Increased risk of hyperlipidemia in patients with major depressive disorder: A population-based study

I-Chia Chien [a,b,*], Ching-Heng Lin [c], Yiing-Jenq Chou [b], Pesus Chou [b,d]

[a] Taoyuan Mental Hospital, Department of Health, Taoyuan, Taiwan
[b] Department of Public Health & Institute of Public Health, National Yang-Ming University, Taipei, Taiwan
[c] Taichung Veteran General Hospital, Taichung, Taiwan
[d] Community Medicine Research Center, National Yang-Ming University, Taipei, Taiwan

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ABSTRACT

Objective: We conducted this study to examine the prevalence and incidence of hyperlipidemia among Taiwanese patients with major depressive disorder (MDD).
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 MDD 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 MDD patients with the general population in 2005. We followed this cohort from 2006 to 2010 to detect incident cases of hyperlipidemia in MDD patients compared with the general population.
Results: The prevalence of hyperlipidemia in patients with MDD was higher than in the general population (14.4% vs. 7.9%, odds ratio 1.67; 95% confidence interval, 1.53–1.82) in 2005. The average annual incidence of hyperlipidemia in patients with MDD was also higher than in the general population (3.62% vs. 2.55%, risk ratio 1.35; 95% confidence interval, 1.24–1.47) from 2006 to 2010. Higher incidence of hyperlipidemia was associated with MDD group, increased age, diabetes, hypertension, and higher socioeconomic status.
Conclusions: Patients with MDD had a higher prevalence and incidence of hyperlipidemia compared with the general population. Younger MDD patients and MDD patients with first-generation antipsychotic exposure or antidepressant exposure had an increased risk of hyperlipidemia compared with individuals in the general population.

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Introduction

Hyperlipidemia involves abnormally elevated levels of one or more lipids and/or lipoproteins in the blood (triglyceride or cholesterol) and pathological lipid qualities, such as elevated levels of low-density lipoprotein, the most common form of dyslipidemia. Hyperlipidemia results from complex interactions between genetic and environmental factors and is highly involved in the process of atherosclerosis and coronary artery disease [1].

A National Health and Nutrition Examination Survey from 1988 to 1994 in the United States revealed that the prevalence of hypertriglyceridemia and low levels of high-density lipoprotein was 30% and 37.1%, respectively [2]. Another Nutrition and Health Survey in Taiwan (1993–1996) showed that the prevalence was 10.2% to 11.2% for hypercholesterolemia and 6.1% to 13.4% for hypertriglyceridemia [3].

One study in Germany found that the prevalence of metabolic syndrome in subjects with MDD was 41%, including hypertriglyceridemia, which affected 43.1%; these rates were higher than in the comparison group [4]. A follow-up study in Finland revealed that females with depressive symptoms had a 2.5-fold greater risk for metabolic syndrome, including a higher prevalence of hypertriglyceridemia (27.7% vs. 18.0%) [5]. Another study showed that a lifetime prevalence of MDD was a significant predictor for the onset of metabolic syndrome (odds ratio, 1.82) [6]. However, a large community study in Australia found no association between MDD and metabolic symptom [7]. Further, another study suggested that metabolic syndrome, particularly the obesity, high triglyceride, and low high-density lipoprotein cholesterol, predicted depressive symptoms [8].

Taiwan implemented the National Health Insurance (NHI) program starting in March 1995, offering a comprehensive, unified, and universal health insurance program to all citizens. Up to 98% of the population of Taiwan joined the NHI program by 2005, and the Bureau of NHI has contracted with 92% of the medical institutions in Taiwan. No comprehensive epidemiologic study of hyperlipidemia in MDD patients has been reported in Taiwan. Therefore, we used the health care service database to analyze the occurrence of hyperlipidemia in patients with

* Corresponding author at: Taoyuan Mental Hospital, Department of Health, No. 71, Longshow Street, Taoyuan City, Taoyuan County 33058, Taiwan. Tel.: +886 3 369 8553; fax: +886 3 360 6929.
E-mail addresses: icchien@typc.doh.gov.tw, lewis777@ms26.hinet.net (I.-C. Chien).

MDD. This study tests the hypothesis of a positive association between MDD and hyperlipidemia. We first compared the prevalence of hyperlipidemia and factors associated with hyperlipidemia between patients with MDD and the general population. Second, we analyzed the associated factors for the prevalent cases of hyperlipidemia. Third, we compared the incidence of hyperlipidemia and factors associated with incident hyperlipidemia in patients with MDD and the general population from 2006 through 2010. Fourth, we analyzed risk factors for the incident cases of hyperlipidemia during the same period.

Methods

Sample

The National Health Research Institute medical claims database includes outpatient care, hospital inpatient care, and prescription drugs. The Institute provided us with a random sample database of 1,000,000 (about 4.5% of the total population) for health-related study. From this, we identified a sample of 766,427 subjects aged ≥18 years in 2005. There were no statistically significant differences in age, sex, and average insured payroll-related amount between the sample group and all enrollees. Insured amount is based on and approximate to the monthly wage of the insured. For the insured group of wage earners, the total monthly premium of an insured family is the insured amount times the premium rate (4.55%) times the employee contribution rate (30%) times the (1 + number of dependents). This study was approved by the Institutional Review Board of Taoyuan Mental Hospital.

Definition of MDD

The diagnosis of MDD was coded according to the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic criteria in the NHI program in Taiwan. Study subjects with one primary diagnosis of MDD (ICD-9-CM: 296.2 or 296.3) for either outpatient or inpatient care during 2005 were identified [9,10].

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) for either outpatient or inpatient care or with medications for treatment of hyperlipidemia were identified. Hypolipidemic drugs included HMG-CoA reductase inhibitors (simvastatin, lovastatin, pravastatin, fluvastatin, atorvastatin, and rosuvastatin), fibric acid derivatives (clofibrate, bezafibrate, aluminum clofibrate, gemfibrozil, fenofibrate, simfibrate, and etofibrate), bile acid sequestrants (cholestyramine, colestipol, and dextran sulfate sodium), nicotinic acid and derivatives (niceritrol, nicofuranose, acipimox, and nicomol), and other lipid-modifying agents (probucol, ezetimibe, and soysterol) [11].

Prevalence of hyperlipidemia

With respect to the prevalence of hyperlipidemia in the general population, the denominator was the number of total study subjects in 2005, and the numerator was the number of prevalent cases of hyperlipidemia in 2005. With regard to the prevalence of hyperlipidemia in MDD patients, the denominator was the number of total MDD subjects in 2005, and the numerator was the number of prevalent cases of hyperlipidemia in patients with MDD in 2005.

Incidence of hyperlipidemia

Both patients with MDD and the general population with new cases of hyperlipidemia from 2006 to 2010 for this fixed cohort and no 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.

Definition of diabetes

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

Definition of hypertension

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

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). 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 three categories according to 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.

Statistical analysis

The differences in prevalence of hyperlipidemia between patients with MDD and the general population according to different age groups, sex, insurance amount, region, and urbanicity were tested by logistic regression adjusted for the other covariates, which included age, sex, insurance amount, region, and urbanicity. Namely, one logistic regression analysis was performed for the entire population, then 17 additional analyses done on various subpopulations according to different stratification. Multiple logistic regression was used to analyze the associated factors for cases of hyperlipidemia in 2005. We also calculated the annual incidence rate of hyperlipidemia in patients with MDD and the general population from 2006 to 2010. The differences in incidence of hyperlipidemia between patients with MDD and the general population according to different age groups, sex, antipsychotic use, antidepressant use, and mood stabilizer use were tested by Cox regression adjusted for the other covariates, which included age, sex, insurance amount, region, and urbanicity. Finally, a Cox regression model was used to detect risk factors for incident hyperlipidemia from 2006 to 2010. SAS version 9.1 was used to analyze the data, and the significance level was set at 0.05.

Results

Table 1 shows the prevalence of hyperlipidemia in patients with MDD and the general population in 2005. The prevalence of hyperlipidemia in patients with MDD was higher than that in the general population (14.4% vs. 7.9%; odds ratio [OR] = 1.67; 95% confidence interval [CI], 1.53 to 1.82; $P < 0.001$) in 2005. Compared with the general population, MDD patients had a higher prevalence of hyperlipidemia in the following groups: age 18–39, age 40–59, age ≥60; all insurance amount groups; persons living in all regions except eastern region; and persons living in urban, suburban, and rural areas.

Table 2 shows the logistic regression analysis of factors associated with the prevalence of hyperlipidemia. A higher prevalence of hyperlipidemia was found in MDD