne disease and a major health problem globally. More than 9 million people diagnosed with tuberculosis with 1.5 million death in 2014 (Lewandowski, 2015). In the poor and vulnerable population, as high as one in three people is diagnose with tuberculosis (Lönnroth et al., 2010). Even though TB incidence has reduced by an average of 1.5% per year since 2000, however, this need to be further improved to achieve a 4-5% annual decline in order to reach the 2020 milestones of the "End TB Strategy" (WHO, 2016). According to Health Indicators 2014 published by Ministry of Health, Malaysia, incidence rate of tuberculosis in Malaysia was 82.10 per 100,000 population (MOH, 2015). As for Kedah state, it contributes around 5% of all cases in Malaysia with incidence rate of 63.58 per 100,000 population (Malaysia, 2015). Recent data published in the end of 2015 by Ministry of Health, Malaysia on tuberculosis mortality rate in Malaysia is 5.33/100,000 population. Kedah has exceeded this national limit with mortality rate of tuberculosis was as high as 6.65 per 100,000 population. Kedah is a state in Malaysia where it's neighbouring country is Thailand, and commuting between these two countries had always been easy via land transportation. Kedah carries a higher risk of TB as Thailand is listed as top 20 tuberculosis burden country with estimated about 120,000 of its population diagnosed with tuberculosis (WHO, 2016). Even though Malaysia was not listed in the top 30 of tuberculosis burden country, there are activities to actively find and detect new cases, regular and close monitoring of all tuberculosis cases through various tuberculosis prevention and control programme that are being conducted all over the country, headed by Ministry of Health, Malaysia.

On the other hand as of 2014 have about 422 million people living with DM worldwide while the global prevalence nearly doubled from 4.7% in 1980 to 8.5% in 2014 among adults aged 18 and above (World Health Organization, 2016). By 2030, WHO projects that diabetes will become the 7th leading cause of death. From recent Malaysia National Health Morbidity Survey (NHMS) conducted in 2015, the prevalence of diabetes mellitus in Malaysia among adults of 18 years and above was 17.5%. From the same survey, Kedah was the state with the highest prevalence of diabetes with 25.4%. Previously in 1980, prevalence of diabetes was highest among high-income countries, but now it is almost similar in both high- and low-income countries with the latter is catching up fast (Shaw, Sicree & Zimmet, 2010). This includes Malaysia as a developing country having struggle to reduce both diabetes and tuberculosis. With this may cause Kedah to be more susceptible to have increase tuberculosis prevalence too in the future.

Tuberculosis-diabetes is a deadly linkage where person with diabetes have triple risk of developing tuberculosis later in their life in view of their weak immune

system as a result of chronic disease that later will cause latent TB to progress into active TB (Lönnroth et al., 2010). In view of both TB and DM as major global health problem, combating both disease will indirectly reduce its burden. Some studies did not show any relation between DM and the outcome of TB treatment (Dooley & Chaisson, 2009; Ponce-de-Leon et al., 2004; Singla et al., 2006; Wang, Lee, & Hsueh, 2005). However, DM may have a negative impact on the outcome of TB treatment: higher failure rates (Chang et al., 2011; Mboussa et al., 2003; Morsy, Zaher, Hassan, & Shouman, 2003; Ponce-de-Leon et al., 2004) higher rates of all-cause mortality (Fielder et al., 2002; Oursler et al., 2002), and death specifically related to TB (Wang et al., 2009). In one study, after adjusting for other factors, the chance of death was over six times higher in patients with diabetes (Dooley, Tang, Golub, Dorman, & Cronin, 2009). Another study showed an adjusted odds ratio of 7.65 (95% CI 1.89 – 30.95) for treatment failure among DM in comparison to non DM tuberculosis patients after removing the effect of covariants such as non-compliance and drug resistance (Alisjahbana et al., 2007).

In Malaysia, the prevalence of diabetes among tuberculosis patients at tertiary centres range between 14-33% (Gnanasan et al., 2011; Sulaiman et al., 2013). Patients with diabetes mellitus (DM) were more likely to have pulmonary tuberculosis (OR=2.079, p<0.001) (Sulaiman et al., 2013). The evidence for this was seen in large scale studies done in South East Asia by Nissapatorn et al. in 2005. A greater percentage of pulmonary tuberculosis patients (91%, 1509/1651) were in the TB-DM group (Nissapatorn et al., 2005). Four smaller scale studies had conflicting evidence on this matter. A study supporting this view discovered 82% (107/131) of patients diagnosed with pulmonary tuberculosis suffering from either diabetes mellitus, hypertension, ischaemic heart disease or all three conditions (Ibrahim, Jetan, Jamaiah, Rohela, & Nissapatorn, 2010). Three other studies revealed the prevalence of tuberculosis among diabetics between the range of 18 and 30% (Ismail, 2004; Jamalludin, 2003).

1.2 Problem Statement

Diabetes is a chronic, non-communicable disease that weakens the immune system, making people with diabetes three times more likely to get active TB (Lönnroth et al., 2010). Diabetes is escalating, and has affected 382 million in 2013 projected to increase to 592 million by 2035. As diabetes increase, it will cause more and more people to develop TB (Diabetes, 2014).

TB is an infectious disease that spreads from person to person through the air. TB kills more people than any other infectious disease except HIV/AIDS: 1.5 million people worldwide died from TB in 2013. These cases of "active" TB disease emerge out of a massive pool of latent TB infection. One in three people around the world—two billion people—hold a latent TB infection somewhere in their body, where it can remain dormant through one's whole life. Every person infected with TB faces about a 10 percent chance that the infection will activate and spread in the body, giving them the known symptoms of TB: gradual but severe weight loss, night sweats, and the famously bloody cough. At this stage, the infection can spread to people nearby (Lewandowski et al., 2015).

Diabetes is fuelling the spread of TB. This is largely because diabetes rates are trending upwards around the world, and having diabetes increases the risk that a person will get infected with TB. Diabetes is also more difficult to manage in people who have TB. A person who have both diseases is likely to have complications that do not typically exist when either is present on its own.

Successfully addressing TB-DM therefore requires a coordinated response to both diseases at all levels of the health system—from the developing and implementation of national policies, to the management of disease control programs, to the delivery of services to individual patients (Dooley & Chaisson, 2009). Therefore it is important to determine the risk factors of tuberculosis-diabetes comorbidity. Knowing the link between this two serious illnesses will give us a better clearer view on where to act, how to prevent and who's responsibility on combating them.

1.3 Significance of Study

This study may give different perspective of how a medical practitioner typically have on a TB-DM patients. Associated factors that will be studied can lead the healthcare workers to different approaches on combating both diseases together. Being able to contain both disease at once, will have greater impact to the community by reducing the spread of tuberculosis among them especially in overcrowding housing area and low socio-economic community.

The risk factors on tuberculosis infection among diabetes mellitus patients is yet to be discovered as limited study on this relationship done in Kedah. While for Malaysia as a developing country, more comprehensive programme of prevention and control focusing concurrently on both TB-DM need to be done as there are more associated factors being known later on from this study. By knowing the risk factors it will also be helpful for future planning on having intervention programmes to both diabetes and tuberculosis together.

1.4 Research Questions

What are the risk factors associated with having tuberculosis among diabetes mellitus patients?

1.5 Objectives

The objectives of this study can be subdivided into general objective and specific objectives.

1.5.1 General Objective

To determine risk factors associated with risk of tuberculosis (TB) among diabetes mellitus (DM) patients in Chest Clinic of Hospital Sultanah Bahiyah, Alor Setar.

1.5.2 Specific Objectives

1.5.2.1 To describe the socio-demographic factors, diabetic characteristics, diabetic complications, other comorbidities and related factors among diabetes mellitus patients with tuberculosis and diabetes mellitus only patients in chest clinic, Hospital Sultanah Bahiyah, Alor Setar

1.5.2.2 To determine the association between sociodemographic factors (age, gender, ethnic and living house category) and TB among diabetes mellitus patients in chest clinic, Hospital Sultanah Bahiyah, Alor Setar.

1.5.2.3 To determine the association between diabetic characteristics (HbA1c level at TB diagnosis, duration of DM, type of DM treatment, HbA1c level at DM diagnosis and age at DM diagnosis) and TB among diabetes mellitus patients in chest clinic, Hospital Sultanah Bahiyah, Alor Setar.

1.5.2.4 To determine the association between diabetic complications (retinopathy, nephropathy, peripheral vascular disease, neuropathy and coronary heart disease) and TB among diabetes mellitus patients in chest clinic, Hospital Sultanah Bahiyah, Alor Setar.

1.5.2.5 To determine the association between having other comorbidities (Hypertension, Cancer and Dyslipidemia) and TB among diabetes mellitus patients in chest clinic, Hospital Sultanah Bahiyah, Alor Setar.

1.5.2.6 To determine the association between having other related factors (BMI level, smoking, history of contact with TB patient) and TB among diabetes mellitus patients in chest clinic, Hospital Sultanah Bahiyah, Alor Setar.

1.5.2.7 To determine the risk factors of developing tuberculosis among diabetes mellitus patients in chest clinic, Hospital Sultanah Bahiyah, Alor Setar.

1.6 Research Hypothesis

Null hypothesis

There is no association between socio-demographic factors, diabetic characteristics, diabetic complications, other comorbidities and other related factors and risk of developing tuberculosis among diabetes mellitus patients.



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