Increased risk of hyperlipidemia in patients with anxiety disorders: A population-based study

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Abstract

Objective This study examined the prevalence and incidence of hyperlipidemia among patients with anxiety disorders in Taiwan.

Methods We used a large dataset containing random samples, and more than 766,000 subjects who were aged 18 years or older in 2005 were identified. Subjects who had more than one primary or secondary diagnosis of anxiety disorders were identified. Individuals who had a primary or secondary diagnosis of hyperlipidemia or medication treatment for hyperlipidemia were also identified. The prevalence rate of hyperlipidemia in patients with anxiety disorders with that of the general population in 2005 was compared. We then followed this cohort to monitor incident cases of hyperlipidemia in anxiety patients, and assessed whether a difference existed from the general population during the period 2006–2010.

Results A higher prevalence rate of hyperlipidemia in patients with anxiety disorders was observed as compared with the general population (21.3% vs. 7.6%, odds ratio 2.14; 95% confidence interval, 2.07–2.22) in 2005. Additionally, a higher average annual incidence rate of hyperlipidemia in patients with anxiety disorders was also found as compared with the general population (5.49% vs. 2.50%, risk ratio 1.64; 95% confidence interval, 1.58–1.70) from 2006 to 2010.

Conclusions Patients with anxiety disorders had higher prevalence and incidence rates of hyperlipidemia than the general population. Risk factors that were found to be associated with the higher incidence rate of hyperlipidemia among anxiety patients included a greater age, the female gender, and the presence of diabetes and hypertension.

Introduction

Anxiety disorders are mental disorders with a high global prevalence rate [1]. Anxiety disorders and comorbid illnesses are becoming serious issues in many countries and deserve further investigation. Many studies have presented various biological theories that support the existence of interactions between anxiety and comorbid medical illnesses, including irritable bowel syndrome and chronic cardiovascular disease [2]. The available literature also suggests that anxiety disorders should be of concern in patients with other illnesses.
Hyperlipidemia is caused by complicated gene–environment interactions and is prominently involved in the development of atherosclerosis symptoms and coronary artery disease [3]. Generally, hyperlipidemia includes disturbances of lipid quantities and qualities, such as raised triglycerides or cholesterol with regards to the former and elevated low-density lipoprotein related to the latter, and is the most common form of dyslipidemia. According to previous epidemiological study of a US National Health and Nutrition Examination Survey from 1988 to 1994, the prevalence of a low level of high-density lipoprotein and hypertriglyceridemia was 37.1% and 30%, respectively [4]. A study in Taiwan that used data obtained from more than 5,000 subjects during 1993 to 1996 revealed that the prevalence was 10.2–11.2% for hypercholesterolemia and 6.1–13.4% for hypertriglyceridemia [5].

One study of more than 4,000 male US veterans found that generalized anxiety disorder has a positive association with metabolic syndrome (odds ratio [OR], 1.38) [6]. The same study also showed that hypertension, obesity, and triglycerides are the elements of metabolic syndrome that may differentiate subjects with and without generalized anxiety disorder, while diabetes had no correlation [6]. A study in Australia revealed that males with anxiety disorders tended to be correlated with the risk factors of metabolic disorders (OR, 2.22) [7]. Another study of 118 patients with psychiatric/psychologic disorders revealed that long-term follow-up endocrine patients are likely to have a greater risk of psychological distress, and generalized anxiety disorder was found to be the most frequent diagnostic disorder (29%) in these patients [8].

Very few studies have paid attention to the link between anxiety disorders and hyperlipidemia worldwide. Additionally, no inclusive epidemiologic research that focused on hyperlipidemia in patients with anxiety disorders has been reported in an Asian population. Therefore, we used the Taiwan National Health Insurance (NHI) database, which has a coverage of 99% of the population of Taiwan, to investigate the occurrence of hyperlipidemia in patients with anxiety disorders. The current study hypothesized that anxiety disorders and hyperlipidemia have a trend towards a positive association. To test the hypothesis, we first compared the prevalence of hyperlipidemia between patients with anxiety disorders and the control general population. We next inspected the data to identify associated factors for the prevalent cases of hyperlipidemia in patients with anxiety disorders.
disorders. Moreover, we compared the incidence of hyperlipidemia between patients with anxiety disorders and the general population during 2006–2010. Finally, we investigated risk factors for hyperlipidemia incident cases in patients with anxiety disorders during the same period.

Methods

Sample

The Taiwan National Health Research Institute generates a medical claims database, which includes data regarding outpatient care, hospital inpatient care, and prescription drugs. The Institute created a random sample dataset containing data of 1,000,000 subjects (which accounts for ~4.5% of the total number of Taiwan residents), which is made available to researchers for health-related study. From the dataset, we identified a subset of 766,427 subjects who were 18 years or older in 2005. The sample group we identified showed no statistical differences when compared with all enrollees in all aspects we tested, including age, gender and mean insured payroll-related amount. The Institutional Review Board of Taoyuan Mental Hospital has approved this study before starting data collection.

Definition of anxiety disorders

The Taiwan NHI database uses diagnostic coding based on the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic criteria [9]. Patients with anxiety disorders in this study were defined as patients with disorders including anxiety states, panic disorder, generalized anxiety disorder, phobic disorder, obsessive-compulsive disorder, acute stress disorder, and post-traumatic stress disorder (ICD-9-CM: 300.0, 300.2, 300.3, 308.3, and 309.81, respectively) [10, 11]. Patients who had at least two service claims during 2005 for either outpatient or inpatient care, with a primary or secondary diagnosis of an anxiety disorder, were identified.

Definition of hyperlipidemia

Study subjects receiving medication for the treatment of hyperlipidemia, or with one primary or secondary diagnosis of hyperlipidemia (ICD-9-CM: 272.0, 272.1, 272.2, 272.3, or 272.4), under either an outpatient or inpatient care service, were identified. Hypolipidemic drugs recorded included bile acid sequestrants (cholestyramine, colestipol and dextran sulfate sodium), fibric acid derivatives
(aluminium clofibrate, bezafibrate, clofibrate, etofibrate, fenofibrate, gemfibrozil and simfibrate), HMG-CoA reductase inhibitors (atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin and simvastatin), nicotinic acid and derivatives (acipimox, niceritrol, nicofuranose and nicomol) and other lipid-modifying agents (ezetimibe, probucol and soysterol) [12, 13].

**Prevalence of hyperlipidemia**

To calculate the prevalence of hyperlipidemia in the control general population, the formula was:

\[
\text{Prevalence} = \frac{\text{No. of prevalent cases of hyperlipidemia in 2005}}{\text{No. of total study subjects in 2005}}.
\]

To calculate the prevalence of hyperlipidemia in anxiety patients, the calculation formula was:

\[
\text{Prevalence} = \frac{\text{No. of prevalent cases of hyperlipidemia in patients with anxiety disorders in 2005}}{\text{No. of total anxiety subjects in 2005}}.
\]

**Incidence of hyperlipidemia**

Incident hyperlipidemia in this fixed cohort was defined as both patients with anxiety disorders and the general population with new cases of hyperlipidemia from 2006 to 2010, but with no hyperlipidemia diagnosis before 2006. The average annual incidence was calculated from 2006 to 2010 using the following formula: 

\[
\text{Average annual incidence} = \frac{\text{No. of incident hyperlipidemia cases}}{\text{No. of person-years contributed by the study subjects}}.
\]

**Definition of diabetes**

Subjects with diabetes in this study were defined as those who had at least one prescription (insulin or oral hypoglycemic agent) for the treatment of the disease in 2005 [14].

**Definition of hypertension**

Subjects with hypertension in this study were defined as those who had a primary or secondary diagnosis of hypertension (ICD-9-CM: 401–405) combined with treatment using an antihypertensive drug in 2005 [15].

**Measures**

The demographic characteristics of the subjects analyzed in this study included age, gender, region, urbanicity and insurance amount. Subjects were classified into three age categories: 18–39, 40–59 and ≥60 years. Subjects were divided into one of five categories for the insurance amount: fixed
premium, dependent, less than 20,000 New Taiwan Dollars (NTD) (<640 US dollars (USD)), 20,000–39,999 NTD (640–1280 USD), and 40,000 NTD or more (≥ 1281 USD). We used the insurance amount for the analysis rather than socioeconomic status (SES) in this study, and persons with a fixed premium were in the lowest cluster of the SES ranking system. With regards to geographic distribution, four different regions of Taiwan: east, north, central and south, was used to classify the study subjects. Urbanicity was classified into rural, urban, and suburban categories according to household registration system in Taiwan. Antidepressant use, antipsychotic use and mood stabilizer use in the identified subjects were defined as absent or present.

**Statistical analysis**

The differences in the prevalence of hyperlipidemia between patients with anxiety disorders and the general population according to age group, gender, region, urbanicity and insurance amount were examined by logistic regression, with adjustment for the other covariates. Multiple logistic regression was used to analyze the associated factors for cases of hyperlipidemia in anxiety patients in 2005. The differences in the incidence of hyperlipidemia between anxiety patients and the general population according to age group and gender were tested by Cox regression, with adjustment for the other covariates. Finally, a Cox regression model was used to investigate risk factors for incident hyperlipidemia in anxiety patients from 2006 to 2010. SAS version 9.1 was used to analyze the data, and the significance level was set at 0.05.

**Results**

Analyses of the prevalence of hyperlipidemia in anxiety patients and the general population in 2005 (Table 1) indicated that the prevalence of hyperlipidemia in anxiety patients was higher than that in the general population (21.3% vs. 7.6%; OR = 2.14; 95% confidence interval [CI], 2.07 to 2.22; P < 0.001) in 2005. Comparing the results with those of the general population, it was observed that anxiety patients in the following groups had a higher prevalence of hyperlipidemia: all three age groups; both genders; persons living in all regions; persons living in all areas; and all insurance amount groups.
Table 1
Prevalence of hyperlipidemia in patients with anxiety disorders and the general population.

| Variables          | Anxiety disorders (n = 21,808) | General population (n = 731,150) | OR<sup>a</sup> | 95% C.I.     | P value |
|--------------------|---------------------------------|----------------------------------|-----------------|--------------|---------|
|                    | %                               | %                                |                 |              |         |
| Age, years         |                                 |                                  |                 |              |         |
| 18–39              | 6.0                             | 1.7                              | 3.94            | 3.47–4.47    | <0.001  |
| 40–59              | 22.4                            | 9.9                              | 2.70            | 2.56–2.83    | <0.001  |
| ≥ 60               | 28.7                            | 19.9                             | 1.56            | 1.48–1.64    | <0.001  |
| Gender             |                                 |                                  |                 |              |         |
| Male               | 20.5                            | 7.7                              | 2.19            | 2.07–2.32    | <0.001  |
| Female             | 21.7                            | 7.5                              | 2.07            | 1.98–2.17    | <0.001  |
| Insurance amount   |                                 |                                  |                 |              |         |
| Fixed premium      | 21.0                            | 8.4                              | 1.97            | 1.80–2.16    | <0.001  |
| Dependent          | 24.9                            | 9.3                              | 1.85            | 1.73–1.97    | <0.001  |
| < 20,000 NTD (< 640 USD) | 19.5                        | 7.1                              | 2.13            | 2.00–2.27    | <0.001  |
| 20,000–39,999 NTD (640–1280 USD) | 21.1                        | 6.1                              | 2.79            | 2.56–3.05    | <0.001  |
| ≥ 40,000 NTD (≥ 1281 USD) | 18.3                        | 7.4                              | 2.33            | 2.07–2.61    | <0.001  |
| Region*            |                                 |                                  |                 |              |         |
| North              | 22.4                            | 7.5                              | 2.21            | 2.10–2.32    | <0.001  |
| Center             | 18.5                            | 6.5                              | 2.10            | 1.94–2.28    | <0.001  |
| South              | 21.3                            | 7.6                              | 2.13            | 2.06–2.21    | <0.001  |
| East               | 19.3                            | 8.1                              | 1.95            | 1.51–2.53    | <0.001  |
| Urbanicity*        |                                 |                                  |                 |              |         |
| Urban              | 22.3                            | 7.7                              | 2.20            | 2.11–2.30    | <0.001  |
| Suburban           | 19.8                            | 7.4                              | 2.11            | 1.92–2.31    | <0.001  |
| Rural              | 19.6                            | 7.2                              | 2.00            | 1.86–2.15    | <0.001  |
| Total              | 21.3                            | 7.6                              | 2.14            | 2.07–2.22    | <0.001  |

* Data for 17 subjects were missing.
* Adjusted for age, sex, insurance amount, region, and urbanicity.

Table 2 shows the logistic regression analysis of factors associated with the prevalence of hyperlipidemia in anxiety patients. A higher prevalence was found in the older age groups of 40–59 and ≥ 60 years; in persons with hypertension; in persons with diabetes; in persons with antipsychotic use; and in persons with mood stabilizer use.
Table 2
Logistic regression model of factors associated with the prevalence of hyperlipidemia in patients with anxiety disorders in 2005.

| Variable                          | Logistic regression model | 95% CI  |
|-----------------------------------|---------------------------|---------|
|                                  | OR                        |         |
| Age, years                        |                           |         |
| 18–39                             | 1.00                      |         |
| 40–59                             | 3.27<sup>c</sup>          | 2.85–3.74|
| ≥ 60                              | 3.42<sup>c</sup>          | 2.96–3.95|
| Gender                            |                           |         |
| Male                              | 1.00                      |         |
| Female                            | 1.04                      | 0.96–1.11|
| Antipsychotic use                 |                           |         |
| Without                           | 1.00                      |         |
| With                              | 1.09<sup>a</sup>          | 1.00–1.18|
| Antidepressant use                |                           |         |
| Without                           | 1.00                      |         |
| With                              | 1.03                      | 0.95–1.11|
| Mood stabilizer use               |                           |         |
| Without                           | 1.00                      |         |
| With                              | 1.17<sup>a</sup>          | 1.02–1.34|
| Diabetes                          |                           |         |
| Without                           | 1.00                      |         |
| With                              | 3.42<sup>c</sup>          | 3.12–3.74|
| Hypertension                      |                           |         |
| Without                           | 1.00                      |         |
| With                              | 2.15<sup>c</sup>          | 2.00–2.31|
| Insurance amount                  |                           |         |
| Fixed premium                     | 1.00                      |         |
| Dependent                         | 1.14<sup>a</sup>          | 1.02–1.28|
| < 20,000 NTD (< 640 USD)          | 1.00                      | 0.90–1.13|
| 20,000–39,999 NTD (640–1280 USD)  | 1.25<sup>c</sup>          | 1.10–1.42|
| ≥ 40,000 NTD (≥ 1281 USD)         | 1.14                      | 0.98–1.32|
| Region                            |                           |         |
| North                             | 1.28                      | 0.98–1.66|
| Center                            | 0.99                      | 0.76–1.30|
| South                             | 1.19                      | 0.91–1.55|
| East                              | 1.00                      |         |
| Urbanicity                        |                           |         |
| Urban                             | 1.17<sup>c</sup>          | 1.07–1.28|
| Suburban                          | 1.01                      | 0.90–1.13|
| Rural                             | 1.00                      |         |

<sup>a</sup> P < 0.05
<sup>b</sup> P < 0.01
<sup>c</sup> P < 0.001

Table 3 shows the annual incidence of hyperlipidemia in anxiety patients and the general population from 2006 to 2010. The annual incidence of hyperlipidemia for anxiety disorders was higher than that in the general population (5.49% vs. 2.50%; risk ratio [RR] = 1.64; 95% CI, 1.58 to 1.70; P < 0.001). Compared with the general population, anxiety patients had a higher incidence of hyperlipidemia if they were from the following groups: all three age groups; and both genders.
Table 3
Incidence of hyperlipidemia in patients with anxiety disorders and the general population from 2006 to 2010.

| Year       | Anxiety Disorders | General population | RR a | 95% C.I. | P value |
|------------|-------------------|---------------------|------|---------|---------|
|            | Incident cases    | Person-years        | Annual incidence (per 100) | Incident cases | Person-years | Annual incidence (per 100) |
| Age, years |                   |                     |                                |                |           |                        |
| 18–39      | 445               | 17986.5             | 2.47                           | 18970          | 1650194    | 1.15                     | 2.24                     | 2.04–2.46   | < 0.001 |
| 40–59      | 1635              | 23047.5             | 7.09                           | 37227          | 924998.5   | 4.02                     | 1.73                     | 1.64–1.82   | < 0.001 |
| ≥ 60       | 942               | 14033               | 6.71                           | 15987          | 313507.5   | 5.10                     | 1.28                     | 1.20–1.37   | < 0.001 |
| Gender     |                   |                     |                                |                |           |                        |
| Male       | 1051              | 20574.5             | 5.11                           | 36772          | 1413112.0  | 2.60                     | 1.57                     | 1.47–1.67   | < 0.001 |
| Female     | 1971              | 34492.5             | 5.71                           | 35412          | 1475588.0  | 2.40                     | 1.64                     | 1.51–1.72   | < 0.001 |
| 2006–2010  | 3022              | 55067.0             | 5.49                           | 72184          | 2888700.0  | 2.50                     | 1.64                     | 1.58–1.70   | < 0.001 |

a Adjusted for age, gender, insurance amount, region, and urbanicity.

Table 4 shows the Cox regression analysis of risk factors for hyperlipidemia in anxiety patients from 2006 to 2010. A higher incidence was found in the older age groups of 40–59, and ≥ 60 years, in females, in persons with hypertension, in those with diabetes, and in those with a higher SES.
Table 4
Cox regression model of factors associated with the incidence of hyperlipidemia in patients with anxiety disorders from 2006 to 2010.

| Variable                        | Cox regression model | 95% CI          |
|---------------------------------|----------------------|-----------------|
|                                | HR                   |                 |
| Age, years                      | 1.00                 |                 |
| 18–39                           | 1.00                 |                 |
| 40–59                           | 2.41 c               | 2.17–2.69       |
| ≥ 60                            | 1.96 c               | 1.73–2.23       |
| Gender                          |                      |                 |
| Male                            | 1.00                 |                 |
| Female                          | 1.10 a               | 1.02–1.19       |
| Antipsychotic exposure          |                      |                 |
| No                              | 1.00                 |                 |
| Yes                             | 1.00                 | 0.92–1.09       |
| Antidepressant use              |                      |                 |
| No                              | 1.00                 |                 |
| Yes                             | 1.04                 | 0.96–1.13       |
| Mood stabilizer use             |                      |                 |
| No                              | 1.00                 |                 |
| Yes                             | 0.85                 | 0.72–1.01       |
| Diabetes                        |                      |                 |
| Without                         | 1.00                 |                 |
| With                            | 1.48 c               | 1.29–1.68       |
| Hypertension                    |                      |                 |
| Without                         | 1.00                 |                 |
| With                            | 1.73 c               | 1.59–1.87       |
| Insurance amount                |                      |                 |
| Fixed premium                   | 1.00                 |                 |
| Dependent                       | 1.04                 | 0.92–1.18       |
| < 20,000 NTD (< 640 USD)        | 1.13 a               | 1.01–1.28       |
| 20,000–39,999 NTD (640–1280 USD)| 1.19 b               | 1.04–1.36       |
| ≥ 40,000 NTD (≥ 1281 USD)       | 1.10                 | 0.95–1.28       |
| Region                          |                      |                 |
| North                           | 1.00                 |                 |
| Center                          | 0.93                 | 0.85–1.03       |
| South                           | 0.93                 | 0.86–1.02       |
| East                            | 0.84                 | 0.64–1.11       |
| Urbanicity                      |                      |                 |
| Urban                           | 1.00                 | 0.92–1.10       |
| Suburban                        | 0.95                 | 0.84–1.06       |
| Rural                           | 1.00                 |                 |

Discussion

This was the first population-based study that employed a large dataset from the Taiwan NHI to investigate two key parameters, the prevalence and incidence of hyperlipidemia, in patients with anxiety disorders. In order to confirm the role of anxiety disorders in the disease, we also compared these two parameters between patients with anxiety disorders and the general population. The current study revealed that anxiety patients exhibited a 2.14-fold higher prevalence of
hyperlipidemia than the general population, at 21.3% and 7.6%, respectively, in 2005. We also found that anxiety patients had a 1.64-fold higher average annual incidence of hyperlipidemia than the general population, at 5.49% and 2.50%, respectively, from 2006 to 2010. Therefore, our findings supported the hypothesis that a positive association exists between anxiety disorders and hyperlipidemia. To understand the underlying mechanism, the influence of several physiological actions needs to be taken into account. First, raising autonomic arousal in anxiety patients is mediated by the hypothalamic–pituitary–adrenal axis, which augments the release of catecholamines in the blood circulation \[16\]. Psychosocial threat has a negative effect on hormonal homeostasis, and also causes autonomic nervous system problems, which are all hit by the abnormal concentration of catecholamine in the circulatory system. This further causes various health problems, such as hypertension, inflammatory response, insulin resistance and other metabolic disorders \[17\]. One population-based cohort study revealed that women who exhibited high responses to psychological distress, such as tension, anger, and depression, at baseline had an increased risk of developing metabolic syndrome later \[18\]. The available evidence suggests that anxiety is connected to altered cortisol activity, and elevated levels of anxiety symptoms are linked to a less prominent cortisol awakening response \[19\]. Second, individuals with anxiety disorders are likely to have an unhealthy lifestyle, including unhealthy dietary habits, smoking, heavy alcohol use, sleep disturbances, physical inactivity and lack of leisure activity, which may lead to obesity, hyperlipidemia, diabetes, and hypertension \[20\]. One study of psychiatric outpatients in Canada revealed that lifestyle factors related to health status (hypertension, obesity, diabetes mellitus, and hyperlipidemia) and health risks are not only limited to patients with schizophrenia, but also extend to those with bipolar, depressive, and anxiety disorders \[21\]. Additionally, anxiety patients are associated with onset of alcohol dependence with abuse (OR, 3.2) \[22\], which may lead to fatty liver with hyperlipidemia. Alcohol use may lead to the development of nonalcoholic fatty liver disease due to the interaction between alcohol and metabolic disturbances. Long-term alcohol use inhibits the production of insulin or insulin-like growth factor in the liver, which causes steatohepatitis, insulin resistance, and oxidative stress or injury \[23\]. Third, anxiety patients have higher likelihoods of hypertension (OR, 2.61) and
diabetes (OR, 1.23) [10, 11], which may produce complex interactions and are risk factors of hyperlipidemia. Fourth, anxiety patients are more likely to seek medical evaluation, therefore increasing the chance of being diagnosed with hyperlipidemia. On the other hand, the prevalence of hyperlipidemia in anxiety patients and in the general population in this NHI data study was lower than has been reported in community studies [4, 5]. Not all persons with hyperlipidemia seek medical treatment in NHI programs, and assessment for dyslipidemia is not conducted as often as assessments for diabetes and hypertension in outpatient services in Taiwan. Therefore, both physicians and psychiatrists should evaluate dyslipidemia in patients with anxiety disorders and provide comprehensive medical and psychiatric treatment. Study of subjects who had been aware of their elevated cholesterol level for a long period demonstrated that realization of their own risk of disease does lead to persisting beneficial effects on health behavior in comparison with the general population; thus, dietary counseling is recommended for the larger public to positively influence long-term awareness of hyperlipidemia [24]. Our study revealed that anxiety patients had a much higher prevalence of hyperlipidemia in the young adult age groups (age 18–39) than in the general population of the same age group (OR, 3.94). In this age group, the incidence of hyperlipidemia among patients with anxiety disorders was also noted to be much higher than that in the general population (RR, 2.24). According to the available literature, the mean age of onset of anxiety disorders is during the ages of 20-30 years.[1] Younger anxiety patients may have unhealthier lifestyles, greater alcohol use, higher smoking rates, and a higher likelihood of obesity. Younger people may also have a greater likelihood of ignoring their physical status, resulting in the underdiagnosis and undertreatment of hyperlipidemia in this age group. We should pay more attention to ensuring that young adults with anxiety disorders receive necessary lipid profile monitoring, as well as fostering a healthy diet and encouraging more regular exercise.

Considering gender, our study revealed that the prevalence of hyperlipidemia was higher in men (OR, 2.19) and in women (OR, 2.07) with anxiety disorders than in the general population. The incidence of hyperlipidemia was also higher in men (RR, 1.57) and in women (RR, 1.64) with anxiety disorders than in the general population. In addition, based on our results, the incidence of hyperlipidemia among
patients with anxiety disorders was also higher in females than in males (HR, 1.1), and both genders with anxiety disorders were found to have an increased risk of hyperlipidemia. It has been reported that anxiety disorders are twice as common in women as in men [16]. Moreover, a study reported that decreasing levels of psychological distress may help women to avert development of metabolic syndrome [18]. Therefore, more attention should be paid to gender differences in anxiety patients with hyperlipidemia.

Generally, patients with anxiety disorders received antipsychotic treatment for refractory anxiety symptoms or severe insomnia. This study found that anxiety patients receiving antipsychotic medications had a higher hyperlipidemia risk than the control subjects (OR, 1.09). Antipsychotic use has been linked to weight gain, increased free fatty acids secretion in the liver, and enhanced triglyceride synthesis and very-low-density lipoprotein release in the liver [25]. Previous studies have described that some antipsychotic drugs cause individuals to become susceptible to hyperlipidemia owing to increasing weight gain, dietary changes and development of glucose intolerance [26]. A previous study also suggested that this type of drug, which is commonly prescribed, causes patients with schizophrenia or mood disorders to experience an increased risk of hyperlipidemia [27]. Therefore, in order to help patients using antipsychotic medication to detect early on the development of the disease, regular checks of blood lipid levels and proper treatment are necessary.

The current study found that anxiety patients taking mood stabilizer medications had a higher risk of hyperlipidemia than the general population (OR, 1.17). Among common mood stabilizers, valproate increased the risk of metabolic disturbances owing to an increased body mass index, elevated insulin and triglycerides, and lower levels of high-density lipoprotein by affecting brain glucose transport. We suggest including lipid profile testing as a routine examination in anxiety patients treated with mood stabilizers.

Diabetes and hypertension were both found to be risk factors for hyperlipidemia in the current study. Diabetes and hypertension increased the prevalence of hyperlipidemia by 3.42 and 2.15 times, respectively. Diabetes and hypertension also increased the incidence of hyperlipidemia by 1.48 and 1.73 times, respectively. Other metabolic conditions were found to be common among patients with
anxiety disorder in previous studies. Anxiety patients also have increased risks of diabetes and hypertension compared to the general population [10, 11]. Patients with anxiety disorders who have multiple metabolic disturbances, including hyperlipidemia, diabetes, and hypertension, should receive a comprehensive medical evaluation and intervention. 

This study used a large population-based dataset containing random samples to investigate the epidemiology of hyperlipidemia in anxiety patients and the general population. Additionally, we followed this cohort to investigate risk factors of hyperlipidemia in anxiety patients. However, there are still several limitations related to the design of this study: (1) The accuracy of diagnosis from the dataset using claims data—both the prevalence of anxiety disorders and hyperlipidemia are underestimated, and we could not link to medical charts for further justification in the present investigation. (2) No sub-classification of the disorder—subtype differentiation of anxiety disorders was not performed, such as for generalized anxiety disorder, panic disorder, phobic disorder, or obsessive-compulsive disorder, in this study. (3) Lack of detail of disorders and treatment—the comorbidities, duration, severity and psychotropic drug dosage in patients with anxiety disorders relevant to hyperlipidemia were not discussed in the current study. (4) No measures were available for certain factors—no detailed data were available in relation to factors such as alcohol use, smoking, occupation, obesity, or other lifestyle factors that may have strong links to hyperlipidemia. 

Conclusion

Patients with anxiety disorders had a higher prevalence and a greater incidence of hyperlipidemia than the control general population. The higher incidence of hyperlipidemia in anxiety patients was related to a greater age, the female gender, and the presence of diabetes and hypertension. It is necessary for us to focus on the prevention (illness awareness and diet counseling), early detection, and comprehensive treatment of hyperlipidemia in anxiety patients.

Abbreviations

NHI

National Health Insurance; NTD: New Taiwan Dollars

Declarations

Ethics approval and consent to participate
The Institutional Review Board of Taoyuan Mental Hospital has approved this study before starting data collection.

**Consent for publication**

Not applicable.

**Availability of data and materials**

The Taiwan National Health Research Institute generates a medical claims database, which is made available to researchers for health-related study.

**Competing interests**

We have no competing interests.

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**Authors’ contributions**

Dr. IC Chien had designed this study and had written this paper, and Mr. CH Lin was responsible for statistics.

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**Authors' information (optional)**

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References

1. Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM, Wittchen H-U. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. Int J Methods Psychiatr Res. 2012;21:169–84.

2. Roy-Byrne PP, Davidson KW, Kessler RC, Asmundson GJ, Goodwin RD, Kubzansky L, Lydiard RB, Massie MJ, Katon W, Laden SK, Stein MB. Anxiety disorders and comorbid medical illness. Gen Hosp Psychiatry. 2008;30:208–25.

3. Haffner SM. Diabetes, hyperlipidemia, and coronary artery disease. Am J Cardiol. 1999;83:17F–21F.

4. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA. 2002;287:356–59.

5. Chang HY, Yeh WT, Chang YH, Tsai KS, Pan WH. Prevalence of dyslipidemia and mean blood lipid values in Taiwan: results from the Nutrition and Health Survey in Taiwan (NAHSIT, 1993-1996). Chinese J Physiol. 2002;45:187–97.

6. Carroll D, Phillips AC, Thomas GN, Gale CR, Deary I, Batty GD. Generalized anxiety disorder is associated with metabolic syndrome in the Vietnam experience study. Biol Psychiatry. 2009;66:91–3.

7. Sanna L, Stuart AL, Pasco JA, Kotowicz MA, Berk M, Girardi P, et al. Physical comorbidities in men with mood and anxiety disorders: a population-based study. BMC Med 2013;24110. doi:10.1186/1741-7015-11-110.

8. Sonino N, Navarrini C, Ruini C, Ottolini F, Paoletta A, Fallo F, et al. Persistent psychological distress in patients treated for endocrine disease. Psychother Psychosom. 2004;73:78-83.

9. Chien IC, Chou Yj, Lin CH, Bih SH, Chou P. Prevalence of psychiatric disorders among National Health Insurance Enrollees in Taiwan. Psychiatr Serv. 2004;55:691–7.

10. Wu EL, Chien IC, Lin CH. Increased risk of hypertension in patients with anxiety disorders: a population-based study. J Psychosom Res. 2014;77:522–7.

11. Chien IC, Lin CH. Increased risk of diabetes in patients with anxiety disorders: A population-based study. J Psychosom Res. 2016;86:47-52.

12. Chien IC, Lin CH, Chou Yj, Chou P. Increased risk of hyperlipidemia in patients with major depressive disorder: a population-based study. J Psychosom Res. 2013;75:270-4.

13. Hsu JH, Chien IC, Lin CH. Increased risk of hyperlipidemia in patients with bipolar disorder: a population-based study. Gen Hosp Psychiatry. 2015;37:294-8.
14. Chien IC, Hsu JH, Lin CH, Bih SH, Chou YJ, Chou P. Prevalence of diabetes in patients with schizophrenia in Taiwan: a population-based National Health Insurance study. Schizophr Res. 2009;111:17-22.

15. Wu EL, Chien IC, Lin CH, Chou YJ, Chou P. Increased risk of hypertension in patients with major depressive disorder: a population-based study. J Psychosom Res. 2012;73:169-74.

16. Tyrer P, Baldwin D. Generalised anxiety disorder. Lancet. 2006;368:2156-66.

17. Curtis BM, O'Keefe JH Jr. Autonomic tone as a cardiovascular risk factor: the dangers of chronic fight or flight. Mayo Clin Proc. 2002;77:45-54.

18. Raikkonen K, Matthews KA, Kuller LH. The relationship between psychological risk attributes and the metabolic syndrome in healthy women: antecedent or consequence? Metabolism. 2002;51:1573-7.

19. Therrien F, Drapeau V, Beaulieu S, Dore J, Tremblay A, et al. Awakening cortisol response in relation to psychosocial profiles and eating behaviors. Physiol Behav. 2008;93:282-8.

20. Strine TW, Mokdad AH, Dube SR, Gonzalez O, Berry JT, et al. The association of depression and anxiety with obesity and unhealthy behaviors among community-dwelling US adults. Gen Hosp Psychiatr. 2008;30:127-37.

21. Chuang HT, Mansell C, Patten SB. Lifestyle characteristics of psychiatric outpatients. Can J Psychiatry. 2008;5:260-6.

22. Swendsen J, Conway KP, Degenhardt L, Glantz M, Jin R, Merikangas KR, Sampson N, et al. Mental disorders as risk factors for substance use, abuse and dependence: results from the 10-year follow-up of the National Comorbidity Survey. Addiction. 2010;105:1117-28.

23. de la Monte S, Dermak Z, Wands JR. Alcohol, insulin resistance and the liver-brain axis. J Gastroenterol Hepatol. 2012;27:33-41.

24. Einvik G, Ekeberg O, Lavik JG, Ellingsen I, Klemesdal TO, Hjerkinn EM. The influence of long-term awareness of hyperlipidemia and of 3 years of dietary counseling on depression, anxiety, and quality of life. J Psychosom Res. 2010;68:567-72.

25. Sanna L, Stuart AL, Pasco JA, Kotowicz MA, Berk M, Girardi P, et al. Physical comorbidities in men with mood and anxiety disorders: a population-based study. BMC Med 2013;24110. doi:10.1186/1741-7015-11-110.

26. Meyer JM, Koro CE. The effects of antipsychotic therapy on serum lipids: a comprehensive review. Schizophrenia Res. 2004;70:1-17.

27. Olsson M, Marcus SC, Corey-Lisle P, Tuomari AV, Hines P, L'Italien GJ. Hyperlipidemia following treatment with antipsychotic medications. Am J Psychiatry. 2006;163:1821-5.

28. Chang HH, Yang YK, Gean PW, Huang HC, Chen PS, Lu RB. The role of valproate in metabolic
disturbances in bipolar disorder patients. J Affect Disord. 2010;124:319–23.