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Risk of psychiatric disorders in Guillain-Barre syndrome: A nationwide, population-based, cohort study

Nian-Sheng Tzeng[a,b], Hsin-An Chang[a,b], Chi-Hsiang Chung[c,d,e], Fu-Huang Lin[d], Chin-Bin Yeh[a,f], San-Yuan Huang[a,f], Chuan-Chia Chang[a], Ru-Band Lu[a,f,g,h,i,j,k], Yu-Chen Kao[a,l], Hui-Wen Yeh[a,m,n,o], Wei-Shan Chiang[a,p], Wu-Chien Chien[d,e,*]

[a] Department of Psychiatry, Tri-Service General Hospital, School of Medicine, National Defense Medical Center, Taipei, Taiwan, ROC
[b] Student Counseling Center, National Defense Medical Center, Taipei, Taiwan, ROC
[c] Taiwanese Injury Prevention and Safety Promotion Association, Taipei, Taiwan, ROC
[d] School of Public Health, National Defense Medical Center, Taipei, Taiwan, ROC
[e] Department of Medical Research, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, ROC
[f] Graduate Institute of Medical Sciences, National Defense Medical Center, Taipei, Taiwan, ROC
[g] Division of Clinical Psychology, Institute of Allied Health Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan, ROC
[h] Department of Psychiatry, College of Medicine, National Cheng Kung University, Tainan, Taiwan, ROC
[i] Institute of Behavioral Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan, ROC
[j] Department of Psychiatry, National Cheng Kung University Hospital, Tainan, Taiwan, ROC
[k] Center for Neuropsychiatric Research, National Health Research Institute, Zhunan, Miaoli County, Taiwan, ROC
[l] Department of Psychiatry, Tri-Service General Hospital, Song-Shan Branch, National Defense Medical Center, Taipei, Taiwan, ROC
[m] Institute of Bioinformatics and Systems Biology, National Chiao Tung University, Hsin-Chu, Taiwan, ROC
[n] Department of Nursing, Tri-Service General Hospital, School of Nursing, National Defense Medical Center, Taipei, Taiwan, ROC
[o] Department of Nursing, Kang-Ning University (Taipei Campus), Taipei, Taiwan, ROC
[p] Department and Institute of Mathematics, Tamkang University, New Taipei City, Taiwan, ROC

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ABSTRACT

Background: Guillain-Barre syndrome (GBS) is a rare immune-related neurological disorder with high mortality and morbidity, but the comorbid psychiatric disorders garnered little attention in the GBS patients. This study aimed to investigate the association between GBS and the risk of developing psychiatric disorders.

Methods: A total of 18,192 enrolled patients, with 4548 study subjects who had suffered GBS, and 13,644 controls matched for gender and age, from the Inpatient Dataset of 2000–2013 in Taiwan, and selected from the National Health Insurance Research Database (NHIRD). After adjusting for confounding factors, Cox proportional hazards analysis was used to compare the risk of developing psychiatric disorders during the 13 years of follow-up.

Results: Of the study subjects, 471 (10.35%) developed psychiatric disorders when compared to 1023 (7.50%) in the control group. Fine and Gray's competing risk model analysis revealed that the study subjects were more likely to develop psychiatric disorders (crude hazard ratio [HR]: 4.281 (95% CI = 3.819–4.798, $p < 0.001$). After adjusting for gender, age, monthly income, urbanization level, geographic region, and comorbidities, the adjusted HR was 4.320 (95% CI = 3.852–4.842, $p < 0.001$). Dementia, depressive disorders, sleep disorders, and psychotic disorders predominate in these psychiatric disorders. Mechanical ventilation and hemodialysis are associated with a lower risk of dementia when compared to the control groups.

Conclusions: Patients who suffered from GBS had a higher risk of developing psychiatric disorders, and this finding should act as a reminder to the clinicians that a regular psychiatric follow-up might well be needed for those patients.

* Corresponding author at: Department of Medical Research, Tri-Service General Hospital, National Defense Medical Center, 7115R, No. 325, Section 2, Cheng-Kung Road, Neihu District, Taipei City 11490, Taiwan, ROC.
E-mail address: chienwu@ndmctsgh.edu.tw (W.-C. Chien).

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1. Introduction

Guillain-Barre syndrome (GBS) is a rare immune-related neurological disorder [1,2], with a prevalence of around 1.7 per 100,000 person-years in Taiwan [3,4], which might well contribute to their morbidity or mortality [4–6]. Some articles about traumatic stress and psychological sequela [7–9] could also be associated with patients with GBS, but only from limited studies on anxiety, depression, sleep, and psychotic disorder in small sample studies or case reports [10–15], in comparison to another immune-related neurological disorder, multiple sclerosis, which has had more comprehensive studies about the prevalence of anxiety, alcohol abuse, bipolar disorder, depression, substance abuse, and psychotic disorders [16,17].

Psychiatric, or mental disorders, are defined as clinically significant behavioral or psychological syndromes, which are associated with present distress, disability, or an increased risk of suffering death, pain, or disability, and subsequent behavioral, psychological, or biological dysfunctions [18,19]. Previous studies have found that psychiatric disorders, such as dementia, anxiety disorders, depressive disorders, bipolar disorders, sleep disorders, psychotic disorders, and posttraumatic stress disorder or acute stress disorder, are associated with occupational injury [20], epilepsy [21], substance use disorders [22], and patients who have had weight control surgery [23]. Psychological stressors, or injury to the brain in the diseases, might contribute to these associations in injury, diseases, substance use disorders, or a post-surgery state. However, the association between GBS and psychiatric disorders has not, as yet, been studied. Therefore, a nationwide, population-based study is necessary for the association between GBS and the risk of psychiatric disorders for the clinicians who actually cared for these patients.

The National Health Insurance (NHI) Program was launched in Taiwan in 1995, and as of June 2009, it included contracts with 97% of the medical providers with approximately 23 million beneficiaries, or > 99% of the entire population [24,25]. The National Health Insurance Research Database (NHIRD), which contains all claims data of the beneficiaries, uses the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes to record diagnoses [26]. All diagnoses of psychiatric disorders in Taiwan are made by board-certified psychiatrists. An Inpatient Dataset in 2000–2013 was selected from the NHIRD, as several studies have demonstrated the accuracy and validity of the diagnoses [27–29]. Therefore, we used the NHIRD to study the association between GBS and the risk of psychiatric disorders.

2. Methods

2.1. Data sources

The present study used the NHIRD to identify inpatients with a discharge diagnosis of GBS, based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) code (357.0) during 2000–2013. The NHI Administration randomly reviews the records of ambulatory care visits and in-patient claims periodically to verify the accuracy of the diagnoses [30].

2.2. Study design and sampled participants

This study was of a population-based, matched-cohort design. Patients with newly diagnosed GBS were selected from the Inpatient Dataset from January 1, 2000, to December 31, 2013, according to a diagnosis of GBS (ICD-9-CM 357.0). The patients with GBS before 2000 were excluded. In addition, the patients diagnosed with dementia, depressive disorders, anxiety disorders, bipolar disorders, sleep disorders, psychotic disorders, posttraumatic stress disorder (PTSD), and acute stress disorder before 2000, or before the first visit for GBS, were also excluded. All patients aged < 20 were also excluded. All patients with other neurological disorders who were admitted for conditions that were similar to GBS, such as chronic inflammatory demyelinating polyneuropathy (357.81), critical illness polyneuropathy (357.82), critical illness myopathy (359.81), polyneuropathy because of other diseases (e.g., porphyria and diphtheria; 357.4), acute poliomyelitis (045, 045.1), myasthenia gravis, other myasthenic syndrome (358.0, 358.01, 358.1, 358.8), acute transverse myelitis (323), acute alcohol intoxication (303.0), and poisoning by drug and biologic substances (960, 979) were excluded, with reference to one previous study related to GBS [4]. The patient's unique identifier was used to ensure that we only evaluated data for the first admission in cases with multiple admissions. A total of the patients that were enrolled, including 4548 subjects with GBS and 13,644 controls without GBS, were matched for age, gender, and index year (Fig. 1).

2.3. Ethics

This study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). The Institutional Review Board of the Tri-Service General Hospital approved this study and waived the need for individual written informed consent (IRB No. 2-105-05-082).

2.4. Covariates

The covariates included gender, age groups (20–29, 30–39, 40–49, 50–59, 60–69, ≥ 70 years), geographical area of residence (north, center, south, and east of Taiwan), urbanization level of residence (levels 1 to 4), and monthly income (in New Taiwan Dollars [NT$]; < 18,000, 18,000–34,999, ≥ 35,000). The urbanization level of residence was defined according to the population and various indicators of the level of development. Level 1 was defined as a population of > 1,250,000, and a specific designation as political, economic, cultural, and metropolitan development. Level 2 was defined as a population between 500,000 and 1,249,999, and as playing an important role in the politics, economy, and culture. Urbanization levels 3 and 4 were defined as a population between 149,999 and 499,999, and < 149,999, respectively [31]. Use of a mechanical ventilator was defined as ICD-9-CM procure codes 96.7 (invasive mechanical ventilator), and 93.9 (non-invasive mechanical ventilator). Use of a therapeutic plasma exchange was defined as the ICD-9-CM procedure code 99.71.

2.5. Comorbidity

Comorbidities were assessed using the Charlson Comorbidity Index (CCI), which categorizes comorbidities using ICD-9-CM codes, scores each comorbidity category [1,2,32–35], and combines all scores to calculate a single comorbidity score. A score of zero indicates that no comorbidities were found, and higher scores indicate higher comorbidity burdens [25]. The five major complications that we evaluated were cardiac complications, pulmonary complications, respiratory failure necessitating endotracheal intubation, systemic infection, and thrombotic complications.

2.6. Outcome measures

All of the study participants were followed from the index date until the onset of dementia (ICD-9-CM codes: 290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.41, 290.42, 290.43, 290.8, 290.9, and 331.0), anxiety disorders (ICD-9-CM 300), depressive disorders (ICD-9-CM 296.2-296.3, 300.4, 311), bipolar disorders (ICD-9-CM 296.0, 296.4-296.8), sleep disorders (ICD-9-CM 307.4, 780.5), psychotic disorders (ICD-9-CM 295, 297-298), and posttraumatic stress disorder (PTSD) and acute stress disorder (ICD-9-CM 308, 309.81), withdrawal from the NHI program, or the end of 2013.