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Diabetes mellitus in patients with pulmonary tuberculosis in an aging population in Shanghai, China: Prevalence, clinical characteristics and outcomes

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ABSTRACT

Aims: To determine the prevalence of diabetes mellitus among pulmonary tuberculosis patients and the difference of clinical characteristics and outcomes between pulmonary tuberculosis patients with and without diabetes mellitus in an aging population in Shanghai, China.
Methods: This is a retrospective population-based study. 201 newly diagnosed pulmonary tuberculosis patients in Changning District, Shanghai during 2007–2008 were included. Clinical characteristics and outcomes were collected. Determination of diabetes mellitus was based on the medical records before pulmonary tuberculosis was diagnosed.
Results: The prevalence of diabetes mellitus among pulmonary tuberculosis patients was 19.9% (40/201). Pulmonary tuberculosis patients with diabetes mellitus were more likely to be old (≥50, OR = 5.23, 95% CI = 2.07–13.25), to have pulmonary cavities (OR = 3.02, 95% CI = 1.31–6.98), to be sputum smear positive (OR = 2.90, 95% CI = 1.12–7.51), and to have extension of anti-tuberculosis treatment duration (OR = 2.68, 95% CI 1.17–6.14). Besides, they had a higher 2nd month sputum smear positive proportion (OR = 2.97, 95% CI 1.22–7.22) and a higher 5-year recurrence rate (OR = 5.87, 95% CI 1.26–27.40).
Conclusions: High prevalence, severe clinical characteristics and poor outcomes of pulmonary tuberculosis patients with diabetes mellitus highlight the necessity of early bi-directional screening and co-management of these two diseases in Shanghai, China.

1. Introduction

It has long been documented (Root, 1934) that diabetes mellitus (DM) is associated with the incidence of active pulmonary tuberculosis (PTB). Recently, a meta-analysis reported that the risk of developing active PTB in people with DM was three times as high as in those without (Jeon & Murray, 2008). Globally speaking, in 2013, an estimated 15% of adult PTB cases were attributed to DM, among which more than 40% were in India and China (Lönnroth et al., 2014).

China's national tuberculosis survey (Wang, Zhang, Ruan, et al., 2014) (2010) revealed that it had more than halved smear-positive tuberculosis prevalence from 1990 to 2010. However, PTB epidemic remains serious since the reduction in the prevalence of all pulmonary cases between 2000 and 2010 was slight (Technical guidance group of the fifth national TB epidemiological survey, 2012). Concurrently, the DM (mainly type 2) prevalence is soaring due to drastically ongoing globalization, urbanization, population growth and aging. A national study from June 2007 through May 2008 estimated that the age-standardized prevalence of total DM was 9.7%, which had reached an epidemic proportion (Yang, Lu, Weng, et al., 2010). According to a meta-analysis, DM not only increases the risk of active PTB but indicates poor PTB outcomes as well. It showed that PTB patients with DM had higher risk of failure and death combined, death, relapse than those without and were more likely to remain sputum smear positive at 2–3 months after initiating treatment for PTB (Baker, Harries, Jeon, et al., 2011). Thus, the double burden of these two diseases might result in a great challenge for the control of PTB in China. Nevertheless, the population and epidemic of these two diseases are quite different in various regions in China (Wang et al., 2014; Yang et al., 2010). The association between DM and PTB (e.g., prevalence, clinical characteristics and outcomes) in Shanghai, the most developed area in China and also a city with the deepest degree of population aging nationwide, has never been studied (Hongguang, Min, Shiwen, et al., 2015; Wang, Ma, Han, et al., 2013; Li, Lin, Mi, et al., 2012).

Conflicts of interest: none.

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Shanghai has a relatively low PTB incidence proportion (27.9/100,000, 2008). But the prevalence of type 2 DM is rising rapidly from 10.2% (Li, Lu, Jia, Li, et al., 2006) in 2002 to 15.6% in 2009 among residents aged from 35 to 74 years, which is also far beyond the average of the whole nation. We conducted this retrospective population-based study to determine the prevalence of DM among PTB patients in an aging population in Shanghai. The differences of clinical characteristics and outcomes between PTB patients with and without DM were also analyzed to provide information for care for PTB patients complicated with DM.

2. Methods

2.1. Study setting and population

We selected Changning District, a downtown area in Shanghai, as the study setting because its high population aging degree (the proportion of 60 years and above people among population has reached 21.7% in 2009 (Shanghai Statistical Bureau, 2010)) had resulted in rising burdens of DM and PTB.

In Changning district, all suspected cases of PTB detected in a general hospital or a community health center were referred to the district tuberculosis hospital where sputum smear, sputum culture, chest radiograph and other necessary tests were carried out and the diagnosis was made.

According to the Guideline for National TB Control Program issued by Ministry of Health, confirmed PTB cases included individuals who had positive sputum smear, positive sputum culture, or pulmonary lesions of tuberculosis that had been confirmed by pathological examination. Individuals who had negative sputum smear and culture were clinically diagnosed as PTB if other pulmonary diseases could be excluded or their chest radiograph supported active PTB and they had either of the below: 1. suspected PTB signs like cough, expectoration, haemoptysis; 2. strong purified protein derivative (PPD) skin test reaction; 3. positive TB anti-body; 4. extra-pulmonary tuberculosis confirmed by pathological examination.

PTB patients were categorized as new or previously treated cases based on their anti-TB treatment history. In general, new PTB patients were treated using standard regimen including 2 months of isoniazid, rifampicin, pyrazinamide, and ethambutol (or streptomycin), then 4 months of isoniazid and rifampicin (2HRZE(S)/4HR). The duration of anti-TB therapy could be extended, depending on radiological and bacteriological data that were available and the clinical judgment of the attending doctor. All of the pretreatment positive cultures in the district tuberculosis hospital were sent to the Tuberculosis Reference Laboratory at Shanghai Municipal CDC, where drug susceptibility testing and species identification were routinely performed.

Determination of DM was based on the medical records before PTB was diagnosed. Patients confirmed for DM in general hospitals previously was categorized as “with DM”. Others were categorized as “without DM”. DM was treated using oral drugs or insulin prescribed by doctors in general hospitals. HIV test was not routinely performed for PTB.

All diagnosed PTB patients living in Changning District were mandatorily reported to the tuberculosis surveillance system at Changning District Center for Diseases Control and Prevention (CDC) who was in charge of the implementation of treatment supervision and patient support.

In this retrospective population-based study, we included all new PTB patients who lived in Changning district during 2007–2008. Patients who were infected with non-tuberculosis mycobacteria (NTM) were excluded from the analysis.

2.2. Data collection and statistics

Information on demographic characteristics such as age, sex, alcoholism and smoking history was collected by trained health care workers using a previously designed questionnaire when they visited the patients. Clinical characteristics (e.g., comorbidity, pulmonary cavities, sputum smear and culture results, drug resistance, treatment duration) and outcomes were completed by doctors through medical records review. Successful treatment outcome is defined as a cure and/or treatment completion, according to international definitions. A poor treatment outcome is defined as death, default, treatment failure, transfer out to another jurisdiction, or other outcomes (e.g., discontinued TB treatment on medical advice). Recurrence was determined by retrieval from tuberculosis surveillance system. Treatment duration was defined as the time from initial to the end of the anti-TB chemotherapy. The medium treatment duration was 243 days (interquartile range 190–283.5) in our study. Patients who had been treated for more than 240 days were considered as those with extension of anti-TB treatment duration.

Descriptive and analytical statistics were performed. We used chi-square test or Fisher’s exact test to compare clinical characteristics and outcomes between PTB patients with and without DM. Univariate and multivariate analysis were performed to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for factors associated with clinical characteristics. Variables with p values of <0.05 in univariate analysis entered the multivariate logistic regression model. The dependent variable was either PTB patients with DM or PTB patients without DM. The independent variables were sex, age (categorized as $<50, \geq 50$), smoking history, pulmonary cavities, sputum smear status and extension of anti-TB treatment duration. A p-value of less than 0.05 was considered significant. All of the analyses were performed using SPSS software (SPSS Inc., Chicago), version 17.0.

2.3. Ethical approval

The study was approved by the Ethical Review Committee at Shanghai Municipal Center for Disease Control and Prevention. Written informed consent was obtained from each patient.

3. Results

3.1. Epidemiological and clinical characteristics of PTB patients with and without DM

During the study period, 201 newly diagnosed PTB patients were included in the analysis. The majority were male (64.2%) and the median age was 48 years (range 15–86). 40(19.9%) had DM before PTB diagnosis. The median history of DM was 3 years (range 1–20). Table 1 showed that in the univariate analysis, PTB patients with DM were more likely to be old (older than 50, $p < 0.001$), to be male ($p = 0.002$), to have smoking history ($p = 0.011$) and to have cavities on initial chest radiography ($p < 0.001$) when compared with those without DM. Likewise, there was a higher likelihood for PTB patients with DM to have positive sputum smears and cultures ($p < 0.001$, respectively) and extension of anti-TB treatment duration ($p = 0.002$). The difference in hepatitis B, alcoholism, pleurisy and drug resistance patterns didn’t meet significance ($p > 0.05$). In a multivariable logistic regression model, being older than 50 (adjusted OR = 5.23, 95% CI = 2.07–13.25), having pulmonary cavities (adjusted OR = 3.02, 95% CI = 1.31–6.98), being sputum smear positive (adjusted OR = 2.90, 95% CI = 1.12–7.51) and having extension of anti-TB treatment duration remained significant (adjusted OR = 2.68, 95% CI = 1.17–6.14).

3.2. Treatment outcomes of PTB patients with and without DM

All of the 201 patients accepted anti-TB treatment. Table 2 shows the outcomes during/at the end of treatment and after treatment was completed. 2nd month sputum smear positive was more often in PTB patients with DM than in those without DM (OR = 2.97, 95% CI 1.22–7.22). Although the proportion of 2nd month sputum culture positive in PTB patients with DM was higher, the difference wasn’t significant ($p > 0.05$).

In the PTB without DM group, 157 (97.5%) patients got successful outcomes, among which 105 (65.2%) were cured, 52 (32.3%) completed

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