



Research paper

Increased risk of chronic obstructive pulmonary disease in patients with bipolar disorder: A population-based study



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ABSTRACT

Background: We conducted this nationwide study to examine the prevalence and incidence of chronic obstructive pulmonary disease (COPD) among patients with bipolar disorder in Taiwan.

Methods: We used a random sample of 766,427 subjects who were aged ≥ 18 years in 2005. Patients with at least one primary diagnosis of bipolar disorder were identified. Study participants with one primary or secondary diagnosis of COPD for either ambulatory or inpatient care were also identified. We compared the prevalence of COPD in patients with bipolar disorder and the general population in 2005. In addition, we further investigated this cohort from 2006 to 2010 to detect incident cases of COPD in patients with bipolar disorder compared with the general population. The factors associated with COPD among patients with bipolar disorder were also analyzed.

Results: The prevalence of COPD in patients with bipolar disorder was higher than in the general population in 2005 (5.68% vs. 2.88%, odds ratio 2.03; 95% confidence interval, 1.53–2.67). The average annual incidence of COPD in patients with bipolar disorder was also higher than in the general population (2.03% vs. 1.03%, risk ratio 1.94; 95% confidence interval, 1.65–2.29) from 2006 to 2010.

Limitations: Some risk factors for COPD such as substance use, obesity, or lifestyle pattern were not available in this study.

Conclusions: Patients with bipolar disorder had a higher prevalence and incidence of COPD compared with the general population. Higher prevalence of COPD among bipolar patients was associated with increased age, males, hypertension, and second-generation antidepressant use.

1. Introduction

Bipolar disorder is a severe and impairing neuropsychiatric illness with early onset in life, and delayed diagnosis and treatment have been reported (Hirschfeld et al., 2003). The larger burden of other medical conditions among patients with serious mental disorders (e.g., schizophrenia or bipolar disorder) has been widely investigated (Kilbourne et al., 2004), and these patients are at higher risk of hospitalization or repeat hospitalizations (Davydow et al., 2016). Chronic obstructive pulmonary disease (COPD) involves persistent airway obstruction and usually progresses to cause lifetime debilitation. The incidence of COPD is high, and it is an increasingly prevalent medical condition worldwide (Adeloye et al., 2015) which has been causing significant morbidity and mortality. According to one long-term follow-up study from 2000 to 2012, COPD was listed as one risk factor for hospital-based mortality

(Schoepf and Heun, 2014). In fact, COPD may be considered a medical condition with systemic influence and extra-pulmonary comorbidities, such as muscle dysfunction, metabolic disturbance, vascular damage or events, and psychiatric distress, which all complicate the treatment and prognosis of COPD (Decramer et al., 2009). Patients with COPD and with psychiatric disorders are at risk of exacerbations, which means the interactions of both body and mind should be considered as a whole.

Some studies have already been undertaken concerning COPD and mental disorders, and data from the Canadian Community Health Survey of a sample of 36,984 participants revealed that chronic lung conditions were related to mood and some anxiety disorders (Patten and Williams, 2007). According to one large-scale study in which 19 countries were enrolled, depression, generalized anxiety, and alcohol abuse were highly associated with COPD, and the cumulative risk of COPD after diagnosis of multiple mental health disorders was

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continuously monitored over a lifetime (Rapsey et al., 2015).

It has been reported that about 32.4% to nearly 60% of adults with bipolar disorder had one or more other medical conditions, and these were related to impaired psycho-social function (Kilbourne, 2009). Of note, patients with bipolar disorder died 8.5–9 years earlier than the general population, and respiratory diseases were one of the leading causes of premature death (Crump et al., 2013). In connection with the occurrence of serious mental illness such as schizophrenia and bipolar disorder, a national study of 8028 adults in Finland, who underwent spirometry, found that a third of patients with schizophrenia and non-affective psychosis had either restrictive or obstructive lung disease (compared with 16.3% in the general population) (Partti et al., 2015). Another cross-sectional survey with a random sample revealed that COPD prevalence was as high as 22.6% in 200 adults with serious mental illness (Himmelhoch et al., 2004). In addition, it has been reported that patients with schizophrenia had 1.66 and 1.83 times higher prevalence and incidence of COPD than the general population in Taiwan (Hsu et al., 2013). One cross-sectional study for general medical conditions by the Veterans Administration showed that 10.6% of patients with bipolar disorder were diagnosed with COPD (Kilbourne et al., 2004). According to one report of administrative claims data from 1996 to 2001, the prevalence of chronic pulmonary disease was 2.32 times higher in patients with bipolar disorder (Carney and Jones, 2006).

We conducted this nationwide study to investigate the epidemiology of COPD in patients with bipolar disorder. First, we compared the prevalence of COPD between patients with bipolar disorder and the general population in 2005. Second, we investigated factors associated with COPD in patients with bipolar disorder. Third, we compared the incidence of COPD in patients with bipolar disorder and the general population from 2006 to 2010. Finally, we also detected risk factors for COPD in patients with bipolar disorder during this period.

2. Methods

2.1. Sample

The medical claims database of the National Health Research Institute includes data on ambulatory care, hospital inpatient care, and prescription drugs. The Institute provided a randomly sampled database of 1,000,000 patients for this study. From this database, 766,427 individuals aged ≥ 18 years in 2005 were entered in this study. This study was approved by the Institutional Review Board of Jinan Mental Hospital. No statistically significant differences in age, sex, or average insured payroll-related amount were present between the sample group and all enrollees.

2.2. Definition of bipolar disorder

The diagnosis of bipolar disorder was coded according to the international Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic criteria of the National Health Insurance (NHI) program in Taiwan. Study subjects with one primary diagnosis of bipolar disorder (ICD-9-CM: 296.0, 296.1, 296.4, 296.5, 296.6, 296.7 or 296.8) for either outpatient or inpatient care during 2005 were identified (Chien et al., 2004; Hsu et al., 2015).

2.3. Definition of chronic obstructive pulmonary disease

Study subjects with one primary or secondary diagnosis of COPD (ICD-9-CM: 491 or 492) for either ambulatory or inpatient care were identified (Hsu et al., 2013).

2.4. The prevalence of COPD

For the prevalence of COPD in the general population, the

numerator was the number of prevalent cases of COPD in 2005, and the denominator was the number of total study subjects in 2005. For the prevalence of COPD in bipolar patients, the numerator was the number of prevalent cases of COPD in patients with bipolar disorder in 2005, and the denominator was the number of total bipolar disorder subjects in 2005.

2.5. The incidence of COPD

From this fixed cohort, both patients with bipolar disorder and individuals in the general population who were diagnosed with new COPD from 2006 to 2010 (and no COPD diagnosis before 2005) were defined as incident COPD. The annual incidence was calculated consequently.

The numerator was the number of incident COPD cases and the denominator was the number of person-years contributed by the study subjects. Subjects who did not have COPD by the end of a year contributed 1 person-year and those who developed COPD during the year contributed one half person-year.

2.6. Measures

Demographic characteristics, including age, sex, insurance amount, region, urbanicity, antipsychotic use, antidepressant use, mood stabilizer use, diabetes, hypertension, and hyperlipidemia were obtained directly from the NHI database. Age was classified into one of six categories: 18–29, 30–39, 40–49, 50–59, 60–69, and ≥ 70 years. The medical insurance amount was assigned to one of five categories: fixed premium, dependent, less than US\$ 640 (NTD 20,000), US\$ 640–1280 (NTD 20,000–NTD 39,999), and US\$ 1281 or more (NTD 40,000 or more). The insurance amount was used to indicate socioeconomic status in this study, and individuals with a fixed premium belonged to the lowest socioeconomic status group. For geographic distribution, the study subjects were grouped by region: north, central, south, or east. Urbanicity was divided into three categories—urban, suburban, and rural—according to the household system (determined by population density) in Taiwan.

2.7. Statistical analysis

The differences in the prevalence of COPD between patients with bipolar disorder and those in the general population, according to different age groups, sex, insurance amount, region, and urbanicity, were tested by logistic regression, adjusted for the other covariates. Factors associated with the prevalence of COPD among patients with bipolar disorder in 2005 were adjusted by a logistic regression model. For the longitudinal analysis from 2006–2010, the differences in the incidence of COPD between patients with bipolar disorder and those in the general population based on age group and sex were tested by Cox regression, adjusted for the other covariates. Finally, we used a Cox regression model to detect risk factors for COPD in patients with bipolar disorder from 2006 to 2010. SAS version 9.1 was used to analyze the data, and the significance level was set at 0.05.

3. Results

Table 1 shows the prevalence of COPD in patients with bipolar disorder and those in the general population in 2005. The prevalence of COPD in patients with bipolar disorder was higher than that observed in the general population in 2005 (5.68% vs. 2.88%; OR 2.03; 95% confidence interval, 1.53–2.67; $P < 0.001$). Compared with the general population, patients with bipolar disorder exhibited a higher prevalence of COPD in the following groups: those aged 18–29, 30–39, 40–49, 50–59, and ≥ 70 years; both sexes; all insurance amounts except that of less than US\$ 640 (NTD 20,000) and US\$ 1281 or more (NTD 40,000 or more); all geographic regions; and living in all areas.

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