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Schizophrenia in type 2 diabetes mellitus: Prevalence and clinical characteristics

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ABSTRACT

Background: This study investigated the prevalence and characteristics of schizophrenia in patients with type 2 diabetes mellitus (T2DM) in Taiwan.
Methods: National Health Insurance claims data for patients with principal diagnoses of schizophrenia and T2DM were analysed.
Results: Compared with patients with schizophrenia in the general population (GP), those with schizophrenia and T2DM were more likely to have higher Charlson comorbidity index (CCI) scores and multiple comorbidities, and were older. The prevalence of schizophrenia was significantly higher in patients with T2DM than in the GP from 2000 to 2010. In addition, during this period, the prevalence of schizophrenia in patients with T2DM increased from 0.64% to 0.85%; such an increase in the GP was also observed. A high prevalence of schizophrenia was observed in patients with T2DM aged less than 60 years old; those residing in eastern Taiwan; those with incomes of ≤NT\$17,280, NT\$17,281–NT\$22,880, NT\$22,881–NT\$28,800, and NT\$36,301–NT\$45,800; and those with CCI > 2.
Conclusions: Our study found the prevalence of schizophrenia is higher in patients with T2DM than in the GP, particularly those with earlier ages less than 60 years old. Public health initiatives are necessary to prevent and treat schizophrenia in patients with T2DM, specifically for those with the aforementioned and premature death risk.

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1. Introduction

Schizophrenia is a psychotic disorder that is often chronic and negatively affects a patient's quality of life [1]. Schizophrenia has a lifetime prevalence of 1.0%–1.5% [2,3]. Schizophrenia is associated with substantial premature death and mortality rate twice as high as that of the general population (GP) [4–6]. One meta-analysis by Carsten Hjorthøj and colleagues showed that patients with schizophrenia die 14.5 years earlier than general population and noted an urgent need for interventions to bridge the mortality gap for patients with schizophrenia, in particular to deal with metabolic syndrome and risks of vascular complications.

Diabetes mellitus (DM) is an endocrine and metabolic disorders with impaired insulin secretion and insulin resistance leading to hyperglycemia and may cause macrovascular and microvascular complications [7]. DM and its complications impose a heavy burden not only at the personal level but also the global level [8,9]. In Asia, type 2 DM (T2DM) became a major public health concern for ethnic Chinese populations in mainland China, Hong Kong, Taiwan, and Singapore, and the prevalence of T2DM among the adult ethnic Chinese populations in these countries has reached 20% [8,10].

Schizophrenia has high endogenous risk with diabetes [11]. In 1879, Sir Henry Maudsley in Pathology of Mind wrote, 'Diabetes is a

disease which often shows itself in families in which insanity prevails' [12]. In addition, leading researchers such as Kraepelin E. (1983) and Bleuler, E. (1911) had discussed whether altered energy metabolism should be part of the disease picture of schizophrenia [13]. Long before antipsychotic drugs became a standard type of therapy, studies had shown abnormal glucose tolerance in patients with 'dementia praecox' (schizophrenia) [11,14,15]. Rajkumar et al. found individuals with schizophrenia were at an approximately three times higher risk of diabetes than the general population before receiving any antipsychotics mediations (drug-naïve). This finding demonstrated that diabetes is associated with schizophrenia independently of treatment with antipsychotic drugs [11].

Existing evidences for the genetic correlation between schizophrenia and T2DM were still mixed. One current study used data from genome-wide association studies to test the presence of causal relationships between schizophrenia and T2DM and found no causal relationships or shared mechanisms between schizophrenia and impaired glucose homeostasis [16]. On the other hand, many studies suggested schizophrenia and T2DM may share genetic (such as TCF7L2 Gene) and familial risk factors [13,17,18]. Gene pathways that have been associated with T2DM and schizophrenia may include calcium, g-secretase-mediated ErbB4, adipocytokine, insulin, and AKT signaling [19]. The genetic variants may increase both the risk of diabetes and vulnerability to schizophrenia [20].

Many studies have examined incidence or prevalence of diabetes in patients with schizophrenia given the possible onset of schizophrenia is much earlier than the T2DM [21–25]. However, very few have investigated the prevalence of schizophrenia among patients with T2DM. The prevalence of schizophrenia in patients with T2DM will not only reflect the proportion of a T2DM population that has onset risk of schizophrenia at a certain point of time before they developed T2DM, but also will reflect the potential premature mortality risks that may affect the duration of the schizophrenia in patients with T2D. Therefore, this study aimed to investigate the prevalence of schizophrenia in patients with T2DM using the Taiwan National Health Insurance (NHI) database and provide information on public health promotion efforts. Specifically, we first investigated the prevalence of schizophrenia in patients with T2DM from 2000 to 2010 and then compared factors for schizophrenia associated with these patients and the general population. Finally, we analysed the risk factors associated with schizophrenia in patients with T2DM.

2. Methods

2.1. Data source

The Taiwan NHI program is a mandatory, single-payer system that was established in 1995; approximately 98% of Taiwanese residents are enrolled in the NHI program, and almost all medical care providers in Taiwan, including those employed at medical and primary care centres, are contracted by the NHI Administration (NHIA) to provide outpatient and inpatient services. All health care providers make claims to the NHI to receive monthly reimbursements for their medical fees. Related claim records include inpatient, ambulatory, and home care visits and associated information such as patient demographic characteristics, clinical details, health care utilisation, and expenditure.

2.2. Sample

This retrospective cohort study analysed a random sample of patients selected from all NHI enrolees from 2000 to 2010. In 2010, the NHI program provided the medical claims data of 1 million randomly selected patients (approximately 4.5% of all enrolees) for research on health services. The registration and claims data collected by the NHI

program for these patients constitutes the Longitudinal Health Insurance Database 2010 (LHID 2010). The sample group did not significantly differ from all enrolees in terms of age, sex, or average insured payroll-related amount. This study analysed a sample of 715,756 patients aged ≥20 years from the LHID 2010.

2.3. Definitions of T2DM and schizophrenia

The Taiwan NHI claims data are based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes. These data provided a useful structure for using ICD-9-CM diagnostic codes to identify patients with T2DM and schizophrenia. This study analysed patients who had at least two service claims for ambulatory care or one service claim for inpatient care for a principal diagnosis of T2DM (ICD-9-CM codes 250.x0 and 250.x2) [26–28]. To deal with patients may have a diagnosis of schizophrenia in one but none of the subsequent contacts, we followed Chien et al. approach and defined schizophrenia as a record of at least one outpatient or inpatient service claim for a principal diagnosis of schizophrenia (ICD-9-CM code 295.xx) from 2000 to 2010 [21,29,30].

2.4. Prevalence of schizophrenia

The prevalence of schizophrenia in the GP was calculated by dividing the number of patients with schizophrenia by the total number of study patients. The prevalence of schizophrenia in patients with T2DM was calculated by dividing the total number of patients with T2DM by the number of patients with schizophrenia.

2.5. Measurements

The demographic characteristics of the patients, including age, sex, residential area, residential urbanisation level, income, comorbidities, Charlson Comorbidity Index (CCI), and duration of DM, were obtained from each patient file retrieved from the NHI database. Patients were classified into seven age groups, namely 20–30, 31–40, 41–50, 51–60, 61–70, 71–80, and ≥80 years. Residential area was classified into five geographical regions of Taiwan, namely northern, central, southern, and eastern Taiwan and offshore islets or other areas. Urbanisation level was categorised as rural or urban. Average monthly income was classified into six categories: ≤NT$17,280, NT$17,281–NT$22,880, NT$22,881–NT$28,800, NT$28,801–NT$36,300, NT$36,301–NT$45,800, and >NT$45,800. Comorbidities included myocardial infarction, congestive heart failure, peripheral vascular disease, hemiplegia or paraplegia, renal disease, and cerebrovascular disease. The CCIs were defined as 0, 1–2, and >2. The duration of DM (years) was classified into four categories: ≤3, 3–6 (including the sixth year), 6–9 (including the ninth year), and >9.

Oral antidiabetic therapy (ADT) was categorised into five groups: metformin (anatomical therapeutic chemical [ATC] code A10BA), sulfonylureas (ATC code A10BB), meglitinides (ATC code A10BX), thiazolidinediones (ATC code A10BG), and an α-glucosidase inhibitor (ATC code A10BF). Insulin injection therapy was classified as rapid-acting (ATC code A10AB), intermediate-acting (ATC code A10AC), long-acting (ATC code A10AE), and combination (ATC code A10AD) therapy.

2.6. Statistical analysis

The distribution of characteristics was compared among the three groups of patients, namely T2DM with schizophrenia, T2DM without schizophrenia, and the GP. Chi-squared (χ^2) and t tests were conducted to determine categorical and continuous variables, respectively. Generalised linear mixed models assuming a