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Increased risk of hypothyroidism and hyperthyroidism in patients with major depressive disorder: A population-based study

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ABSTRACT

Objective: To determine the prevalence and incidence of hypothyroidism, hyperthyroidism, and risk factors in patients with major depressive disorder (MDD).
Methods: The National Health Research Institute provided a database of 1,000,000 random subjects for health service studies. We identified subjects aged ≥18 years who had at least 1 service claim during 2005 with a primary diagnosis of MDD or with a primary or secondary diagnosis of hypothyroidism or hyperthyroidism. We also compared the incidence of hypothyroidism and hyperthyroidism among patients with MDD and the general population from 2006 through 2010.
Results: The prevalence of hypothyroidism in patients with MDD was higher than that in the general population (1.20% vs. 0.30%; odds ratio, 3.08; 95% confidence interval, 2.35–4.03) in 2005. The prevalence of hyperthyroidism was also higher in patients with MDD than in the general population (2.46% vs. 0.79%; odds ratio, 2.77; 95% confidence interval, 2.29–3.35) in 2005. The annual incidence of hypothyroidism was higher in patients with MDD than that in the general population (0.40% vs. 0.13%; risk ratio, 2.47; 95% confidence interval, 2.00–3.06). The annual incidence of hyperthyroidism was also higher in patients with MDD than that in the general population (0.72% vs. 0.32%; risk ratio, 2.06; 95% confidence interval, 1.75–2.43).
Conclusions: Patients with MDD had a higher prevalence and a higher incidence of hypothyroidism or hyperthyroidism than the general population. Female sex was a risk factor for hypothyroidism and hyperthyroidism in MDD.

Introduction

Hypothyroidism is one of the most common endocrine disorders encountered in clinical practice. The prevalence of hypothyroidism measured with different surveys varies between 1% and 4.6% [1,2]. The prevalence of hypothyroidism increases with age [1] and is higher among patients older than 65 years, with 1.7% of these having overt hypothyroidism and 13.7% having subclinical hypothyroidism [2]. Hypothyroidism is nearly 10 times more common in females than in males [2,3]. The prevalence of hyperthyroidism in the community is about 1.2% [4,5]. The reported prevalence of hyperthyroidism in elderly persons ranges widely, from 0.4% to 2% [1,5]. Hyperthyroidism is also approximately 10 times more common in women than in men [1,5].

It has long been recognized that thyroid hormones play an important role in neuropsychiatric manifestations, such as mood disturbances, cognitive impairment, and other psychiatric symptoms [6]. The psychiatric symptoms of hypothyroidism are generally well recognized but overlap with some of the symptoms of major depressive disorder (MDD), including low appetite, energy changes, sleep disruption and tiredness, poor concentration, depressed mood, impaired memory, and other cognitive defects [7,8]. Therefore, severe hypothyroidism can mimic melancholic depression. With regard to hyperthyroidism, affective psychosis (e.g., depression and mania) can result from thyrotoxicosis [9], and a significant number of patients with hyperthyroidism have long been noticed to meet diagnostic criteria for major depressive episode [1,10,11]. Hyperthyroidism may present differently depending on the age of the patient. In younger patients, hyperthyroidism typically manifests as hyperactivity or anxious dysphoria [12], whereas in the elderly, it can manifest as apathy or depression, referred to as apathetic hyperthyroidism [13].

However, the causal relationship between depression and overt thyroid dysfunction is still speculative and requires confirmation from further studies. One recent study indicated that patients with

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psychiatric disorders, especially depression, have elevated rates of thyroid disease [14]. However, this study only enrolled individuals aged >55 years, limiting the generalizability of the findings to the general population. Another large study of patients with recurrent MDD showed that patients with MDD had higher rates of thyroid disease than controls [15]. In contrast, another study revealed that respondents with MDD did not have a statistically significant higher incidence of thyroid disease than respondents without MDD [16]. Another major limitation of both studies is that they depended on self-report of thyroid disorders, making the results difficult to interpret [17]. Therefore, these inconsistent findings do not clarify the casual association between MDD and overt thyroid dysfunction.

Taiwan implemented the National Health Insurance (NHI) program in March 1995, offering a comprehensive, unified, and universal health insurance program to all citizens. As much as 98% of the population of Taiwan has joined the NHI program since 2005, and the Bureau of NHI has contracted with 91% of the medical institutions in Taiwan.

This study uses national insurance data to test the hypothesis that individuals with MDD have increased risk of overt thyroid disorders, including both hyperthyroidism and hypothyroidism. We determined the prevalence of hypothyroidism and hyperthyroidism in persons with MDD in 2005 and compared factors associated with hypothyroidism and hyperthyroidism between patients with MDD and the general population. We also compared the incidence of hypothyroidism and hyperthyroidism among patients with MDD and the general population from 2006 through 2010. Finally, we analyzed the risk factors for hypothyroidism and hyperthyroidism in this cohort during the same period.

Methods

Sample

The National Health Research Institute provided a database of 1,000,000 random subjects (about 4.5% of the population), including data related to outpatient care, inpatient care, dental services, and prescription drugs. Longitudinal Health Insurance Database 2005 contains the original claim data of 1,000,000 beneficiaries random sampling from the NHI Research Database in 2005. There were no statistically significant differences in age, sex, or average insured payroll-related amount between the sample group and all enrollees. Subjects <18 years of age in 2005 were excluded from the current study, leaving 766,427 subjects. This study was approved by the Institutional Review Board of Taoyuan Mental Hospital.

Definition of MDD

The diagnostic coding used by the NHI in Taiwan follows the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic criteria. We identified subjects who had at least 1 service claim during 2005 for outpatient or inpatient care with a primary diagnosis of MDD (ICD-9-CM: 296.2 or 296.3).

Definition of hypothyroidism

Subjects who had a primary or secondary diagnosis of hypothyroidism (ICD-9-CM: 243 or 244) in 2005 and during 2006–2010, for either outpatient or inpatient care, were identified as having a diagnosis of hypothyroidism.

Definition of hyperthyroidism

Subjects who had a primary or secondary diagnosis of hyperthyroidism (ICD-9-CM: 242) in 2005 and during 2006–2010, for either outpatient or inpatient care, were identified as having a diagnosis of hyperthyroidism.

Prevalence of hypothyroidism or hyperthyroidism

Prevalence was defined as any history of existing or prior hypothyroidism or hyperthyroidism at the entry date in 2005, not all the (incident) number of cases in 2005. The denominator was the total number of study subjects in 2005, and the numerator was the number of cases of hypothyroidism in 2005. The prevalence of hyperthyroidism in 2005 was calculated using the same method as hypothyroidism.

Incidence of hypothyroidism or hyperthyroidism

Subjects with newly diagnosed hypothyroidism and no hypothyroidism diagnosis before 2006 were referred to as incident case patients, and we calculated the incidence for 2006–2010. The numerator was the number of incident cases of hypothyroidism, and the denominator was the number of person-years contributed by the study subjects. The incidence of hyperthyroidism was calculated using the same method as hypothyroidism.

Measures

Demographic data, such as age, sex, antipsychotic use, antidepressant use, mood stabilizer use, insurance amount, region, and population density, were directly obtained from individual BNHI files. Three categories of age were defined: 18–39, 40–59, and ≥60 years. Antipsychotic use was classified as no antipsychotic use, first-generation antipsychotic use, and second-generation antipsychotic use. Antidepressant use was classified as no antidepressant use, first-generation antidepressant use (tricyclic antidepressants), and second-generation antidepressant use. Mood stabilizer use was defined as present or absent. Insurance amount was classified into 5 categories: fixed premium, dependent, less than US $640 (NTD 20,000), US $640–$1280 (NTD 20,000–39,999), and US $1281 (NTD 40,000) or more. We used the insured amount as a proxy for socioeconomic status. For geographical distribution, study subjects were classified as residing in 1 of 4 regions: northern, central, southern, or eastern Taiwan. Population density was classified as urban, suburban, or rural.

Statistical analysis

We used logistic regression to test differences in the prevalence of hypothyroidism and hyperthyroidism between patients with MDD and the general population according to age group and sex. We adjusted for the other covariates, which included age, sex, insurance amount, region, and urbanicity. We used Cox regression to test differences in the incidence of hypothyroidism and hyperthyroidism between patients with MDD and the general population according to age group

Table 1
Prevalence of hypothyroidism in persons with major depressive disorder and in the general population

Variable	MDD, % (n=4593)	General population, % (n=761,834)	OR[a]	95% CI	p
Age, years					
18–39	0.88	0.18	4.05	2.42–6.78	<0.001
40–59	1.42	0.37	3.17	2.14–4.70	<0.001
≥60	1.32	0.48	2.45	1.43–4.17	<0.001
Sex					
Male	0.24	0.10	1.92	0.71–5.16	0.1961
Female	1.73	0.49	3.23	2.44–4.27	<0.001
Total	1.20	0.30	3.08	2.35–4.03	<0.001

Abbreviations: CI, confidence interval; MDD, major depressive disorder; OR, odds ratio.
[a] Odds ratio adjusted for other covariates, including age, sex, insurance amount, region, and urbanicity.