Seizure 50 (2017) 160–165

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

National trend survey of hospitalized patients with febrile seizure in the United States

Yusuke Okubo[a,b,*], Atsuhiko Handa[c]

[a] Harvard TH Chan School of Public Health, Boston, USA
[b] Department of Social Medicine, National Research Institute for Child Health and Development, Tokyo, Japan
[c] Department of Pediatrics, Massachusetts General Hospital for Children and Harvard Medical School, Boston, USA

ARTICLE INFO

Article history:
Received 11 February 2017
Received in revised form 15 June 2017
Accepted 20 June 2017
Available online xxx

Keywords:
Epidemiology
Febrile seizure
Kids inpatient database

ABSTRACT

Purpose: Several studies have reported the prevalence and incidence of febrile seizure (FS) among children in the USA and other countries. However, recent trends in FS among hospitalized children, hospital course, and risk factors for its severity remain unknown at a national level in the USA.
Method: Hospital discharge records of patients with FS aged <6 years were obtained for the years 2003, 2006, 2009, and 2012 from the Kid's Inpatient Database. Data were weighted to estimate the annual hospitalization rates with respect to gender and race/ethnicity in the United States. Multivariable logistic regression was conducted to ascertain factors associated with FS severity.
Results: A decreasing trend in total annual hospitalization rates due to FS was observed, ranging from 59.0 per 100,000 children in 2003 to 40.8 per 100,000 children in 2012 ($p < 0.001$). Winter predominance of hospitalizations was observed ($p = 0.001$). Hispanic children and children admitted to hospitals in northeast region were less likely to be severely affected. Age, gender, health insurance status, and household income level were not associated with FS severity.
Conclusions: Total hospitalization rates due FS is decreasing, and race/ethnicity and geographic locations of the patients were associated with FS severity.
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1. Introduction

Febrile seizure (FS), the most frequent seizure observed in children, is characterized by episodes of convulsions that occur in association with fever in children aged less than 6 years in the absence of a central nervous system (CNS) infection or an electrolyte imbalance [1–5]. FS is believed to be a benign seizure syndrome distinct from other neurologic disorders [4].

Several studies have investigated the epidemiology of FS, including its prevalence, and gender-, age-, and race/ethnicity-specific variations. The incidence of FS peaks at the age of 18 months, and is 2%–9% among all children [1–5]. The incidence is the highest among children living in Asian and Pacific Island countries, and is higher in boys than girls, with a male-to-female ratio of 1.1–2.0 [2–8]. In addition, seasonal variation has been reported in Finland, Japan, and the USA, and the highest incidence observed in winter, and the lowest in summer [7,8]. However, the USA's national data remain unclear regarding the epidemiology and hospital course of inpatients with FS.

To address these gaps in knowledge, the present study was conducted to investigate annual hospitalization rates due to FS and identify its epidemiological characteristics (differences in gender, race/ethnicity, geographic locations, and seasonal variations) in the entire USA. We also determined the mean cost of hospitalization and mean length of hospital stay, stratified by year of admission, and ascertained factors that were associated with FS severity.

2. Methods

2.1. Study population and participation

We analyzed data of hospital discharge records about patients aged 6 years or younger with FS for the years 2003, 2006, 2009, and 2012 using the US representative Kids Inpatient Database (KID). The Agency for Healthcare Research and Quality (AHRQ) compiled the data, and the Healthcare Cost and Utilization Project (HCUP) generated the database in collaboration with public and private statewide data organizations [9,10]. The KID is a large national all-

* Corresponding author at: Harvard T.H. Chan School of Public Health, 158 Longwood Avenue, Boston 02115, USA.
E-mail address: sunning_dale@yahoo.co.jp (Y. Okubo).

http://dx.doi.org/10.1016/j.seizure.2017.06.020
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payer hospital pediatric discharge database. The KID is designed to generate robust national estimates of annual pediatric hospitalizations, and is aimed to present hospital use, outcome, and healthcare cost [9,10]. The KID sampling frame was constructed based on all US short-term, non-federal, general, and specialty hospitals participating in the HCUP [9,10]. The KID had approximately 3 million pediatric discharges in each sample from 36 states in 2003, 38 states in 2006, and 44 states in 2009 and 2012 [11–14]. Discharge weight (DISCWT) variables were provided with the KID to obtain the national estimates of hospitalizations in the United States [9,10].

Hospitalizations with FS were identified using *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9CM) code (780.31: febrile convulsions (simple), unspecified, and 780.32: complex febrile convulsions) in the primary or secondary diagnosis fields, and they were weighted with DISCWT variables to calculate the estimated number of hospitalizations in the entire United States.

2.2. Measurements of variables

Patient characteristics included age, gender (male or female), and race/ethnicity (black, Hispanic, white, Asian or Pacific Islanders, others (Native American and other types), and unknown). Patient socioeconomic status consisted of primary payer information (private, Medicare/Medicaid, other types (self-pay, no insurance, or no information)), and median household income quartiles for counties of residence (see Supplement 1). We excluded patients with chronic medical conditions (congenital heart, kidney, pulmonary, endocrine, hematologic, gastrointestinal, and neurologic diseases; cancer or leukemia; and autoimmune disease) using pediatric complex chronic conditions classification system version 2 [15].

Hospital characteristics included hospital regions (Northeast, Midwest, South, or West), hospital types (urban teaching, urban nonteaching, or rural), and hospital sizes (small, medium, or large). The definitions of hospital sizes are different across the location of the hospital (Supplement 2).

2.3. Outcomes

The outcomes of interest were FS-associated annual hospitalization rates with respect to gender and race/ethnicity. Annual FS-associated hospitalization rates were calculated; the number of hospitalizations as the numerator and the corresponding population of each subgroup as the denominator according to the US census in 2003, 2006, 2009 and 2012 [16–20]. The number of hospitalizations by months was also obtained during 2003–2012. Total costs were calculated from total hospitalization charges using cost-to-charge ratio according to the HCUP recommendations [9–14].

Severity of illness was captured from the hospitalization's All Patient Refined-Drug-related Groups (APR-DRG) code [9–14]. The system of DRG was developed and used for Medicare as a prospective payment system to classify hospital cases into 1 of approximately 500 groups to have similar hospital resource use. APR-DRG is a refinement of the system, and it accounts for severity of illness and risk of mortality. Severity of illness in APR-DRG was categorized into four groups (minor, medium, major or extreme), and it was determined by combinations of clinical information, including patient characteristics, primary diagnosis, comorbidity, and procedures that the patients received. We defined major-to-extreme severity of illness defined by APR-DRG as severe, and mild-to-medium severity of illness as non-severe, and ascertained factors (age, gender, race/ethnicity, socioeconomic status and geographic location) associated with severity, after adjusting for patient and hospital characteristics, and years of admissions.

2.4. Statistical analysis

Descriptive statistics, including continuous and categorical data, were summarized. The number of FS-related hospitalizations and the proportions of hospitalizations by month were calculated using DISCWT. We determined annual hospitalization rates with respect to gender and race/ethnicity, and calculated 95% confidence interval, assuming a normal approximation to a Poisson distribution. We used chi-square test for linear-trend analyses of annual hospitalization rates between 2003 and 2012. Two-way analysis of variance (ANOVA) was performed to check the seasonal variations.

To investigate the secular trends for healthcare cost and length of hospital stay in days from the years 2003 to 2012, we constructed multivariable linear regression model adjusting for patient and hospital characteristics with the reference year of 2003. Multivariable logistic regression with dichotomous outcome (severe or non-severe) was conducted to investigate the factors associated with severity. The results were adjusted for patient and hospital characteristics as well as years of admissions, and were reported with 95% confidence intervals. Statistical significance was two-sided $p < 0.05$ for all tests. All data were analyzed using STATA software version 14.1 (StataCorp LP, Texas, USA).

3. Results

We identified a total of 16,337 patient discharges in 2003, 13,986 discharges in 2006, 13,169 discharges in 2009, and 11,505 discharges in 2012 among children aged 6 years or younger with FS in the USA. Table 1 described the characteristics of age, gender, race/ethnicity, socioeconomic status, and hospital characteristics among children hospitalized children FS. The mean age and male-to-female ratios did not change over the study period. The proportions of children with unknown race/ethnicity decreased from 22.4% in 2003 to 7.0% in 2012. More than 90% of children were covered by private insurance or Medicare/Medicaid. Patients with very-low or low median income levels were more likely to be hospitalized with FS. The majority of patients with FS were hospitalized in urban teaching hospital (54.3%–68.4%) with large bed size (54.0%–66.0%). Mean length of hospital stays in days significantly changed from 2.26 days in 2003 to 2.01 days in 2012 ($P_{trend} < 0.001$). The mean health care costs for hospitalizations significantly increased from 2870 USD in 2003 to 3792 USD in 2012 ($P_{trend} < 0.001$).

The annual FS-associated hospitalization rates with respect to gender and race/ethnicity were summarized in Table 2. The total annual hospitalization rates showed a decreasing trend, ranging from 59.0 per 100,000 children in 2003 to 40.8 per 100,000 children in 2012 ($p < 0.001$). The annual hospitalization rates in boys were consistently greater than those in girls with male-to-female ratio of 1.14–1.22. Significant downward linear-trends of the annual rates were observed among black children, ranging from 59.2 per 100,000 children in 2003 to 51.4 per 100,000 children in 2012 ($p < 0.001$), and among Hispanic children, ranging from 69.9 per 100,000 children in 2003 to 44.8 per 100,000 children in 2012 ($p < 0.001$). The hospitalization rates among white children and children of Asian or Pacific Island ancestry did not show upward or downward linear-trends over the period.

Fig. 1 showed the proportions of FS-associated hospitalizations by months and years. The winter seasonality predominance was observed ($p = 0.001$). We conducted a sensitivity analysis among hospitalized patients with FS in December stratified by year of admission to investigate the higher proportions of hospitalizations

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