The risk of tuberculosis in patients with diabetes mellitus from an Asian tertiary hospital

Dr Yang Yong

Epidemiology

Singapore General Hospital

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education
research

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Introduction: TB

Tuberculosis (TB) is a critical health problem globally.

It is the ninth leading cause of death worldwide and the leading cause from a single infectious agent, ranking above HIV/AIDS.

In 2016, there were an estimated 1.3 million TB deaths among HIV-negative people and an additional 374 000 deaths among HIV-positive people.

An estimated 10.4 million people fell ill with TB in 2016

WHO report 2017

Introduction: DM

- **The International Diabetes Federation has predicted that the number of individuals with diabetes will increase from 240 million in 2007 to 380 million in 2025, with a further 418 million people having impaired glucose tolerance (IGT).**
  - **van der Leeuw J et al. J Am Heart Assoc. 2016 May 31;5(6).**

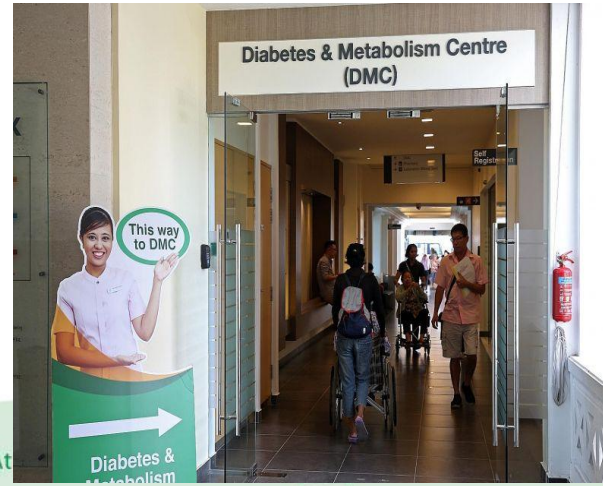
War against diabetics: Singapore

In 1998, among adults aged 18 to 69, 9% had DM; In 2010, 11% has DM

Among older people, the incidence is even higher

The number of diabetics under 70 is expected to rise to 670,000 by 2030 and to one million by 2050

Diabetes is expensive, with about $1 billion a year - expected to climb to $1.8 billion by 2050



War against diabetics. MOH (singapore): 30 Nov 2017

Risk of TB in DM

The risk of TB development in subjects with DM is higher than that in the general population.

In DM patients with TB, an increased risk of poor TB treatment outcomes, including treatment failure, death, and relapse

Reis-Santos B, et al. (2014) PLoS ONE 9(7): e100082.
Baker MA, et al. (2011). BMC Med 9:81.

Risk of TB in DM

Estimated to increase the risk of active TB disease about 3-fold and may impact TB-related mortality

A 2011 meta-analysis estimated that mortality was more likely among patients with TB and DM (TB-DM) compared with those without DM (unadjusted risk ratio [RR], 1.9; 95% confidence interval [CI], 1.3-2.4).

Jeon CY, Murray MB. PLoS Med 2008;5(7):e152.
Dooley KE, Chaisson RE. Lancet Infect Dis 2009;9(12):737e46.
Baker MA, et al. (2011). BMC Med 9:81.

Machenism of the risk

This increased risk of developing TB is thought to occur as a result of an impairment in the immune response among individuals with DM.

- **Diminishes the immune function of human body**
- **Causing decreased protein synthesis and**
- **Increased protein consumption,**
- **Decreased ability to produce immunoglobulin and hindering lymphocyte transformation for immune protection.**

Young. J Epidemiol Community Health 2012;66:519e523

Gaps

Limited data is avalable in Asian population

No data is available in local patients population

Resulted data may be of help in clinical management of DM and TB

Vital info for developing appropriate govenrment policy in the fighting agaist diabetics strategy and allocating resources

Young. J Epidemiol Community Health 2012;66:519e523

Objectives

To assess the rate of TB in patients with DM in an Asian patient population

To investigate the risk of DM on the development of TB using the hospital's administrative database

Methods: data

- Retrospective database study
- All inpatients ≥21 years between 2004 and 2015
- Demographic information: age, gender, ethnicity,
- Clinical data: admission and discharge date,10 ICD-9/10-AM diagnosis and 10 procedure codes (ICD-10-AM from 2012), discharge department and status, and disposition at discharge
- Index admission: latest admission

Methods: case definition--TB

- IICD-9-AM codes 010–018 and 647.3
  - Pulmonary TB (010-012, 018)
  - Extrapulmonary TB (013-017) /Pulmonary + Extrapulmonary TB
- ICD-10-AM codes: A15-A19
  - Pulmonary TB (A15-A16)
  - Extrapulmonary TB (A17-A19) /Pulmonary + Extrapulmonary TB
- Checked the medical records of all 50 TB cases for positive *M. tuberculosis* culture with 100% accuracy

Zgibor JC, et al. *Diabetes Res Clin Pract* 2007;75:313-9,
Dentan. *Clinical Infectious Diseases* 2014;58(4):495–501
Yang Y, et al. *Rheumatol Int*. 2017 Jun;37(6):1027-33

Methods: case definition--DM

- **ICD-9-AM code: 250**
- **ICD-10-AM: E10-E14**
  - **Positive predictive value of 95% for identifying true cases of diabetes**
    - **Zgibor JC, et al. *Diabetes Res Clin Pract* 75:313-9, 2007**
    - **Dentan. Clinical Infectious Diseases 2014;58(4):495–501**

Methods: Comorbidities

- Cardiovascular disease
- Cerebrovascular disease
- Lung disease
- Renal disease
- Liver disease
- Cancer
- Nutritional deficiency
- HIV infection

Yu, Y. B., (2012) Thromb Haemost 108(2): 225-235
Herring AA, et al (2008) International journal of health services: planning, administration, evaluation 38 (4):641-652

Statistical analysis I

•Categorical variables: %	Chi Square test
•Continuous variables: mean ± SD	ANOVA
•LOS: geometric mean (GM) 95%CI	Kruskal-Wallis H test
•Significant level	P<0.05

Statistical analysis II

- **Logistic regression model:**
  - **Adjustments: age groups, gender, ethnicity, admission class, and other comorbid conditions such as cardiovascular disease, renal disease, liver disease, cerebrovascular disease, cancer, nutritional deficiency and HIV infection.**
- **Hosmer–Lemeshow chi-square goodness-of-fit test: model assessment**
- **Area under the receiver operating curve (ROC): presented**

Results: summary

Table 1 The demographic and clinical characteristics of hospitalized patients with DM

	Non-DM, n=326258	DM, n=80493	p†
Age, mean year (SD)	50.3 (18.1)	64.7 (12.9)	<0.001
<65, %	76.7	49.4	<0.001
≥65, %	23.3	50.6	
Female sex, %	50.3	47.1	<0.001
Ethnicity, %			
Chinese	71.4	67.3	<0.001
Malay	10.4	13.3	
India	7.9	12.9	
Other	10.3	6.4	
Admission class, %			
A	18.1	10.7	<0.001
B	57.2	56.3	
C	24.7	33.0	
Medical management, %	44.4	68.3	0.105
Surgical management, %	55.6	31.7	
Cardiovascular disease, %	3.9	12.4	<0.001
Cerebrovascular disease, %	3.3	7.3	<0.001
Lung disease, %	2.2	2.5	0.057
Renal disease, %	2.0	13.6	<0.001
Liver disease, %	0.8	2.1	<0.001
Cancer, %	12.0	11.7	0.245
Nutritional deficiency, %	0.1	0.1	0.876
HIV infection, %	0.2	0.1	0.062
ICU admission, %	2.9	4.5	<0.001
Hospital mortality, %	1.4	2.7	<0.001
Hospital length of stay, day*	2.6 (2.6, 2.7)	4.5 (4.2, 4.9)	<0.001

DM, Diabetes mellitus. * Geometric mean (95% confidence interval). †p value was calculated using Chi-Square test except p value for age was calculated using two sample t-test and hospital length of stay using Mann-Whitney U test.

Rate of tuberculosis

Table 2 The prevalence of tuberculosis in patients with DM

	Non-DM, n=326258	DM, n=80493	p†
Tuberculosis, %	0.55	0.71	<0.001
Pulmonary*, %	0.44	0.62	<0.001
Extrapulmonary, %	0.11	0.08	0.053

DM, Diabetes mellitus. * If pulmonary and extrapulmonary tuberculosis, classified as pulmonary. †p value was calculated using Chi-Square test.

Associations of TB with DM
by logistic regression

Table 3 Regression analysis assessing associations of TB with DM in hospitalized patients

	OR	95% CI of OR		p
Age group, years				
<65	Reference			
≥ 65	1.3	1.2	1.4	<0.001
Female sex	0.5	0.4	0.5	<0.001
Ethnicity				
Chinese	Reference			
Malay	1.4	1.3	1.6	<0.001
India	0.9	0.8	1.1	0.285
Others	1.9	1.7	2.2	<0.001
Admission class				
A	Reference			
B	1.6	1.4	1.9	<0.001
C	3.2	2.7	3.7	<0.001
Cardiovascular disease	0.3	0.2	0.4	<0.001
Cerebrovascular disease	0.4	0.3	0.6	<0.001
Lung disease	1.8	1.5	2.2	0.001
Renal disease	1.3	1.1	1.6	0.001
Liver disease	1.0	0.7	1.5	0.808
Cancer	0.4	0.4	0.5	<0.001
Nutritional deficiency	10.0	6.1	16.4	<0.001
HIV infection	18.6	14.7	23.6	<0.001
Diabetes mellitus	1.2	1.1	1.3	<0.001

Logistic regression was used for analysis. OR, odds ratio; CI, confidence interval. Hosmer and Lemeshow Test, X2=12.2, df = 8, p=0.143. Area under the receiver operating curve (ROC) = 0.68, p<0.001.

Conclusion

- **DM patients were found to have higher rates of TB in this group of Asian patient population.**

- **Active screening for latent TB should be considered for DM patients**


Thank you !