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Diabetes mellitus increased all-cause mortality rate among newly-diagnosed tuberculosis patients in an Asian population: A nationwide population-based study

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ABSTRACT

Aims: To investigate the effect of diabetes mellitus (DM) on all-cause mortality among patients with newly-diagnosed tuberculosis (TB) in an Asian population. We also identified risk factors for mortality in these patients.

Methods: The data were obtained from the National Health Insurance Research Database and included 9831 newly-diagnosed TB individuals and 1627 TB mortality cases in the period of 2000–2010. The mortality data were divided into a DM group and a non-DM group. We measured the incidence density of mortality and identified the risk factors of mortality.

Results: The all-cause mortality of newly-diagnosed TB patients progressively increased with an average rate of 16.5% during 2000–2010. DM is an independent risk factor for all-cause mortality with HRs 1.17–1.27 by various models. TB patients with ages above 75 years had the highest risk of mortality (HR = 11.93) compared with those under 45 years. TB patients with heart failure, peripheral vascular disease, ischemic heart disease, cerebral vascular disease, hypertension, chronic kidney disease, pulmonary disease, liver disease, cancer, peptic ulcer disease, gout, and autoimmune disease had higher mortality compared to those without the aforementioned factors.

Conclusions: The one-year all-cause mortality after TB diagnosis was high among TB patients in Taiwan and it tended to increase in the past decade. While treating these newly-diagnosed TB patients, it is crucial to detect the factors predisposing to death, such as old age, male gender, certain kinds of aforementioned factors and diabetes.

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1. Introduction

Nowadays, tuberculosis (TB) remains a major public health issue worldwide. Although the TB mortality rate has fallen by 45% since 1990, there were an estimated 1.3 million TB deaths globally in 2012 [1]. The TB mortality rate among countries is variable, ranging from less than one death per 100,000 population to more than 40 deaths per 100,000 population [1]. Approximately 75% of global TB deaths occurred in the African and South-East Asia in 2012 [1]. In Taiwan during the period of 2004–2008, the average TB incidence was 68 per 100,000 population and the average TB mortality rate was 36 per 1000 TB population per year (annual regional TB induced mortality/annual regional TB incidence) [2].

Regarding the case-fatality rates of TB, it was reported from 1.8% to 83% in different study populations [3]. In the regions of high TB incidence and high human immunodeficiency virus (HIV) prevalence, risk factors of death for TB patients were HIV positivity, advancing immunosuppression, sputum with acid fast stain smear-negative disease and malnutrition. In the regions of low TB incidence and low HIV prevalence, risk factors of death were non-infective comorbidities, sputum with acid fast stain smear-positive disease, alcohol misuse and substance misuse [3].

Diabetes mellitus (DM) is prevalent moderately in Taiwan with an increased prevalence from 4.31% to 6.38% in the period of 2000–2008 [4], and it has a great impact on TB treatment outcomes. A systematic review had revealed that DM increased the risk of the poor outcome which composed of treatment failure and death, death during TB treatment, and relapse after successful completion of treatment [5]. In the previous study, we found that the prevalence of DM among newly-diagnosed TB patients in Taiwan was progressively increasing in the period of 2000–2010, with an average rate of 27.9% [6]. However, studies about the impact of DM on TB mortality in Taiwan are scarce. Our primary objective was to determine whether DM is the risk factor of all-cause mortality among newly-diagnosed TB patients in Taiwan by using Taiwan's secondary data. Our secondary objective was to investigate the TB all-cause mortality rate and its risk factors.

2. Materials and methods

2.1. Study design and setting

This study was a cohort study by analyzing secondary data. The Taiwan National Health Insurance (NHI) was established since 1995 and has been enrolling more than 99% of Taiwan population. We obtained our study data from the National Health Insurance Research Database (NHIRD), which was released by the National Health Research Institute (NHRI) for research purposes. The database includes information on the clinical visits for each insurant, such as birth date, sex, date of visits, diagnoses based on the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) and prescription drugs. This study used a sub-dataset of one million randomly sampled subjects in the NHI program in 2000 with all of their medical records from 1996 to 2011. The details of the NHIRD have been described in previous studies [7].

2.2. Study participants

We included patients with newly-diagnosed TB (ICD-9-CM 010-018) in the period from January 1, 2000 to December 31, 2010 (Fig. 1). To confirm TB cases, the patient must have had at least three outpatient visits with a TB diagnosis (ICD-9-CM 010-018) or at least one hospitalization with a discharge diagnosis of TB. The earliest date of TB diagnosis was defined as the index date for each subject. Patients with incomplete age or sex information were excluded (n = 2). Similarly, to confirm DM cases, the patient must have had at least three outpatient visits with a DM diagnosis (ICD-9-CM 250) or at least one hospitalization with a discharge diagnosis of DM, either before the index date or within 6 months after the index date.

TB patients were separated into a DM group and a non-DM group depending on their baseline DM status. The DM group was defined as patients with DM before TB diagnosis or with DM within 6 months after TB diagnosis (n = 2738). The non-DM group was defined as patients without DM before TB diagnosis and without DM within 6 months after TB diagnosis (n = 7093). From the index date of TB diagnosis, we tracked patient's data for one year or until the date of their death (Fig. 1).

2.3. Data sources, variables and outcomes

The main outcome of this study was to determine whether DM is the risk factor of all-cause mortality among newly-diagnosed TB patients. The secondary objective was to investigate the TB all-cause mortality rate and the risk factors of mortality for DM and non-DM group. The incidence density of mortality was defined as mortality of TB patients that developed over one year after TB diagnosis. The median survival time of TB deaths was calculated as the duration from the index date to the death date. Death was defined as withdrawal of the patient from the NHI program according to previous study [8].

Sites of TB infection were according to the ICD-9-CM codes, namely pulmonary TB (ICD-9-CM 010 only, 011 only or both), pulmonary TB combined with extra-pulmonary TB (011 plus any of 012-018), and extra-pulmonary TB (any of 012-018, without 011).

We determined the comorbidities by the ICD-9-CM codes from inpatient and outpatient diagnosis files, which included heart failure (ICD-9-CM 482), peripheral vascular disease (443.9), ischemic heart disease (410–414), cerebral vascular disease (430–436), hypertension (401–405), dyslipidemia (272.0–272.4), chronic kidney disease (585–586), pulmonary disease (490–496), liver disease (570–573), malignancy (140–208), HIV infection (042, V08), peptic ulcer disease (531–534), gout (274), and autoimmune disease (710–714). The definition