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Brain & Development xxx (2018) xxx–xxx

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Original article

# Incidence of childhood epilepsy: A population-based study in rural Japan

Kentaro Okamoto [a,b,*], Mitsumasa Fukuda [c], Isao Saito [d], Isaku Horiuchi [e], Tomoko Okazawa [f], Eiichi Ishii [c]

[a] Department of Regional Pediatrics and Perinatology, Ehime University Graduate School of Medicine, Toon, Ehime 791-0295, Japan
[b] Department of Pediatrics, Uwajima City Hospital, 1-1 Gotenmachi, Uwajima, Ehime 798-8510, Japan
[c] Department of Pediatrics, Ehime University Graduate School of Medicine, Toon, Ehime 791-0295, Japan
[d] Department of Community Health Systems Nursing, Ehime University Graduate School of Medicine, Toon, Ehime 791-0295, Japan
[e] Department of Pediatrics, Asahigawasou South Ehime Hospital, 607, Naganoichi, Kihoku, Ehime 798-1333, Japan
[f] Okazawa clinic, 1976, Mishohirajo, Ainan, Ehime 798-4110, Japan

Received 9 June 2017; received in revised form 10 August 2017; accepted 5 June 2018

**Abstract**

*Introduction:* Epilepsy is a common childhood neurological condition and a major public health concern worldwide. A higher incidence of epilepsy is reported in low- and middle-income countries, particularly in rural areas. However, no Japanese reports on the incidence of childhood epilepsy have been published in the past 25 years. We estimated the annual incidence of epilepsy in children aged 1–14 years in Uwajima, a city in a rural, relatively isolated area of Japan.

*Methods:* Candidates were extracted from Japan's public insurance database following the International Classification of Diseases code for epilepsy. Epilepsy was defined as two or more unprovoked seizures more than 24 hours apart, as per the International League Against Epilepsy definition. The study sample was divided into three cohorts based on age at diagnosis: 1–4, 5–9, and 10–14 years. The incidence of epilepsy was calculated as the number of children with epilepsy divided by the person-years in each cohort.

*Results:* The annual incidence rate of epilepsy in children aged 1–14 years was 70.4/100,000 children (95% confidence interval, 44.8–96.0). There was no significant difference in incidence between boys and girls. This rate was similar to those reported in other countries, although the incidence in children aged 1–4 years was slightly higher in our study than in other countries.

*Conclusion:* The annual incidence of childhood epilepsy in rural areas of Japan is generally comparable with rates of childhood epilepsy reported in other countries.


*Keywords:* Childhood epilepsy; Incidence; Japan; ILAE definition; Rural

## 1. Introduction

Epilepsy is a serious neurologic disorder that is common in children [1]. A better understanding of its epidemiology will help in developing care systems that go beyond seizure control and address aspects of children's social, emotional, and developmental wellbeing [2]. New findings may influence how physicians determine an effective course of treatment for pediatric patients, as well as the information they can provide parents and caregivers regarding the risks, recurrence, and long-term prognosis [1]. Although some epidemiological

* Corresponding author at: Department of Regional Pediatrics and Perinatology, Ehime University Graduate School of Medicine, Shitsukawa, Toon, Ehime 791-0295, Japan.
*E-mail address:* kentaro206@gmail.com (K. Okamoto).

https://doi.org/10.1016/j.braindev.2018.06.003
0387-7604/

studies have addressed the incidence and prevalence of epilepsy in children, comparison between studies is challenging because of differing methods, definitions of epilepsy, participants' age range, and inclusion of children with febrile seizures [3]. Guidelines for epidemiologic research were published in 1993 by the International League Against Epilepsy (ILAE), and are usually used for definitions of epilepsy [1,3].

Most studies on the incidence of childhood epilepsy are restricted to new-onset epilepsy before age 16 years [3]. These studies report rates ranging from 41–187 per 100,000 children, and consistently show that the incidence is highest in the first year of life and declines to adult levels by age 10 years [3]. Nearly all studies found that the incidence did not differ between boys and girls, but was higher in low- and middle-income countries (LMICs), particularly in rural areas [3].

Although the prevalence of childhood epilepsy has been investigated in Japan [4], there have been no reports on the incidence of childhood epilepsy in the past 25 years, meaning there are no available studies that used the ILAE classification system. Our study addressed this gap by estimating the incidence of childhood epilepsy in a rural area of Japan, and comparing this with rates reported in other countries.

## 2. Materials and methods

### 2.1. Methods

This population-based study was performed using data on Uwajima, a city in a typical rural area in Japan and with a population of about 83,000 people and little population transfer. Uwajima is geographically isolated from other large cities and is surrounded by mountains and the sea, making it particularly suitable for this population study. A previous report indicated that 92.0% of the children with epilepsy in Uwajima and surrounding areas had visited or been referred to Uwajima City Hospital [5]. A seizure is an emergency and a threatening symptom, which generally results in an ambulance being called. Uwajima City Hospital is the only hospital in the area that accepts children carried by ambulances on a full time basis. Around 94.5% of ambulances that carried children who lived in Uwajima went to Uwajima City Hospital (unpublished data). Uwajima City Hospital is a teaching hospital, and is the largest hospital in the region and the only hospital in the city that treats children with epilepsy. Two general hospitals and one general practitioner's office from surrounding towns also participated in our study. These institutions treat children with epilepsy from surrounding areas. This suggests that almost all children with epilepsy in the study area had visited participating institutions. To increase the accuracy of our data, children with epilepsy from surrounding areas were excluded from the present analyses. This research was approved by the Ethics Committee of Uwajima City Hospital (approval number: 1411-218).

Three population-based cohorts were identified using life-table analysis, based on observation and new diagnoses between 2007 and 2015 (Fig. 1). All included children were born and newly diagnosed with epilepsy in Uwajima: children aged 1–4 years at diagnosis were born between 2006 and 2010 (n = 3,006); those aged 5–9 years were born between 2002 and 2005 (n = 2,609); and those aged 10–14 years were born between 1997 and 2000 (n = 3,261).

In Japan, all individuals have public health insurance. Children with epilepsy are assigned the public insurance term "epilepsy" for examinations or therapy in both outpatient and hospital settings. We extracted 159 candidates from the public insurance database using the International Classification of Diseases code for epilepsy. Two independent specialists in epilepsy and childhood neurology (K.O., M.F.) reviewed candidates' history, neurologic examination results, electroencephalograms (EEG), magnetic resonance imaging, and laboratory examination results.

### 2.2. Diagnosis and type of epilepsy

Epilepsy was diagnosed using two diagnostic criteria. The first was the classical criterion that is common in clinical use that defines epilepsy according to the ILAE guidelines [6] as two or more unprovoked seizures separated by at least 24 hours. Therefore, we excluded children with febrile (provoked) seizures and convulsions related to mild gastroenteritis. We defined the age at diagnosis as the age at which the second unprovoked seizure took place. The second criterion was a newly established practical clinical definition of epilepsy [7] based on: (a) at least two unprovoked seizures occurring >24 h apart, (b) one unprovoked seizure and a probability of further seizures similar to the general risk of recurrence (at least 60%), or (c) diagnosis of an epileptic syndrome [8].

To determine the type of epilepsy, we used the 1989 ILAE classification [9], which is widely used in population-based and childhood-epilepsy studies, despite some significant shortcomings [10].

### 2.3. Statistical analyses

To determine the incidence of epilepsy, we established three age-based cohorts: cohort 1, children born between 1997 and 2000 (aged 10–14 years at diagnosis); cohort 2, those born between 2002 and 2005 (aged 5–9 years at diagnosis); cohort 3, those born between 2006 and 2010 (aged 1–4 years at diagnosis). Using regional age-specific mortality rates, the living population aged 1–4 years, 5–9 years, and 10–14 years between 1997

Please cite this article in press as: Okamoto K et al. Incidence of childhood epilepsy: A population-based study in rural Japan. Brain Dev (2018), https://doi.org/10.1016/j.braindev.2018.06.003