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Tuberculosis and Associated Factors among Type 2 Diabetic Patients In Perak: A Case Control Study

(Tuberkulosis dan Faktor Berkaitan dalam Kalangan Pesakit Diabetis Jenis 2 di Perak: Suatu Kajian Kes Kawalan)

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ABSTRACT

This is a case-control study conducted with diabetic patients in Kinta, Kampar and Larut-Matang-Selama districts of Perak, Malaysia. We intended to determine the factors contributing to the development of active tuberculosis among diabetes patients. Cases were culture-proven and registered in the Malaysian National Tuberculosis Surveillance Registry (MyTB) from 2012 to 2018. Controls were diabetes patients identified from the National Diabetes Registry and were matched with cases based on the clinic in which they were registered at a ratio of 1:1. 119 cases and 119 controls were included in this study. Multivariate analysis was used to identify clinical factors associated with tuberculosis. Patient had increased odds of having tuberculosis if they had higher glycaemic (HbA1c) levels (OR=1.41, 95% CI 0.22-0.96, p<0.001) or nephropathy (OR=8.91, 95% CI 2.31-34.05, p<0.001). The odds ratio was lower if they have diabetes for at or more than 5 years (OR=0.46, 95% CI 0.22-0.96, p=0.04) and older (OR=0.96, CI 0.92-0.99, p=0.02). In conclusion, this study suggests that routine screening for tuberculosis in patients with diabetes should consider the diabetic duration, glycemic control, presence of nephropathy, and age of the patient.

Keywords: Case-control study; diabetic associated factors; diabetic nephropathy; type 2 diabetes mellitus; tuberculosis

ABSTRAK

Ini adalah sebuah kajian kes kawalan yang melibatkan pesakit diabetes di daerah Kinta, Kampar dan Larut-Matang-Selama Perak, Malaysia. Kajian ini bertujuan untuk menentukan faktor yang menyumbang kepada perkembangan tuberkulosis aktif dalam kalangan pesakit diabetes. Kes bermaksud pesakit yang terbukti mendapat jangkitan tuberkulosis melalui kultur yang didaftarkan di Sistem Maklumat Tuberkulosis Kebangsaan (MyTB) dari tahun 2012 hingga 2018. Kawalan adalah pesakit diabetes yang dikenal pasti daripada Sistem Maklumat Diabetes Kebangsaan dan dipadankan dengan kes berdasarkan klinik dengan pesakit-pesakit tersebut didaftarkan dan dalam nisbah 1: 1. Kajian ini melibatkan 119 kes dan 119 kawalan. Analisis multivariat digunakan untuk mengenal pasti faktor klinikal yang berkaitan dengan tuberkulosis. Pesakit berisiko untuk tuberkulosis jika mereka mempunyai tahap glisemik (HbA1c) yang tinggi (OR=1.41, 95% CI 0.22-0.96, p<0.001) atau masalah ginjal (OR=8.91, 95% CI 2.31-34.05, p<0.001). Kebarangkalian pesakit untuk mendapat tuberkulosis berkurangan sekiranya mereka mempunyai diabetes 5 tahun atau lebih (OR=0.46, 95% CI 0.22-0.96, p=0.04) dan berumur (OR=0.96, CI 0.92-0.99, p=0.02). Kesimpulannya, kajian ini menunjukkan bahawa pemeriksaan rutin tuberkulosis pada pesakit diabetes harus mempertimbangkan tempoh diabetes, kawalan glisemik, keadaan ginjal dan usia pesakit.

Kata kunci: Diabetes; faktor berkaitan diabetes; kajian kes kawalan; masalah ginjal; tuberkulosis

INTRODUCTION

Tuberculosis has affected humans for thousands of years and has a long history (Daniel 2006). It remains a threat, surpassing human immunodeficiency virus (HIV) as the leading cause of death worldwide from infectious diseases (World Health Organization 2018). Tuberculosis is an airborne infectious disease caused by *Mycobacterium tuberculosis.* Despite strong efforts in the past decade towards controlling tuberculosis-related morbidity and mortality, there were as many as 10.0 million new tuberculosis cases and 1.3 million deaths worldwide reported in 2017 (World Health Organization 2018). Malaysia is considered a high tuberculosis burden country, with an estimated incidence of 93 cases per 100,000 population (World Health Organization 2019). In 2016, 25,005 were cases reported, and the number continues to rise (World Health Organization 2019).

Studies have shown that diabetes mellitus increases the risk of active tuberculosis three-fold, which complicates efforts to curb the pandemic (Leung et al. 2008). The World Health Organization estimated that up to 15% of tuberculosis globally is related to diabetes mellitus, and its prevalence is expected to rise in developed

and developing countries (World Health Organization 2011). The National Health and Morbidity Survey 2015 showed that the prevalence of diabetes in Malaysia has increased from 15.2% in 2011 to 17.5% in 2015, meaning that about 3.5 million Malaysian people above 18 years old have diabetes (Institute for Public Health 2015). There were over 3,492,600 cases of diabetes reported among adults in 2017 (International Diabetes Federation 2019). The dual epidemics of tuberculosis and diabetes in Malaysia are expected to cause a surge in tuberculosis cases; thus, implementing a cost-effective screening program is vital to control the pandemic.

It is well known that diabetes increases the risk of tuberculosis, but the risk increases differently in low and high tuberculosis burden countries. Two cohort studies in Australia and China reported that people with diabetes had 1.5 to 3 times higher risk of developing tuberculosis compared to people without diabetes (Dobler et al. 2012; Wang et al. 2013). A cross-sectional study in Taiwan and a retrospective population-based study in China reported that the prevalence of diabetes among newly diagnosed patients with tuberculosis was as high as 27.9% and 19.9%, respectively (Ko et al. 2017; Wu et al. 2016). In Malaysia, the prevalence of tuberculosis in patients with diabetes ranges from 14% to 33% (Swarna Nantha 2012).

Diabetes increases the risk of tuberculosis, but not all diabetic patients develop active tuberculosis. Factors influencing the development of tuberculosis have been explored in several studies (Alkabab et al. 2015; Dobler et al. 2012; Dooley et al. 2009; Leung et al. 2008). There is evidence that poor glycaemic control increases the risk of contracting tuberculosis (Ko et al. 2017). A cohort study demonstrated that diabetic patients with HbA1c of more than 7% had 3 times the tuberculosis hazard risk (Leung et al. 2008). In the Middle East, about one in two diabetic patients with HbA1c of more than 8% have tuberculosis (Alkabab et al. 2015). In addition, a longer disease duration and the use of insulin were found to be associated with a higher chance of developing tuberculosis among diabetics (Alkabab et al. 2015; Dobler et al. 2012; Dooley & Chaisson 2009).

To date, there is little agreement on screening for tuberculosis among people with diabetes worldwide and in Malaysia. The World Health Organization recommends symptom-based approach in which chest radiograph and sputum examination will be done in those with symptoms suggestive of tuberculosis (World Health Organization 2011). This has been practiced in many countries including China and India (Lin et al. 2015, India Tuberculosis-Diabetes Study Group 2013). In addition, the World Health Organization recommends systematic screening for tuberculosis among diabetic patients from countries with high prevalence of tuberculosis (World Health Organization 2011). Thus, the Ministry of Health Malaysia recommends systematic approach using chest radiograph, tuberculin skin test or Interferon Gamma Release Assay in asymptomatic high-risk individuals including diabetics (MaHTAS 2012). In 2015, the national data showed that among 340,000 diabetes patients screened for tuberculosis, 32% were screened using chest radiograph and the remaining tests were based on symptoms. However, the yield was low, with only 742 or 0.22% positive for tuberculosis (Disease Control Division 2016). A similar pattern was seen in Perak in the same year, as out of 25,454 chest radiographs performed among diabetics, only 74 or 0.29% were diagnosed with active tuberculosis (Perak State Health Department 2015).

Debate continues about the best strategies to screen for tuberculosis among diabetic patients as the yield was low either using the chest radiograph and symptoms based or chest radiograph alone as seen in the national and Perak data. More importantly, studies on factors that increase the likelihood of tuberculosis among diabetics have been limited. Thus, the aim of this study was to identify factors associated with having active tuberculosis among diabetes patients in Perak. Specifically, this study examined the association between active tuberculosis and clinical factors like glycaemic control, disease duration, insulin use, and diabetic complications. By identifying these factors, this study hopes to be able to suggest a more targeted group of diabetic patients to be screened for tuberculosis.

Materials and Methods

Study Setting

This was a case-control study involving type 2 diabetic patients registered under 16 government health clinics in the districts of Kinta, Kampar, and Larut-Matang-Selama in Perak. The patients were identified through the National Tuberculosis International System (MyTB) and the National Diabetes Registry. MyTB is a registry for new tuberculosis cases detected in Malaysia and contains data on socio-demographic characteristics, type of tuberculosis, direct smear, culture and sensitivity, treatment, and outcomes. The tuberculosis data are captured manually on medical cards and a medical assistant then updates it in the registry upon diagnosis and every two months until each patient has completed treatment. The National Diabetes Registry monitors the quality of care received by diabetic patients and has data on socio-demographic characteristics, co-morbidities, treatment regimens, and diabetic complications. Similar to tuberculosis, the diabetes data are recorded manually on medical cards and a medical assistant would updates the registry at six-monthly intervals.

STUDY POPULATION

CASE DEFINITION AND SAMPLING

The cases were Malaysians aged 18 years and above, diagnosed with type 2 diabetes mellitus and culture-confirmed tuberculosis. A total of 287 patients with culture-confirmed tuberculosis diagnosed from 2012 to 2018 in the MyTB registry were identified. Patients with immune suppression (e.g. HIV) were excluded from this study. From this sampling frame, every second patient was systematically selected for inclusion.

CONTROL DEFINITION AND SAMPLING

Controls were Malaysians aged 18 years and above, with type 2 diabetes mellitus but without tuberculosis. From the National Diabetes Registry, 1190 patients were registered during the same period and from this sampling frame, every tenth patient was systematically sampled for inclusion. The ratio for cases and controls was 1 to 1 and matched based on the health clinic at which they were registered.

SAMPLE SIZE

This sample size was calculated based on the assumption that 70% of the diabetic population has poor glycaemic control with elevated HbA1c level of more than 6.5%, and the odds of them to have tuberculosis was 3 times higher compared to diabetics with good glycaemic control (Chew et al. 2011; Dooley & Chaisson 2009). Using a sample size calculator for case-control studies with study power of 90%, significance level of 5%, and the ratio for cases to controls was 1:1. The minimum number of samples required for cases and controls was 112.

STUDY VARIABLES AND DATA COLLECTION

The presence of tuberculosis in the cases was defined as culture-confirmed tuberculosis. The duration of diabetes was calculated by subtracting the year of diagnosis from 2018, the year of data collection. The diabetic complications documented included retinopathy, proteinuria, nephropathy (defined as serum creatinine >106 mmol/L), ischemic heart disease and cerebrovascular disease (stroke). Treatment regime was defined as treatment with oral anti-diabetics only or with insulin. As for the demographic data, age was calculated from the date of birth and documented in years, sex as female or male and ethnicity as Malay, Chinese or Indian. This information was extracted from the National Diabetes Registry. In the event of incomplete information from the registry, the researcher obtained the required information from the patient's diabetic cards, obtained from their respective clinic. The HbA1c value for cases was at diagnosis of TB, while the HbA1c value for controls was the latest available value.

STATISTICAL ANALYSIS

Data management and analysis were performed using IBM SPSS Version 23.0® (Armonk, NY: IBM Corp). Continuous data were summarized as means and standard deviations if normally distributed, or medians and interquartile ranges if otherwise. Categorical data were presented as frequencies with percentages. Demographic and clinical characteristics were compared between cases and controls, using the Chi-square test for categorical variables and the independent samples t-test for continuous variables. Prior to statistical analysis, the treatment regimens were grouped into oral hypoglycaemic agent (OHA) and insulin use, if insulin was used either in combination with OHA or insulin alone. Multivariate logistic regression analysis was used to determine the association between tuberculosis and clinical factors such as duration of diabetes, HbA1c level, insulin use, and micro and macro complications, adjusting for socio-demographic factors. A P value of <0.05 was set as significant.

ETHICAL GOVERNANCE

The study was approved by the Medical Research and Ethics Committee (MREC) of the Ministry of Health Malaysia [(5) KKM/NIHSEC/P17-784) and by the Universiti Kebangsaan Malaysia ethics committee (UKM FPR.4/244/FF-2017-323). The ethics committees waived the needs of obtaining individual patient consent as this study used secondary data. Master lists linking patients' identification numbers and names were stored securely and not shared. No personal data or unique identifiers were recorded in the data collection forms.

RESULTS

The study included 238 patients, of which 119 were tuberculosis cases and 119 were controls. Table 1 compares the demographic and clinical characteristics of cases and controls. The patients in cases appeared to be younger (56 ± SD 12.4 years) compared to the control group (62.9 ± SD 10.5 years). The mean HbA1c was higher (9.5 ± SD 2.5 %) in cases compared to controls (7.9 ± SD 1.93 %). The median duration of diabetes in cases (3 ± IQR 2-9 years) was 3 years shorter than controls (6 ± IQR 4-12 years). In terms of insulin usage, the proportion of patients on insulin was higher in cases (37.8%) compared to controls (28.5%).

TABLE 1. Clinical and demographic characteristics of cases and controls

Variable		Cases (Type 2 Diabetics with TB) (n=119)	Controls (Type 2 Diabetics without TB) (n=119)	*p*-value
Demographic characteristics				
Age	mean (SD)	56.0 (12.4)	62.7 (10.5)	<0.001[a]
Gender	Male	82 (68.9)	60 (50.4)	
	Female	37 (31.1)	59 (49.6)	
Ethnicity	Malay	72 (60.5)	50 (42.0)	
	Chinese	24 (20.2)	41 (34.5)	
	Indian	23 (19.3)	28 (23.5)	
Clinical characteristics				
Duration of diabetes (years)	<5	62 (52.1)	42 (35.3)	0.009[b]
	≥5	57 (47.9)	77 (64.7)	
HbA1c, mean (SD)**		9.5 (2.5)	7.9 (1.93)	<0.001[a]
Treatment				
Metformin use	Yes	97 (81.5)	103 (86.6)	0.29[b]
	No	22 (18.5)	16 (13.4)	
Sulphonylurea use	Yes	73 (61.3)	63 (52.9)	0.19[b]
	No	46 (38.7)	56 (47.1)	
Insulin use	Yes	45 (37.8)	34 (28.6)	0.13[b]
	No	74 (62.2)	85 (71.4)	
Microvascular complications				
Proteinuria***	Positive	40 (41.7)	32 (33.0)	0.21[b]
	Negative	56 (58.3)	65 (67.0)	
Nephropathy	Yes	18 (15.1)	7 (5.9)	0.02[b]
	No	101 (84.9)	112 (94.1)	
Retinopathy	Yes	7 (5.9)	8 (6.7)	0.79[b]
	No	112 (94.1)	111 (93.3)	
Macrovascular complications				
Ischaemic heart disease	Yes	12 (10.1)	7 (5.9)	0.23[b]
	No	107 (89.9)	112 (94.1)	
Cerebrovascular disease	Yes	2 (1.7)	2 (1.7)	1.00[c]
	No	117 (98.3)	117 (98.3)	

*Data shown are frequencies (column percentages) unless otherwise indicated. ** Missing data for HbA1c, n=7 for Cases and n=1 for Controls. *** Missing data for Proteinuria, n=23 for Cases and n=22 for Controls

[a]Independent t-test. [b]Pearson's Chi-squared test. [c] Fisher Exact Test

Table 2 shows the associations between clinical factors (duration of diabetes, level of HbA1c, insulin use, proteinuria, nephropathy, retinopathy, ischaemic heart disease, and cerebrovascular disease) and tuberculosis. Simple logistic regression analysis was used for each variable to get the crude odds ratio. The duration of diabetes, HbA1c level and presence of nephropathy were statistically significant from this analysis. Subsequently, each variable was adjusted for socio-demographic characteristics including age, gender, and ethnicity using multiple logistic regression analysis. Those with diabetes for five or more years had a 50% risk reduction (OR=0.50, 95% CI 0.30-0.84, p=0.01) compared to those with a shorter duration of diabetes. After adjustment for socio-demographic characteristics, the risk to have tuberculosis in diabetics with the duration of diabetes at or more than 5 years was reduced to 43% (OR=0.57, 95% CI 0.32-1.00, p=0.05). For each percentage increment in HbA1c, the odds ratio of developing tuberculosis increased by 1.4 times (OR=1.39, 95% CI 1.22-1.58, p<0.001) and after adjusted for socio-demographic variables it remained almost similar (OR=1.34, 95% CI 1.17-1.55, p<0.001). There were no increased odds of tuberculosis associated with insulin use, before (OR=1.52, 95% CI 0.88-2.62, p=0.13) and after adjusting for socio-demographic characteristics (OR=1.71, 95% CI 0.94-3.14, p=0.07). Patients with nephropathy had almost 3 times higher odds (OR=2.85, 95% CI 1.14-7.11, p=0.03) of developing active tuberculosis compared to those without nephropathy and the odds increased to 5.5 times after adjusted for socio-demographic characteristics (OR=5.55, 95% CI 1.98-15.59, p <0.001).

TABLE 2. Crude and adjusted odds ratios of tuberculosis among diabetic patients

Variable	Univariate analysis					Multivariate analysis#				
	B	S.E.	Wald	Unadjusted OR (95% CI)	p-value	B	S.E.	Wald	Adjusted-OR (95%CI)	p-value
Diabetes ≥ 5 years [Diabetes < 5 years]	-0.69	0.27	6.76	0.50(0.30,0.84)	0.01	-0.56	0.29	3.81	0.57 (0.32, 1.00)	0.05
HbA1c level	0.33	0.07	25.37	1.39 (1.22, 1.58)	<0.001	0.29	0.07	17.30	1.34 (1.17, 1.55)	<0.001
Insulin use [No]	0.42	0.28	2.28	1.52 (0.88, 2.62)	0.13	0.56	0.31	3.40	1.71 (0.94, 3.14)	0.07
Retinopathy [No]	-0.14	0.54	0.07	0.87 (0.30,2.47)	0.96	-0.12	0.59	0.04	0.89 (0.28, 2.84)	0.84
Proteinuria [No]	0.37	0.30	1.55	1.45(0.81,2.61)	0.21	0.40	0.33	1.48	1.49(0.79,2.81)	0.22
Nephropathy [No]	1.05	0.47	5.05	2.85 (1.14, 7.11)	0.03	1.71	0.53	10.59	5.55 (1.98, 15.59)	<0.001
Ischaemic heart disease [No]	0.59	0.49	1.40	1.79(0.68, 4.73)	0.24	0.73	0.54	1.82	2.07 (0.72, 6.00)	0.18
Cerebrovascular disease [No]	0.00	1.01	0.00	1.00 (0.14, 7.22)	1.00	0.17	1.08	0.03	1.19 (0.14, 9.86)	0.88

#Multivariate analysis: adjusted for socio-demographic characteristics: age, gender, and ethnicity.

[-] reference group

TABLE 3. Factors associated with tuberculosis among diabetic patients

Variable	B	S.E.	Wald	Adjusted OR (95% CI)	*p*-value
Age	-0.04	0.18	5.74	0.96 (0.92,0.99)	0.02
Gender					
Male [Female]	0.43	0.38	1.26	1.53 (0.73,3.23)	0.39
Ethnicity					
Malay [Chinese]	0.09	0.42	0.05	1.09(0.48,2.48)	0.26
Indian [Chinese]	-0.70	0.54	1.68	0.50 (0.17,1.43)	0.24
Duration of diabetes					
≥5 years [<5 years]	-0.78	0.37	4.33	0.46 (0.22,0.96)	0.04
HbA1c level	0.34	0.10	11.82	1.41 (1.16,1.72)	<0.001
Treatment					
Insulin [OHA]	-0.26	0.45	0.34	0.77(0.32,1.85)	0.56
Diabetes complications					
Proteinuria [No]	0.31	0.40	0.63	1.36 (0.64,2.91)	0.43
Nephropathy [No]	2.19	0.68	10.23	8.91 (2.31,34.05)	<0.001
Retinopathy [No]	-0.54	0.78	0.49	0.58 (0.13,2.66)	0.48
Ischaemic heart disease [No]	1.13	0.79	2.03	3.09 (0.65,14.64)	0.15
Cerebrovascular disease [No]	0.62	1.17	0.28	1.86 (0.19,18.47)	0.60

*OHA-oral hypoglycaemic agent

Subsequently, a multiple logistic regression analysis was conducted in which all the clinical and sociodemographic variables were analysed at once using the enter method (Table 3). Patients diagnosed with diabetes for less than 5 years, those with higher HbA1c and those with nephropathy had increased odds of having contracted tuberculosis. In this analysis, diabetic duration of at or more than five years was related to a 54% reduction in tuberculosis risk (OR=0.46, 95% CI 0.22-0.96, p=0.04). The HbA1c level has consistently been associated with higher odds of developing active tuberculosis, and the risk was 1.4 times higher than those with a lower HbA1c level (OR=1.41,95% CI 1.16,1.72, p<0.001). The association between tuberculosis and nephropathy was further strengthened through this analysis. The odds for active tuberculosis were almost 9 times higher (OR=8.91, 95% CI 2.31, 34.05, p<0.001) than those for patients without nephropathy. Age was significantly associated with tuberculosis. With increasing age, tuberculosis risk was reduced by 4% each year (OR=0.96, 95% CI 0.92, 0.99, p=0.02).

DISCUSSION

This study aimed to identify factors which increase the likelihood of TB among diabetic patients, in order to allow for better-targeted screening. Generally, there is no standardized definition for long-standing diabetes mellitus due to the difficulties to determine the exact duration of the disease since its onset. A duration of 5 years or more from the diagnosis of diabetes is considered long-standing. In this study, those with diabetes for less than 5 years had higher odds to develop tuberculosis compared to those with longer duration. This is consistent with a retrospective population-based study in China that showed that mean duration of diabetes among those newly diagnosed with active tuberculosis was also less than 5 years (Wu et al. 2016). This result could be because the glycaemic levels of those with newly diagnosed diabetes or those with shorter duration of diabetes may still not be very well controlled, thus, leading to low immunity which predisposes them to tuberculosis infection. This hypothesis is consistent with the findings of this study showing that an elevated HbA1c was associated with 1.4 times odds of developing active tuberculosis. This was further supported by a study in Hong Kong that showed an elevated HbA1c greater than 7% increased the risk of developing active tuberculosis by 3 times among diabetics compared to those with lower HbA1c levels (Leung et al. 2008).

In this study, insulin use has not been associated with the development of tuberculosis, in concordance with the findings reported in a cohort study conducted in England (Pealing et al. 2015). However, this is in contrast with the studies conducted in Australia and Tanzania that found that insulin dependent diabetic patients had higher odds of developing active tuberculosis (Dobler et al. 2012; Swai et al. 1990). This could be due to the cases studied being among those with shorter duration of diabetes and younger age group. These groups of people

are usually least likely to be on insulin, tending to be on oral hypoglycaemic agent medication instead.

Another important result found in this study was that nephropathy increased the odds of developing tuberculosis by almost 9 times compared to those without nephropathy. This result is consistent to a systematic review that showed the risk of developing active TB among patients who had end stage renal failure was 3.6 times higher risk compared to their counterparts (Al-Efraij et al. 2015). Similar findings were also observed in a study conducted in India which showed that patients with end stage renal failure, either with or without dialysis, were more likely to develop active tuberculosis (Abdelreheem et al. 2014). A study in England had shown that the time recorded from the diagnosis of end stage renal failure to the development of active tuberculosis was about 12 months (Ostermann et al. 2016). However, this study had insufficient data to stage the chronic kidney diseases (CKD) and none of patients with nephropathy were on dialysis. Nonetheless, this study managed to show that it is important to monitor patients with nephropathy for tuberculosis. This is in agreement with the recommendation by the British Thoracic Society to screen patient for tuberculosis using tuberculin skin test in those with chronic kidney disease, regardless of stage (Milburn et al. 2010). However, other factors like diabetic treatment regime, proteinuria, retinopathy, ischemic heart disease, cerebrovascular disease, gender, and ethnicity were found not to be associated with active tuberculosis among diabetic patients.

This study found age plays an important role in the epidemiology of tuberculosis. Younger patients had a higher risk of contracting tuberculosis compared to an older age group. The risk of contracting tuberculosis was reduced by 4% with every one-year increment of age. This is consistent with the local data showing that TB notification age peaks between 20 and 60 years, followed by a decline after 60 years of age (Swarna Nantha 2012). Similarly, a study conducted in Cape Town, South Africa on age-structured transmission of TB showed that the incidence of TB peaks between the ages of 30 and 50 in the HIV negative population (Blaser et al. 2016). However, this is in contrast to the common understanding that immunity declines with increasing age and thus increases the risk of infection (Shaw et al. 2013). It is not well understood why tuberculosis incidence rates decline with increasing age; perhaps patients above 60 years may have acquired the immunological protective effect from a previous tuberculosis infection. More research is needed to understand this relationship.

The strength of this study was that the data were obtained systematically from the national registries, which may eliminate selection biases. However, there are a few limitations as well. As this study used retrospective data, the actual causal relationship between diabetes and tuberculosis could not be determined. A cohort study would be a better design to investigate associated factors by choosing subjects with a similar background and clinical characteristics and follow them up over a period. In this study, confounding factors such as level of education, occupation and household income were not available for inclusion in the analysis. The current study was also limited by the lack of information to calculate the estimated glomerular filtration rate, and thus this study could not stage the chronic kidney disease. It would be useful to assess the stages of chronic kidney disease and investigate the susceptible stages associated with the presence of tuberculosis. However, this study may guide the clinicians in tuberculosis screening among diabetics.

CONCLUSION

This research extends our knowledge on factors that increased the likelihood of having tuberculosis among type 2 diabetes patients. Clinical factors significantly associated with tuberculosis infection included duration of diabetes, HbA1c level and nephropathy, while age was the only demographic factor significantly associated with the infection. Patients with nephropathy who were not on dialysis had a nine times higher risk of developing tuberculosis.

Therefore, this study would like to suggest for the routine screening for tuberculosis among patients with diabetes, physicians should consider the duration of disease, glycemic control, presence of nephropathy, and age. Screening for tuberculosis in specific patient populations may be more practical and cost-effective, but further studies are required to examine the effectiveness of this targeted screening program.

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