General Hospital Psychiatry 37 (2015) 294–298

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: http://www.ghpjournal.com

Increased risk of hyperlipidemia in patients with bipolar disorder: a population-based study

Jer-Hwa Hsu, M.D. [a], I-Chia Chien, M.D., Ph.D. [b,c,*], Ching-Heng Lin, Ph.D. [d]

[a] Chia-Yi Hospital, Ministry of Health and Welfare, 600 Chiayi City, Taiwan
[b] Tsaotun Psychiatric Center, Ministry of Health and Welfare, 54249 Nantou County, Taiwan
[c] Department of Public Health and Institute of Public Health, National Yang-Ming University, 112 Taipei City, Taiwan
[d] Taichung Veteran General Hospital, 407 Taichung City, Taiwan

ARTICLE INFO

Article history:
Received 9 February 2015
Revised 2 April 2015
Accepted 3 April 2015

Keywords:
Prevalence
Bipolar disorder
Hyperlipidemia
National Health Insurance
Taiwan

ABSTRACT

Objective: We conducted this nationwide study to examine the epidemiology of hyperlipidemia among Taiwanese patients with bipolar disorder.
Methods: We used a random sample of 766,427 subjects who were ≥18 years old in 2005. Subjects with at least one primary diagnosis of bipolar disorder were identified. Individuals with a primary or secondary diagnosis of hyperlipidemia or medication treatment for hyperlipidemia were also identified. We compared the prevalence of hyperlipidemia in patients with bipolar disorder with the general population in 2005. Furthermore, we investigated this cohort from 2006 to 2010 to detect the incident cases of hyperlipidemia.
Results: The prevalence of hyperlipidemia in patients with bipolar disorder was higher than that of the general population [13.5% vs. 7.9%; odds ratio, 1.75; 95% confidence interval (CI), 1.52–2.02] in 2005. The average annual incidence of hyperlipidemia in patients with bipolar disorder was also higher than that of the general population (4.37% vs. 2.55%; risk ratio, 1.66; 95% CI, 1.47–1.87) from 2006 to 2010.
Conclusions: Patients with bipolar disorder had a higher prevalence and incidence of hyperlipidemia compared with the general population. Patients with bipolar disorder coexisting hypertension exhibited a higher likelihood of hyperlipidemia.

1. Introduction

Hyperlipidemia is strongly associated with the pathophysiology of cardiovascular disease via atherosclerosis, which is a clear threat to human health worldwide (i.e., reduced life expectancy, high mortality from cardiovascular illness). It is important to know the prevalence and incidence of hyperlipidemia among individuals with bipolar disorder [1,2]. Findings from the National Health and Nutrition Examination Survey showed that the age-adjusted prevalence of hypertriglyceridemia and low HDL (*h*igh-*d*ensity *l*ipoprotein) cholesterol for US adults was 30% and 30.7%, respectively [3]. According to the Nutrition and Health Survey in Taiwan from 1993 to 1996, the prevalence of hypercholesterolemia and hypertriglyceridemia were estimated to be 6.1% to 24.4%, respectively, in different age groups of both sexes [4]. Furthermore, a large growth of metabolic syndrome had been reported in Taiwan in the past decades, from 13.6% to 25.5%, which was attributable to the uptake of Western and industrialized lifestyles and behaviors [5].

Bipolar disorder is viewed as a major mental illness and is more prevalent than schizophrenia [6,7], which not only severely affects patients' emotions, behaviors and daily functioning but also causes a heavy care burden for families and society. Bipolar patients possess a substantial risk of more general medical comorbidities at an earlier age occurrence than the general population [8,9]. All-cause mortality was 2-fold higher for patients with bipolar disorder compared with the general population [10]. Furthermore, cardiovascular disease was identified as the leading cause of the premature natural death. One population-based longitudinal study had found that the incidence of cardiovascular morbidity for patients with bipolar disorder was 1.66 times as high in comparison to the general population in Canada [11]. Among risk factors associated with metabolic syndrome, which highly predict the development of cardiovascular disease, the prevalence of hyperlipidemia was high in patients with bipolar disorder. According to a previous study in Taiwan, the prevalence of hypertriglyceridemia and low HDL was 36.8% and 53%, respectively, in bipolar patients [12]. The reported age-specific prevalence of metabolic syndrome was 26.5% in Italian bipolar patients, with a prevalence of 34% and 28.5% of hypertriglyceridemia and low HDL, respectively [13].

The increased risk for metabolic syndrome in patients with bipolar disorder is generally reported in comparison to the general population worldwide, and this co-occurrence results in complex and poorer treatment outcomes [14]. In a cross-sectional analysis of an administrative claims database of patients with bipolar disorder, the adjusted rate of high triglyceride levels and low HDL levels was 2.09 and 2.77 times

* Corresponding author. Tsaotun Psychiatric Center, Ministry of Health and Welfare, No. 161, Yu-Pin Road, Tsaotun Township, 54249 Nantou County, Taiwan. Tel.: +886-49-255-0800; fax: +886-49-256-1240.
E-mail addresses: icchien@ttpc.mohw.gov.tw, lewis777@ms26.hinet.net (I.-C. Chien).

http://dx.doi.org/10.1016/j.genhosppsych.2015.04.003
0163-8343/

higher than the comparison group, respectively [15]. Carney et al. reported a significantly higher rate of cardiovascular disease in patients with bipolar disorder compared to the general population, but the prevalence of hyperlipidemia did not differ between these two groups [8]. One 2-year follow-up study showed that the metabolic syndrome rate significantly increased from 28.6% to 44.3% in Italy; however, the rate of lipid level change did not reach statistical significance [16].

Although hyperlipidemia has a critical role in metabolic disturbance and cardiovascular disease, lower treatment and assessment rates of hyperlipidemia compared to other metabolic abnormalities such as diabetes and hypertension have become an issue deserving attention in patients with mental disorders [17,18], and there has yet to be a comprehensive hyperlipidemia survey among patients with bipolar disorder in Taiwan.

Taiwan implemented a National Health Insurance (NHI) program in March 1995, offering a comprehensive, unified and universal health insurance program to all citizens [19]. We conducted this nationwide study to investigate the epidemiology of hyperlipidemia in patients with bipolar disorder. First, we compared the prevalence of hyperlipidemia between patients with bipolar disorder and the general population in 2005. Second, we investigated factors associated with hyperlipidemia in patients with bipolar disorder. Third, we compared the incidence of hyperlipidemia in patients with bipolar disorder and the general population from 2006 to 2010. Finally, we detected risk factors for hyperlipidemia in patients with bipolar disorder during this period.

2. Methods

2.1. Sample

The National Health Research Institute medical claims database includes outpatient care, inpatient care and prescription drug data. The Institute provided us with a random sample database of 1,000,000 individuals (approximately 4.5% of the total population) for a health-related study. Based on the dataset, we identified a sample of 766,427 subjects aged ≥18 years in 2005. There were no statistically significant differences in respect to age, sex and average insured payroll-related amount between the sample group and all enrollees. This study was approved by the institutional review board of Jianan Mental Hospital.

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 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.

2.3. Definition of hyperlipidemia

Study subjects with one primary or secondary diagnosis of hyperlipidemia (ICD-9-CM: 272.0, 272.1, 272.2, 272.3 or 272.4) during either outpatient or inpatient care or with medications for the treatment of hyperlipidemia were identified. Hypolipidemic drugs included HMGCoA reductase inhibitors, fibric acid derivatives, bile acid sequestrants, nicotinic acid and derivatives and other lipid-modifying agents [20].

2.4. Prevalence of hyperlipidemia

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

2.5. Incidence of hyperlipidemia

Both patients with bipolar disorder and the general population with new cases of hyperlipidemia from 2006 to 2010 in this fixed cohort without a hyperlipidemia diagnosis before 2006 were defined as incident hyperlipidemia. The average annual incidence was calculated from 2006 to 2010. The numerator was the number of incident hyperlipidemia cases and the denominator was the number of person-years contributed by the study subjects. Subjects who became an incident case of hyperlipidemia during the year contributed one-half person-year to the denominator [21].

2.6. Definition of diabetes

Study subjects who had at least one prescription (oral hypoglycemic agents or insulin) for the treatment of diabetes in 2005 were considered to have a diagnosis of diabetes.

2.7. Definition of hypertension

Study subjects who had a primary or secondary diagnosis of hypertension (ICD-9-CM: 401–405) combined with antihypertensive drug treatment in 2005 were considered to have hypertension.

3. Measures

Demographic characteristics included age, sex, insurance amount, region and urbanicity. Age was classified into one of three categories: 18–39, 40–59 and ≥60 years. The insurance amount was divided into one of five categories: fixed premium, dependent, less than US$640 [20,000 New Taiwan Dollar (NTD)], US$640–1280 (20,000–39,999 NTD) and US$1281 or more (40,000 NTD or more). The insurance amount was used instead of socioeconomic status (SES) in this study, and persons with a fixed premium were in the lowest SES group. For geographic distribution, the study subjects were grouped by region: north, central, south or east. Urbanicity was divided into urban, suburban and rural categories according to the household system in Taiwan. Antipsychotic use was grouped as no antipsychotic use, first-generation antipsychotic use and second-generation antipsychotic use. Antidepressant use and mood stabilizer use were defined as present or absent.

3.1. Statistical analysis

The differences in the prevalence of hyperlipidemia between patients with bipolar disorder and the general population according to different age groups, sex, insurance amount, region and urbanicity were tested by logistic regression adjusted for other covariates in 2005. We also calculated the annual incidence rate of hyperlipidemia in patients with bipolar disorder and the general population from 2006 to 2010.

For patients with bipolar disorder, logistic regression was used to analyze the factors associated with the prevalence of hyperlipidemia prevalence in 2005 and incidence from 2006 to 2010, including age, sex, antipsychotics use, antidepressant use, mood stabilizer use, diabetes, hypertension, insurance amount, region and urbanicity. SAS version 9.1 was used to analyze the data, and the significance level was set at 0.05.

4. Results

Table 1 shows the prevalence of hyperlipidemia in patients with bipolar disorder and the general population in 2005. The prevalence of