Original Article

Comorbidity of narcolepsy and depressive disorders: a nationwide population-based study in Taiwan


**Department of Child and Adolescent Psychiatry, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan**
**Department of Psychiatry, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan**
**Department of Psychiatry, School of Medicine and Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan**
**Department of Psychiatry, College of Medicine, National Yang-Ming University, Taipei, Taiwan**
**Institute of Statistical Science, Academia Sinica, Taipei, Taiwan**
**Department of Biopharmaceutical Sciences, National Yang-Ming University, Taipei, Taiwan**
**Department of Psychiatry, College of Medicine, National Yang-Ming University, Taipei, Taiwan**
**Community Medicine Research Center, Keelung Chang Gung Memorial Hospital, Keelung, Taiwan**
**Department of Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA**
**Department of Chinese Medicine, College of Medicine, Chung Gung University, Kwei-Shan, Taoyuan, Taiwan**
**Department of Ophthalmology, Chang Gung Memorial Hospital, Keelung, Keelung, Taiwan**
**Institute of Molecular Biology, Academia Sinica, Nankang, Taipei, Taiwan**
**Department of Nursing, Research Center for Food and Cosmetic Safety, Research Center for Chinese Herbal Medicine, College of Human Ecology, Chang Gung University of Science and Technology, Taiwan**
**Department of Nutrition and Health Sciences, Research Center for Food and Cosmetic Safety, Research Center for Chinese Herbal Medicine, College of Human Ecology, Chang Gung University of Science and Technology, Taiwan**

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**Abstract**

Objective: Narcolepsy is a chronic sleep disorder that is likely to have neuropsychiatric comorbidities. Depression is a serious mood disorder that affects individuals’ daily activities and functions. The current study aimed to investigate the relationship between narcolepsy and depressive disorders.

Methods: The study consisted of patients diagnosed with narcolepsy between January 2002, and December 2011 (n = 258), and age-matched and gender-matched controls (n = 2580) from Taiwan’s National Health Insurance database. Both the patients and the controls were monitored through December 31, 2011, to identify the occurrence of a depressive disorder. A multivariate logistic regression model was used to assess the narcolepsy’s potential influence on the comorbidity of a depressive disorder.

Results: During the study period, 32.7%, 24.8%, and 10.9% of the narcoleptic patients were comorbid with any depressive disorder, dysthymic disorder, and major depressive disorder, respectively. When compared to the control subjects, the patients with narcolepsy were at greater risks of having any depressive disorder (aOR 6.77; 95% CI 4.90–9.37), dysthymic disorder (aOR 6.62; 95% CI 4.61–9.57), and major depressive disorder (aOR 6.83; 95% CI 4.06–11.48). Of the narcoleptic patients that were comorbid with depression, >50% had been diagnosed with depression prior to being diagnosed with narcolepsy. Conclusions: This nationwide data study revealed that narcolepsy and depression commonly co-occurred. Since some symptoms of narcolepsy overlapped with those of depressive disorders, the findings serve as a reminder that clinicians must pay attention to the comorbidity of narcolepsy and depression.

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* Corresponding author. Department of Child and Adolescent Psychiatry, Kaohsiung Chang Gung Memorial Hospital, No. 123, Ta-Pei Road, Kaohsiung, Taiwan. Fax: +886 7 7326817.
** Corresponding author. Community Medicine Research Center, Keelung Chang Gung Memorial Hospital, Keelung, Taiwan. E-mail address: wangliangjen@gmail.com (L.-J. Wang).

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1. Introduction

Narcolepsy is a lifelong disabling sleep disorder that is characterized by excessive daytime sleepiness (EDS), cataplexy, sleep paralysis, fragmented nocturnal sleep, and hypnagogic hallucination [1]. Patients suffering from narcolepsy complain of excessive daytime sleepiness nearly every day, which may develop into irresistible sleep episodes. Cataplexy, another core symptom of narcolepsy, is characterized by the sudden loss of muscle tone, which is often prompted by intense emotion or excitement. The lifelong prevalence of narcolepsy is approximate 1 in 2000 in the general population, and this condition can severely hinder daily activities [2,3]. Furthermore, the high probability of having a comorbid condition, such as obesity, epilepsy, other sleep disorder, anxiety, and depression, significantly impacts a narcoleptic patient’s daily function, and may result in delayed diagnosis and improper treatment [1,4].

Depression is a common but serious mood disorder; symptoms affect an individual’s feelings, thoughts, drive, and ability to handle daily activities and functions [5]. Therefore, identifying depression among narcoleptic patients is vital for providing adequate intervention. Vignatelli et al. found that the presence of depressive symptoms was the major independent predictor of health-related quality of life over a 5-year period in narcoleptic individuals [6]. An increased risk of suicide ideation may also be associated with excessive daytime sleepiness, particularly when comorbid with a depressive disorder [7]. However, many studies have reported a high ratio of depressive moods among narcoleptic patients, although the incidence of depressive disorders related to narcolepsy remains unsettled. Ruoff et al. found that narcolepsy is associated with a wide range of mental illnesses, particularly anxiety and depressive disorders [8]. Furthermore, Ohayon et al. suggested that mood and anxiety disorders occurred more frequently among the narcoleptic group than the control group in their study, with major depressive disorder and social anxiety disorder being the most common [9]. Previous studies using self-reported questionnaires, such as Medical Outcome Short Form-36 (SF-36) and Beck Depression Inventory (BDI), have revealed that 45.1–56.9% of narcoleptic patients suffer from depression [10,11]. In contrast, two case-control studies that employed a structured psychiatric interview indicated that the prevalence of depressive disorders among narcoleptic patients was not higher than that of the healthy comparison group [12,13]. For example, Vourdas et al. found that 16% of narcoleptic patients and 18% of the control group had one or more episodes that met the DSM-IV criteria for major depression [12]. Likewise, Fortuyn et al. reported that 7% of narcoleptic patients had a current major depressive episode with 3% of controls [13]. Therefore, it remains controversial as to whether narcolepsy patients have a higher rate of depression.

One possible reason for the discrepancy in the comorbidity rate of narcolepsy and depression is the difficulty of differential diagnosis. Many somatic symptoms of narcoleptic patients (eg, sleep disturbance, fatigue, decreased attention, and weight changes) can also be considered to be depressive symptoms [14], thus posing a diagnostic dilemma when attempting to differentiate these overlapping symptoms between narcolepsy and depressive disorders in clinical settings. As a result, investigating the time sequence of the diagnoses of narcolepsy and depression may help to clarify the complexity among narcoleptic patients comorbid with a depressive disorder. It is assumed that some narcoleptic patients are diagnosed with depression prior to their narcolepsy diagnosis, while depression may be identified later in others.

Therefore, this nationwide population-based analysis was conducted to clarify the co-occurrence rate of narcolepsy and depressive disorders. An epidemiological methodology was also used to examine the time sequence between narcolepsy and depressive disorder diagnoses.

2. Materials and methods

2.1. Data source

The Institutional Review Board at Chang Gung Memorial Hospital approved this study. Data for this study were obtained from the ambulatory claims database of the National Health Insurance Research Database of Taiwan (NHIRD-TW). Implemented in 1995, National Health Insurance (NHI) is the compulsory universal health insurance program in Taiwan. As of the end of 2000, 22.3 million people in Taiwan (>96% of the population) were enrolled in the NHI program. The study used two subsets of the NHIRD-TW, the Longitudinal Health Insurance Database 2000 (LHID 2000) and the Longitudinal Health Insurance Database 2005 (LHID 2005), which contain the original claims data for 1 million beneficiaries randomly sampled from the 2000 and 2005 Registry of Beneficiaries of the NHIRD-TW, respectively. Therefore, the LHID 2000 and LHID 2005 contain data about all the medical procedures and prescriptions for 2 million people (approximately 5%) in Taiwan. The reliability of the diagnostic codes in the NHIRD has already been proven in previous studies [15,16].

2.2. Study subjects

All patients diagnosed with narcolepsy between January 1, 2002, and December 31, 2011, in the LHID 2000 and LHID 2005 database were recruited as the patient group (n = 258). A narcolepsy diagnosis was defined as at least one NHI claim record per visit with the presence of the International Classification of Diseases, ninth revision, Clinical Modifications (ICD-9-CM) code of 347.XX. The index date was established as the date when narcolepsy was first diagnosed, and the patients’ medical records were monitored until a depressive disorder was diagnosed or until December 31, 2011.

For each patient in the patient group, a matching control was randomly chosen from the LHID 2000 or LHID 2005 using the propensity score matching technique (the ratio of narcolepsy cases to controls was 1:10). Age and sex were applied as covariates, to determine the propensity score using a multivariable logistic regression model. January 1, 2002, was set as the initial observation date, and the 2580 control subjects were monitored from this entry date until December 31, 2011, or a diagnosis of a depressive disorder.

2.3. Comorbidities and outcomes

The following relevant disorders were identified to be commonly comorbid with narcolepsy in this study [1,4]: attention-deficit hyperactivity disorder (ADHD) (ICD-9-CM code 314.X), obesity (ICD-9-CM code 278.X), epilepsy (ICD-9-CM code 345), and intellectual disability (ICD-9-CM codes 317 to 319).

The results of this study were determined using a diagnosis of any depressive disorder, including major depressive disorder (ICD-9-CM code 296.2X, which corresponds to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision [DSM-IV-TR] [17] diagnosis of major depressive disorder), dysthymic disorder/neurotic depression (ICD-9-CM code 300.4, which corresponds to the DSM-IV-TR diagnosis of dysthymic disorder), and depressive disorder NOS (ICD-9-CM code 311, which corresponds to the DSM-IV-TR diagnosis of depressive disorder NOS).
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