

Policy Forum



Mutual Impact of Diabetes Mellitus and Tuberculosis in China*

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China has a double burden of diabetes mellitus and tuberculosis, and many studies have been carried out on the mutual impact of these two diseases. This paper systematically reviewed studies conducted in China covering the mutual impact of epidemics of diabetes and tuberculosis, the impact of diabetes on multi-drug resistant tuberculosis and on the tuberculosis clinical manifestation and treatment outcome, the yields of bi-directional screening, and economic evaluation for tuberculosis screening among diabetes patients.

Key words: Impact; Tuberculosis; Diabetes mellitus; China

China has a double burden of diabetes mellitus (DM) and tuberculosis (TB). A national survey conducted in 2010 found that the prevalence of DM was 11.6% [95% confidence interval (CI): 11.3%-11.8%] in Chinese adults, and 113.9 million adults were estimated to have DM in China^[1]. China has made substantial progress in TB control in the past two decades, and more than halved the TB prevalence, with a decreased prevalence of smear-positive TB from 170/100,000 to 59/100,000^[2]. However, there is still a significant number of TB cases in China because of its large population size, and it is estimated that there were 0.918 million incident TB cases in 2015^[3]. The evidence for a positive association between DM and TB has been found in many studies regardless of the study design and population, and the two diseases may complicate each other to different extents. Data from the tuberculosis patient information management system also showed that a high percentage of TB patients with DM was observed in some areas in China, and annually increased in several cities^[4-5]. Epidemics and the growing evidence of the link between TB and DM remain a grave global public health concern for researchers

and policy-makers in China.

The purpose of the current study was to systematically review the literature on the association between DM and TB conducted in China and to understand the future needs and policy implication for public health. We searched for studies published from 2,000 with the key words 'tuberculosis/tuberculin', 'diabetes/diabetic', and 'China/Chinese'. Case reports, nursing research, studies with inconclusive results or inaccessible full text were excluded from this current study.

Mutual Relationship between TB and DM in Epidemics

DM and TB have mutual risk factors. A higher prevalence of TB among DM patients and vice versa was consistently observed in many previous studies worldwide^[6].

Impact of DM on TB Among the Chinese, DM patients have a higher incidence of TB. In a cohort study conducted in Taiwan, China, compared to those in randomly selected matched non-diabetic controls, both female and male patients with DM had a significantly higher risk of incidence of TB, with the cumulative incidence of TB being 1.92 cases per 1,000 person-years for females and 3.25 cases per 1,000 person-years for males within a 5 year follow-up duration^[7]. This result was very close to the incidence obtained in another cohort study conducted in Hong Kong, China which yielded 214 cases per 100,000 person-years for culture-confirmed TB and 270 cases per 100,000 person-years for pulmonary TB^[8]. DM patients also had a higher prevalence of TB. In a population-based pilot study for TB screening among DM patients conducted in Shandong province, the prevalence of TB was 342.72/100,000^[9], while the prevalence of TB among DM patients in Taiwan, China was 3.89 per thousand population^[10]. In addition, DM patients

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have a more severe manifestation of TB infection on chest radiograph^[11]. In a tuberculin skin test conducted in Shandong province, a higher prevalence rate of patients with a positive tuberculin test result (mean induration ≥ 5 mm) was found among hospitalized diabetes patients than that among other patients without diabetes^[12].

The impact of DM on TB was identified in many studies, and DM was associated with a three-fold increased risk of incident TB using a meta-analysis in a systematic review^[13]. Studies in China also noted similar findings. A population-based study conducted in Taiwan, China found an adjusted hazard ratio (*HR*) of 1.31 (95% *CI*: 1.23-1.39) for type 2 DM with TB compared with non-diabetic controls^[7]. This risk increased among the elderly. Another cohort study conducted in Hong Kong, China showed that type 2 DM was associated with a modest increase in the risk of culture-confirmed and pulmonary TB (with or without extrapulmonary involvement) in subjects aged 65 years and more, with adjusted *HRs* of 1.91 (95% *CI*: 1.45-2.52) and 1.89 (95% *CI*: 1.48-2.42), respectively^[8]. The risk of developing TB also increased with increasing severity of DM, and > 3 -fold risk was observed among those with ≥ 2 DM-related complications [odds ratios (*OR*), 3.45; 95% *CI*: 1.59-7.50], compared to that among persons without DM^[14].

Limited studies identified the risk factors for TB among DM patients in China. Being male (*OR*: 5.057, 95% *CI*: 1.562-16.377), having a body mass index (BMI) < 18.5 (*OR*: 16.189, 95% *CI*: 2.588-101.260), and having anxiety (*OR*: 5.214, 95% *CI*: 1.772-15.339) were found to be significant risk factors for TB after adjusting for confounding factors^[9]. However, healthy habits (*OR*: 0.333, 95% *CI*: 0.218-0.508), high socioeconomic level (*OR*: 0.508, 95% *CI*: 0.346-0.745), hypertension (*OR*: 0.517, 95% *CI*: 0.350-0.764), good housing condition (*OR*: 0.599, 95% *CI*: 0.413-0.868), and beneficial change of diet after the diagnosis of DM (*OR*: 0.630, 95% *CI*: 0.447-0.889) were shown to be associated with a decreased risk for TB^[15]. In addition, data in the tuberculosis patient information management system showed an increasing trend of DM-TB concurrent rate with age^[16].

Impact of TB on DM Several studies verified the impact of TB on DM. In a descriptive study conducted in peripheral health facilities in Kerala, 32.4% of TB patients were diabetic, and 7% of DM patients were newly diagnosed^[17]. In another cohort study in Georgia, the prevalence of DM (HbA1c \geq

6.5%) and pre-DM (HbA1c $\geq 5.7\%$ -6.4%) was 11.6% and 16.4%, respectively among 318 newly diagnosed patients with TB^[18]. A retrospective cohort study conducted in Malaysia showed that DM was more likely to be present in Chinese, with an *OR* of 1.401 (95% *CI*: 1.079-1.818)^[19].

A higher prevalence of DM among TB patients was also found in the Chinese. A prevalence rate of 12.4% in TB patients with DM was identified by a screening pilot survey in mainland China in 2011-2012^[20]. In two studies conducted in Taiwan, China, an average DM prevalence rate of 27.9% in newly diagnosed TB patients^[21] and 31.2% in newly culture positive pulmonary TB patients^[22] were obtained, which were more than four times the prevalence of DM among the general population. Hospital-based retrospective studies have determined the DM prevalence in urban areas in mainland China. By using medical records, a DM prevalence rate of 19.9% and 12% was observed in Shanghai^[23] and Guangzhou^[24], respectively. The DM prevalence among TB patients decreased in rural areas. In a prospective community-based survey carried out in Shandong province, the prevalence of DM among TB patients aged 18 years old and above was significantly higher than that among non-TB controls (6.3% vs. 4.7%, $P < 0.05$). The DM risk was higher in TB patients than that in the non-TB group (adjusted *OR*: 3.17, 95% *CI*: 1.14-8.84) after adjusting for confounding factors^[25].

Older age was significantly associated with DM, and several new independent factors have been ascertained to be associated with DM, including heart failure (*OR*: 1.27, 95% *CI*: 1.09-1.48), ischemic heart disease (*OR*: 1.23, 95% *CI*: 1.09-1.39), cerebrovascular disease (*OR*: 1.30, 95% *CI*: 1.15-1.48), hypertension (*OR*: 2.32, 95% *CI*: 2.05-2.62), dyslipidemia (*OR*: 3.26, 95% *CI*: 2.88-3.68), chronic kidney disease (*OR*: 1.60, 95% *CI*: 1.33-1.92) and liver disease (*OR*: 1.68, 95% *CI*: 1.51-1.86)^[21]. In addition, DM prevalence increased with age, and compared with TB patients aged under 30 years, adjusted *ORs* were 5.35 (95% *CI*: 2.47-11.57), 9.46 (95% *CI*: 4.61-19.43) and 13.20 (95% *CI*: 6.71-25.96) for those aged 30, 40, and 50 years and above, respectively. Also, TB patients with normal BMI had the lowest DM prevalence (5.8%), in comparison with 7.4% for TB patients with BMI < 18.5 and 7.7% for those with BMI ≥ 24.0 ^[25].

Impact of DM on Multi-drug Resistant TB

Although it was reported that type 2 DM was

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