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Original article

Association of developing childhood epilepsy subsequent to febrile seizure: A population-based cohort study

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Abstract

Purpose: Epilepsy is an important neurological condition that frequently associated with neurobehavioral disorders in childhood. Our aim was to identify the risk of developing epilepsy subsequent to febrile seizure and the association between epilepsy risk factors and neurobehavioral disorders.

Subjects and methods: This longitudinal population-based cohort data included 952 patients with a febrile seizure diagnosis and 3808 age- and sex-matched controls. Participants were recruited for the study from 1996 to 2011, and all patients were followed up for maximum 12.34 years.

Results: The association of epilepsy was significantly higher (18.76-fold) in individuals that experienced febrile seizure compared to controls. Further, of those individuals who experienced febrile seizure, the frequency of subsequent development of epilepsy was 2.15-fold greater in females, 4.846-fold greater in patients with recurrent febrile seizure, and 11.26-fold greater patients with comorbid autism.

Conclusions: Our study showed that being female, comorbid autism with febrile seizure and recurrent febrile seizure had an increased association with development of epilepsy. Increased recognition the association for epilepsy might be warranted in those febrile seizure children with certain characteristics.

Keywords: Epilepsy; Autism; Comorbidity; Recurrent febrile seizure

1. Introduction

Epilepsy is an important spectrum of neurological condition that frequently associated with cognitive impairment and neurobehavioral disorders in childhood.

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With the increasing recognition of epilepsy, many investigators have attempted to identify factors that increase the risk of developing epilepsy [1]. More than 50 million people worldwide have epilepsy [2], and 10–20% of epilepsy patients have had a febrile seizure (FS). FS is the most common convulsion that occurs in childhood; FS affects 2–5% of all children and usually appears between 6 months and 6 years of age [3,4]. Although some studies have found a higher risk of developing epilepsy after FS [5–8], the association between FS and subsequent epilepsy has not been the subject of adequate numbers of population-based studies. Furthermore, the association between epilepsy risk factors and neurobehavioral disorders comorbid with FS has not been investigated in a population-based study.

In the present study, we aimed to determine the association between comorbidities and the subsequent risk of epilepsy in febrile seizure. Therefore, we performed an association study on comorbidities in children with a history of FS and subsequent epilepsy development. Using the National Health Insurance Research Database (NHIRD), we conducted a nationwide population-based study to investigate the relationship between FS and subsequent epilepsy incidence.

2. Subjects and methods

The NHIRD included 99% of the 23 million residents of Taiwan. The National Health Insurance (NHI) program provides for approximately 90% of medical coverage and examinations by board-certified medical physicians and institutions. Therefore, information regarding diseases diagnoses, medication, and familial incomes are accessible. However, the Personal Information Privacy Act required that each patient's original identification number be encrypted in the cohort data.

To our knowledge, the NHIRD database is one of the largest nationwide population-based databases in the world, and its use has resulted in publication of many scientific manuscripts. Our data included 1,000,000 randomly sampled NHIRD insurant registered in 2005, either during hospitalization or subsequent outpatient department visits. These cohort data also included each patient's longitudinal medical records following registration. This study was approved by the Institutional Review Board (IRB-103-0779B) of Chang Gung Medical Hospital.

The study cohort consisted of individuals aged 6 months to 6 years who were diagnosed with FS (International Classification of Diseases, Ninth Revision; ICD-9: code 78031) between January 1996 and December 2011. Exclusion criteria included: previous epilepsy (ICD-9 code: 345x), previous cerebral palsy (343x), or within one month of being diagnosed or concurrently diagnosed with meningitis (320x, 047x, 049x) or encephalitis (062x, 323x). The control group was randomly sampled and selected four times according to the same criteria used for the study cohort, and was matched according to age, sex, and index year (Fig. 1). The primary outcome of the study was the occurrence of decision-making claims of epilepsy (ICD-9-CM code: 345x) as the main diagnosis and anticonvulsant medication prescribed for at least 3 months by a board-certified physician.

Recurrent FS (ICD-9 code: 78031) was defined as the occurrence of FS more than once in the same patient

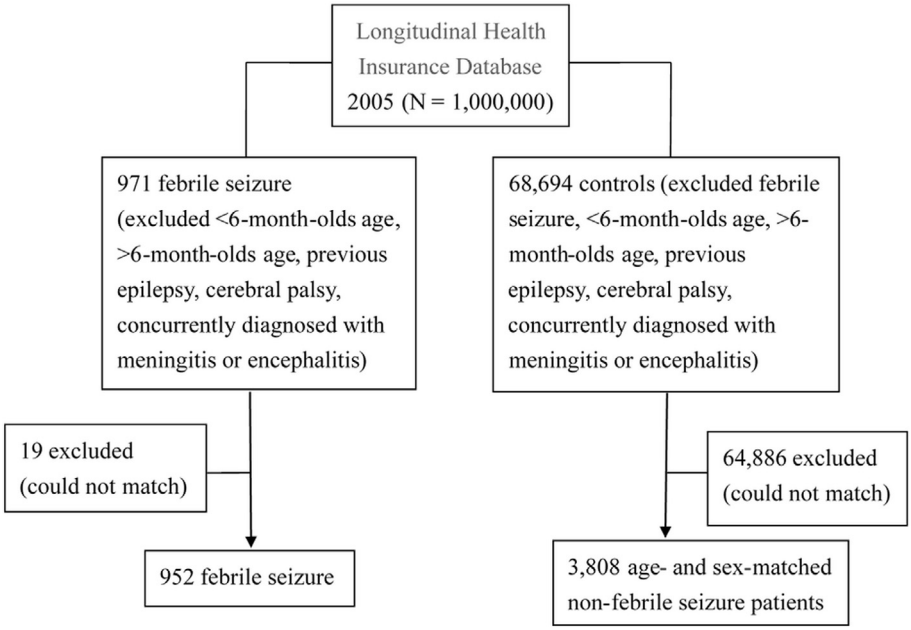

Fig. 1. Research design flow chart of the present study. ICD-9: International Classification of Diseases, Ninth Revision.

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