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Effects of the coronavirus disease outbreak on the development of neurological disorders in children: A comparison of the incidence of febrile seizure and epilepsy using an interrupted time-series approach

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ABSTRACT

Background: With the outbreak of COVID-19, school closures and quarantines following social distancing have brought significant changes to children's lifestyles. Therefore, we aimed to compare the population-adjusted incidence of febrile seizures(FS) and epilepsy before and after the COVID-19 outbreak in Korea and to assess the effects of the COVID-19 outbreak on the incidence by region and age group.

Methods: A retrospective cohort study was conducted using nationwide claims data and covid data from January 2019 to December 2020. The incidence of diseases and difference in incidence before (Jan 20 to Dec 30, 2019) and after (Jan 20 to Dec 30, 2020) the COVID-19 outbreak was measured using rate ratio. An Interrupted time series analysis was used to identify the effect of COVID-19 on trends of FS and epilepsy. Subgroup analysis by age, sex, insurance, and risk of coronavirus by area were conducted.

Results: Following the onset of the pandemic, the number of newly diagnosed FS cases decreased sharply by 69 % (24,182 to 7238), whereas the incidence of epilepsy, increased to 1.02 times (30,286–29,312), when adjusted in proportion to the population. Notably, a greater decrease in the incidence of FS were found in the regions with high-risk of coronavirus. A result of segmented regression analysis proved the decrease was significant and made immediately after the pandemic started($p < 0.001$). In contrast to the incidence of FS, that of epilepsy did not exhibit a significant month-to-month change during the baseline period, immediately after the pandemic started, and during the pandemic.

Conclusions: The COVID-19 outbreak and resulting social distancing measures reduced the incidence of febrile seizure immediately rather than gradually. Unlike in the case of acute febrile seizure, the COVID-19 pandemic had no effect on the incidence of chronic epilepsy.

Introduction

Febrile seizure (FS) and epilepsy are the most common neurological disorders in children; these conditions have similar clinical features but different etiologies [1]. FS is a fever-induced convulsion or seizure that occurs in the absence of a central nervous system infection or metabolic disease. It is the most common type of seizure, affecting 2–14 % of children aged between 6 months and 5 years [2,3]. The direct causes of FS remain unclear, but viral or bacterial infection occurring prior to fever is a potential cause of FS. The role of viral infections in the etiology of FS remains controversial [4,5]. Epilepsy is a condition involving recurrent seizures caused by unprovoked or abnormal neuronal firing owing to non-epileptic events [6]. Epilepsy affects approximately 0.3–1 % of children and adolescents and is chronic in over 80 % of childhood onset cases [7,8].

Coronavirus disease (COVID-19) was first identified in December 2019, and because of its rapid spread, a pandemic was declared by the World Health Organization (WHO) on March 11, 2020 [9]. A surge in the number of COVID-19 cases posed unprecedented public

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health challenges [10]; consequently, South Korea enforced vigilant social distancing to prevent virus transmission. In accordance with social distancing schedule, school closures and quarantine altered the children's lifestyles. Hygiene-related precautions, including the provision of hand sanitizer in public places and use of facemasks, were strictly followed after the national crisis alert, raised on February 23, 2020 [11].

During the period in which attempts were made to minimize the risk of person-to-person virus transmission, the occurrence of diseases caused by viral infections was reported to have reduced [12,13]. Similarly, the incidence of pediatric seizures was reported to have reduced during the COVID-19 outbreak in Hong Kong [14]. This background raised concerns regarding the association between FS development and the prevention of virus transmission. However, during this period, we were not able to confirm whether there was a difference in the incidence of epilepsy, which exhibits similar characteristics to FS. Therefore, we aimed to compare the population-adjusted incidence of FS and epilepsy before and after the COVID-19 outbreak and to assess the effects of the COVID-19 outbreak on the incidence by region and age group.

Methods

This retrospective cohort study, using nationwide data from January 2019 to December 2020, observed the incidence change of FS and epilepsy. The effect of COVID-19 on the incidence of FS and epilepsy was measured using an interrupted time series analysis. The study was approved by the Institutional Review Board of Yonsei University Gangnam Severance Hospital (IRB No. 3–2021–0374), and all methods were performed in accordance with the declaration of Helsinki.

Data sources

All health insurance claims data provided by the Health Insurance Review and Assessment (HIRA) service and data on newly diagnosed COVID-19 provided by the Korea Disease Control and Prevention (KCDC) agency were analyzed. The data were collected between January 2019 and December 2020, which covered the period before and after the start of the pandemic. The healthcare system in South Korea is a universal healthcare system in which 98 % of the population is enrolled in National Health Insurance. The data comprise the history of healthcare services received, including diagnosis, treatment, and drug prescription [15]. The KCDC agency operates the National Notifiable Disease Surveillance System and has been managing and tracking COVID-19 trends from the early stages of the outbreak. The surveillance data comprise epidemiological characteristics of confirmed COVID-19 patients organized by age, sex, and region.

Population values that were used to calculate incidence per population were obtained from Statistics Korea, and the monthly population values were used to calculate the monthly incidence of FS and epilepsy.

Study population

The study population comprised the FS and epilepsy patients aged below 10 years, before and after COVID-19. The first case of COVID-19 in South Korea was confirmed on January 20, 2020, and the period from January 20, 2020, to December 31, 2020, was defined as the post-COVID-19 period. The pre-COVID period was set from January 20, 2019, to December 31, 2019, with the same duration as that of the post-COVID-19 period.

Case ascertainment of FS and epilepsy

Patients with FS and epilepsy were identified using the following International Classification of Diseases (ICD)-10 codes: "FS (R560)," "Convulsion (R568)," and "Convulsion, NEC (R56)" for FS and "Epilepsy (G40)" for epilepsy [16]. A patient with FS was described as a pediatric patient who visited the hospital or was hospitalized for the treatment of FS, with one of the FS codes as the primary condition. For epilepsy patient, a patient who was treated or hospitalized with the epilepsy code as the primary condition and medical history of at least two epileptic episodes annually was included. A washout period of 28 days prior to the hospital visit was applied for FS and epilepsy, and repeated episodes occurring within 28 days were considered as a single episode, even when visits were to different hospitals.

Definition of variables

Regarding age groups, children with atypical FS were considered as one group, and typical FS was evaluated by age. The majority of children do not experience seizures after the age of 5 years [2]; however, FS that persists beyond this age is called atypical FS [17]. Although there are considerable differences among children of the same age, yearly age groups were used because of data availability.

Regarding insurance type, National Health Insurance (NHI) and Medical Aid (MA) were analyzed. The choice of NHI or MA is determined by income level, and MA covers financially and medically indigent individuals subsidized by the government. MA covers 3 % of the general population and 1 % of the pediatric population. [18].

The 13 provinces comprising the Korean cities were divided into high-, medium-, and low-risk regions based on the number of COVID-19 cases in 2020 in each province in relation to the regional population of all age groups. The high-risk areas were Daegu, Seoul, Gyeonggi-do, Incheon, and Gyeongsangbuk-do. Seoul is the most densely populated city in South Korea, and Gyeonggi-do and Incheon are closely connected to Seoul. Daegu was the first city in which a large COVID-19 outbreak occurred, and Gyeongsangbuk-do is adjacent to Daegu [19]. The medium-risk regions were Gangwon-do, Chungcheongnam-do, Gwangju, Chungcheongbuk-do, Jeju, and Ulsan, and low-risk regions were Daejeon, Busan, Jeollabuk-do, Sejong, Gyeongsangnam-do, and Jeollanam-do. The number of COVID-19 patients per 10,000 population for the high-, medium-, and low-risk regions ranged from 32.1 to 9.2, 7.8–5.9, and 5.7–3.0, respectively.

Analysis

Incidence of FS and epilepsy

The population-adjusted incidence of FS and epilepsy was calculated for the two time periods. For each time period, the population-adjusted incidence rate per 10,000 persons was calculated by dividing the total number of patients during the time period by the population size during the time period and multiplying the result by 10,000. The differences in the incidence in each time period were compared using t-tests.

Difference in incidence before and after the COVID-19 outbreak (rate ratio)

The rate ratio was obtained by dividing the incidence rate after the start of the COVID-19 outbreak by that before the outbreak. The adjusted rate ratio reflects changes in the rate ratio in the general population. Since the general pediatric population was different before and after the COVID-19 outbreak, the rate ratio of the general population was set to one, and the corresponding rate ratios were calculated accordingly.

Interrupted time series (ITS)

Segmented regression of ITS analysis was conducted on a monthly basis to assess the incidence of FS and epilepsy before and after the COVID-19 outbreak. An ITS analysis is a powerful statistical method for estimating trend change over time and level change at a specific time point [20]. In this analysis, trend change indicates how the incidence of FS and epilepsy changed over time, including whether it changed immediately or gradually or in the short- or long-term. The level change indicates how much the incidence changed at the time of the COVID-19 outbreak.

The ITS model used in this study was as follows:

$$Yt = B0 + B1 \times Time1 + B2 \times COVID + B3 \times Time2 + e,$$

where Yt is the number of pediatric patients with FS or epilepsy per 10,000 persons, which changes on a monthly basis. Time1 is the baseline period before the COVID-19 outbreak, expressed as a continuous variable from the initiation of the study period. COVID is a dummy variable representing the COVID-19 outbreak with the date set to February 2021, taking the value of 0 before the outbreak and of 1 from the start of the outbreak. Time2 represents a time-series trend after the national crisis alert. This is a continuous variable that starts with 0, takes the value of 1 from the start of the national crisis, and increases by 1 per week thereafter.

Statistical significance was set at $p < 0.05$, and SAS, version 9.4 (SAS Inc., Cary, NC, USA), was used to perform all analyses in the study.

Results

Incidence of FS and epilepsy

During the pre-COVID-19 period, there were 24,182 cases of FS and 30,286 cases of epilepsy. Following the onset of the pandemic, the number of newly diagnosed FS cases decreased sharply by 69 % (adjusted rate ratio: 0.31; 7238 cases), whereas the epilepsy incidence and epileptic episode increased 1.02 times (29,312 cases in 10,128 patients) compared with the pre-COVID-19 incidence ($p = 0.091$ and 0.059, respectively). The incidence of FS did not differ by sex and type of insurance, but there were differences according to age and region ($p < 0.001$). In the case of epileptic episode, significant differences after the pandemic were only observed based on age group (Table 1).

Regarding FS, the higher the risk of COVID-19, the greater the decrease in the incidence of FS. The incidence of FS decreased by 69 %, 65 %, and 50 % during the pandemic in the high-risk, middle-risk, and low-risk areas, respectively. Regarding epilepsy, no trend was observed in relation to the risk of COVID-19. Epilepsy occurred most frequently in the areas with the highest risk of COVID-19 throughout the observation period; however, there was no difference between the middle-and low-risk areas (Fig. 1).

The incidence of FS was higher in boys than in girls; the incidence was the highest in children at the age of 1 year, following which it gradually decreased. In boys, the trend toward a higher incidence was more pronounced in the case of epilepsy; however, the incidence according to age exhibited the opposite trend. The incidence of epilepsy increased with age, and a sharp increase was seen from the age of 5. The medical aid group comprises 1.0 % of the Korean pediatric population[21] and included 1.5 % of the total pediatric patients with FS and 5 % of the total pediatric patients with epilepsy. The proportion of non-relapse patients increased in both the FS and epilepsy groups (Table 1). During the pandemic, the non-relapse rate of FS increased from 87.2 % (18,114) to 91.7 % (6534) and that of epilepsy increased from 90.5 % (2676) to 92.2 % (2357).

Segmented regression model

Table 2 presented the segmented regression estimates of FS incidence in the overall group of FS pediatric patients, seven age-based subgroups, and three risk-based area subgroups. In the overall pediatric FS group, there was no significant month-to-month change in the incidence of FS before the pandemic started (baseline trend) and during the pandemic (baseline trend [ß1]: $p = 0.070$, trend change [ß3]: $p = 0.587$). However, there was a significant decrease in the incidence immediately after the pandemic started (level change [ß2]: $p < 0.001$), which implies that the start of the pandemic was associated with a reduced number of pediatric FS cases. In all seven age-based subgroups, the decline in the incidence immediately after pandemic was significant. The largest absolute decrease was observed in the 1-year-old group, with a reduction of 23.45, while the 6–9-year-old group had the smallest decrease at 0.67. The group under 1 year had an absolute value of 3.0, which was lower than the other typical groups.

Subgroup analyses of FS incidence were performed to identify the age groups or areas in which the incidence was influenced by the COVID-19 pandemic. In some groups, there was a significant increasing trend during the pre-pandemic period; however, this trend was not observed in the overall pediatric population. The trend was observed in age groups older than 2 years and in middle-risk areas (baseline trend [ß1]: $p = 0.012$ for 3 years, $p = 0.001$ for 4 years, $p < 0.001$ for 5 years, $p = 0.004$ for 6–9 years, and $p = 0.026$ for middle-risk areas). In all subgroups, there was a significant reduction in incidence immediately after the pandemic started (level change [ß2]: $p < 0.001$ for all subgroups), and the magnitude of the regression coefficient representing the decrease was the greatest in the 1-year-old subgroup. A significant month-to-month decreasing trend was observed in groups older than 3 years (trend change [ß3]: $p = 0.030$ for 4 years, $p < 0.001$ for 5 years, $p = 0.006$ for 6–9 years), implying an association between the COVID-19 pandemic and a reduction in the number of pediatric FS cases in these age groups.

Table 3 presented the regression analysis estimates of the incidence of epilepsy in the overall pediatric group, seven age-based subgroups, and three risk-based area subgroups. In contrast to FS, the incidence of epilepsy did not exhibit a significant month-to-month change during the baseline period, immediately after the pandemic started, and during the pandemic (baseline trend [ß1]: $p = 0.207$, level change [ß2]: $p = 0.100$, trend change [ß3]: $p = 0.611$]. A non-significant trend was also found in most subgroups, which implies that the COVID-19 pandemic was not associated with the incidence of epilepsy. No significant change in incidence was observed in any subgroup immediately after the pandemic started; however, the 1-year-old subgroup showed a significant increasing trend during the pre-pandemic period and a significant decreasing trend change during the pandemic (baseline trend [ß1]: $p = 0.010$, trend change [ß2]: $p = 0.023$).

Discussion

This nationwide retrospective cohort study showed that the COVID-19 pandemic and resulting social distancing measures had an effect on the incidence of FS but not on epilepsy. Immediately after the start of the COVID-19 outbreak, the decline of incidence was most prominent among typical FS cases aged 1 year or older, while it was significant but relatively small in those under 1 year of age and in cases of atypical FS. In neonates, a wide range of systemic and metabolic derangements such as hypoglycemia and hypocalcemia can increase the risk of FS in addition to infections [22]. Atypical FS may also be influenced by factors such as pre-existing developmental abnormalities and family history other than infections [23]. Another finding was that the decrease in the incidence of FS was more pronounced in high-risk areas, even when the high-risk areas started out with a higher incidence. In these areas, social distancing

Table 1
Pre- and post-COVID-19 demographic and clinical characteristics of pediatric febrile seizure and epilepsy patients.

		Febrile seizure				Epilepsy			
		Before COVID-19[a]	After COVID-19[b]	p-value*	Adjusted rate ratio	Before COVID-19[a]	After COVID-19[b]	p-value*	Adjusted rate ratio
Pediatric population	3950,006	3763,973		1.00	3950,006	3763,973		1.00	
Occurrence	Patients	20,777	7127	< 0.001	0.36	10,380	10,128	0.091	1.02
	Cases	24,182	7238	< 0.001	0.31	30,286	29,312	0.059	1.02
Sex	Boy	11,967	4071	0.482	0.36	9863	9643	0.524	1.03
	Girl	8810	3056		0.36	517	485		0.98
Age groups	< 1 y	1280	660	< 0.001	0.54	544	447	0.004	0.86
	1 y	7947	3408		0.45	538	460		0.90
	2 y	5059	1330		0.28	597	537		0.94
	3 y	2829	645		0.24	751	672		0.94
	4 y	1569	383		0.26	873	865		1.04
	5 y	922	265		0.30	1064	1086		1.07
	6–9 y	1171	436		0.39	6013	6061		1.06
Type of insurance	NHI	20,459	7023	0.670	0.36	10,004	9706	0.588	1.02
	Medical aid	318	104		0.34	523	490		0.98
Area	High-risk	11,498	3404	< 0.001	0.31	7075	6847	0.243	1.02
	Middle-risk	4831	1589		0.35	1304	1352		1.09
	Low-risk	4447	2134		0.50	2001	1929		1.01
Recurrence frequency in epilepsy patients	0	18,114	6534		0.38	2676	2357		0.92
	1	2122	451		0.22	2066	2173		1.10
	2	397	90		0.24	1872	2090		1.17
	3	98	30		0.32	1931	1932		1.05
	> 4	46	22		0.50	1835	1576		0.90

[a]from January 20, 2019 to December 31, 2019; [b] from January 20, 2020 to December 31, 2020 p-value < 0.05 by t-test, as compared with 'after COVID-19'; COVID: coronavirus disease; NHI: National Health Insurance

measures are expected to have been stricter due to the large number of COVID-19 cases. The incidence decreased to 31 % in high-risk areas and to 50 % in low-risk areas after the pandemic started. These findings may indicate that the virus suppression policy had a significant effect on FS pathology through social distancing. However, the policy had no effect on epilepsy pathology. The incidence of epilepsy was not significantly different between the periods before, immediately after, and during the pandemic.

When the national alert level turned severe, KCDC released guidelines for preventing COVID-19. In this context, the public was advised to wash their hands frequently with soap, cover their mouth and nose when coughing and sneezing, use a facemask, and avoid visiting crowded places. People with fever or respiratory symptoms were asked not to go to school or work and to avoid outdoor activities and visits to other regions [11]. During this period, there were also significant changes for children. Schools were closed, or each grade level took turns attending school 1–2 times a week, in accordance with the social distancing schedule. It appears that these circumstances also affected the incidence of FS and epilepsy.

After the onset of the COVID-19 outbreak, the incidence of acute or viral diseases was found to decrease in the pediatric population [24,25]. By contrast, there were no significant changes in the incidence of chronic diseases, such as type 1 diabetes or gastroesophageal reflux disease [26–28]. Our results also support those of previous studies reporting no significant changes in the incidence of chronic epilepsy and an opposite trend in that of FS. Several studies have reported on COVID-19-related effects on other acute diseases, which are similar to those on pediatric FS, and the sudden decline in incidence seen in Korea was confirmed to be the same as worldwide. In Hong Kong, there was a 69.7 % reduction in pediatric seizure-related emergency department visits [14], and the rate of FS diagnosis in the United States decreased by 36.1 % compared to pre-pandemic rates [29]. Since FS is not a concomitant neurological manifestation of COVID-19 in pediatric patients, this does not appear to have affected the incidence rate [30].

There have been no studies on the incidence of pediatric epilepsy during the COVID-19 period. However, several studies conducted in Italy monitored the admission rates for epilepsy in all age groups [31–33]. Studies have reported a reduction in epilepsy-related emergency department access during the lockdown. The reason for this reduction was that telemedicine consultants were providing services during this period in Italy. As the number of telemedicine consultants increased, there were no significant changes in the use of antiepileptic drugs. Telemedicine was not actively implemented in Korea at that time, which is thought to be the reason why there was no effect on the incidence rates.

The decline in the incidence of FS as a result of social distancing may be due to the reduction in the incidence of other infectious diseases that are known to cause FS. During the social distancing period, the incidence of vaccine-preventable diseases, such as influenza, varicella, and mumps, declined in Korea [34,35]. These are the most frequent infections associated with FS in pediatric patients. Fever triggered by these infections causes the release of high levels of cytokines, which can alter brain activity, thereby causing FS [36]. Another reason for the decline in FS incidence may be a reporting bias. Due to the fear of secondary contagion in hospitals, people might be reluctant to visit hospitals in case FS symptoms are not severe. While social distancing, people are also disinclined to visit essential facilities, such as schools or work places, and they would only visit hospitals in case of very severe symptoms. COVID-19 is known to be transmitted even through aerosols and can be transmitted while patients are being treated in hospitals [37,38]. Therefore, patients with relatively severe FS may have visited a hospital and may have been included in the incidence estimation. This health service-related behavioral pattern of avoiding hospitals was also observed during severe acute respiratory syndrome (SARS) epidemic and Ebola outbreak [39,40].

The subgroup analysis of regions stratified by the risk of COVID-19 supported the view that the decrease in the incidence of FS was related to the COVID-19 pandemic. The incidence of FS decreased most rapidly in regions with a high incidence of COVID-19, whereas in the case of epilepsy, the regional COVID-19 incidence did not affect the incidence. In areas with a high risk of COVID-19, social distancing and personal hygiene measures would have been implemented more strictly, and these non-pharmaceutical interventions were strong measures against contracting infection during the pandemic [12]. As the development of chronic epilepsy is not affected by these non-pharmaceutical interventions, there

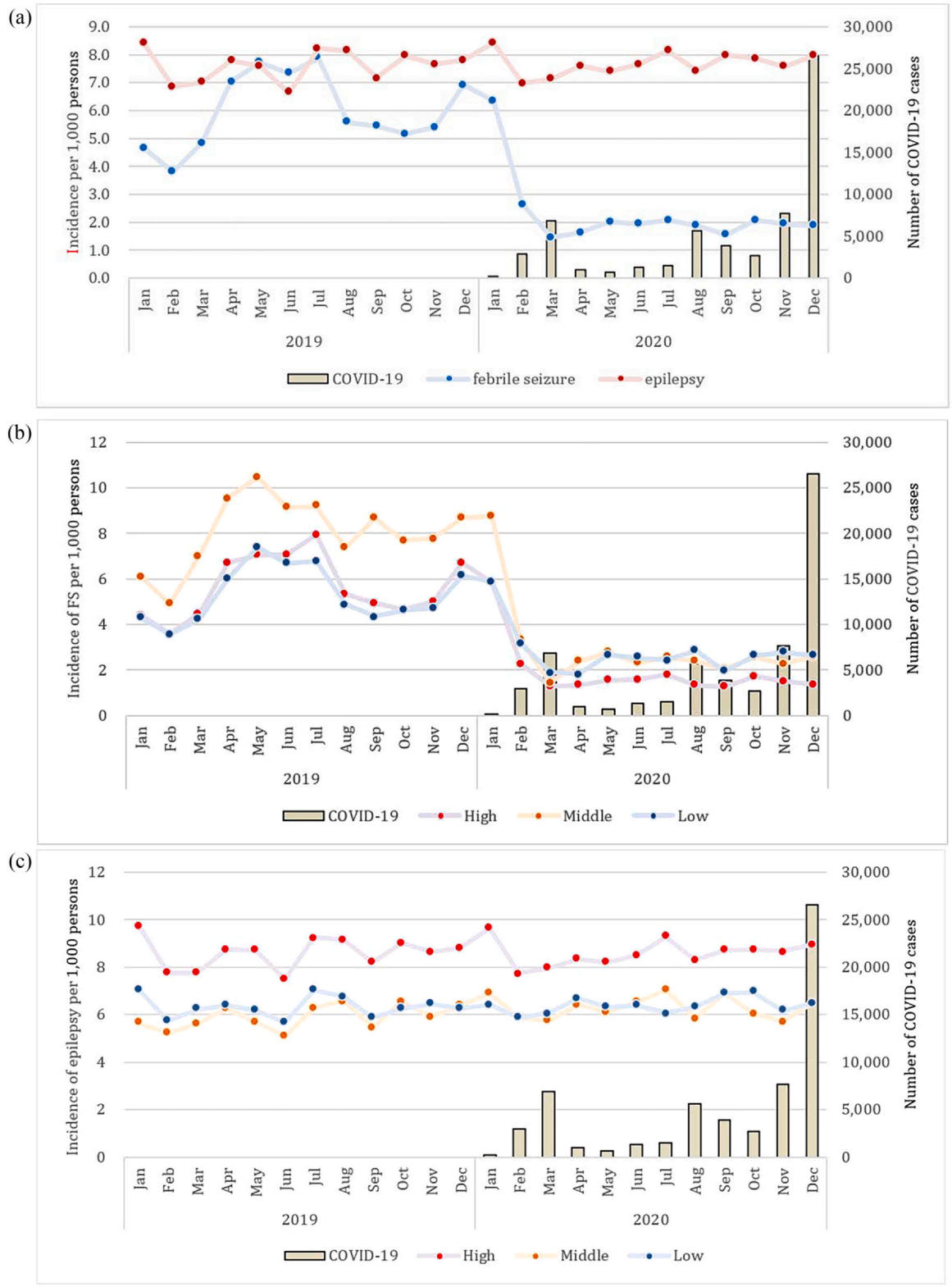

Fig. 1. Time trends of the incidence of FS and epilepsy and number of COVID-19 cases. (**a**) Overall incidence of FS and epilepsy per 1000 persons. (**b**) Incidence of FS per 1000 persons by area according to the risk of COVID-19. (**c**) Incidence of epilepsy per 1000 persons by area according to the risk of COVID-19. The bar graph represented the observed monthly incidence of COVID-19 in all age groups, the blue dots indicated the observed monthly incidence of FS, and the red dots indicated the monthly incidence of epilepsy. The number of cases included only the number of patients who were newly diagnosed with COVID-19 between February 2019 and February 2020 in South Korea. Abbreviations: FS: febrile seizure, COVID-19: coronavirus disease.

was no effect on the incidence. A previous study investigated the effects of the COVID-19 pandemic on complex chronic conditions in children, and the results showed that only the rate of hospital admissions for these conditions decreased. Other characteristics, such as length of stay, costs, and intensive care unit use, were not affected by the pandemic [24]. Although admissions declined due

Table 2
Results of the interrupted time series analysis of the monthly incidence of febrile seizure.

	Intercept	Baseline trend	Level change	Trend change	Season 1	Season 2	Season 3
All patients	4.28 (0.83)*	0.15 (0.08)	-5.55 (0.95)*	-0.06 (0.11)	1.22 (0.69)	1.20 (0.58)	0.44 (0.58)
< 1 y	3.95 (0.56)*	0.05 (0.05)	-3.00 (0.64)*	0.02 (0.08)	0.59 (0.47)	0.62 (0.39)	0.51 (0.39)
1 y	19.76 (4.80)*	0.54 (0.45)	-23.45 (5.51)*	0.11 (0.67)	7.90 (4.01)	7.01 (3.37)	1.97 (3.39)
2 y	11.68 (2.97)*	0.49 (0.28)	-17.04 (3.40)*	-0.23 (0.41)	2.36 (2.48)	3.50 (2.08)	0.21 (2.09)
3 y	5.50 (1.12)*	0.29 (0.10)*	-8.56 (1.28)*	-0.25 (0.16)	1.14 (0.93)	1.52 (0.78)	0.10 (0.79)
4 y	2.89 (0.46)*	0.18 (0.04)*	-4.69 (0.53)*	-0.15 (0.06)*	0.58 (0.39)	0.30 (0.32)	0.31 (0.33)
5 y	1.25 (0.26)*	0.15 (0.02)*	-2.83 (0.30)*	-0.15 (0.04)*	0.55 (0.22)*	0.32 (0.18)	0.67 (0.19)*
6–9 y	0.51 (0.08)*	0.03 (0.01)*	-0.67 (0.10)*	-0.02 (0.01)*	0.15 (0.07)*	0.10 (0.06)	0.26 (0.06)*
High-risk area	4.01 (0.84)*	0.14 (0.08)	-5.38 (0.97)*	-0.07 (0.12)	1.16 (0.70)	1.30 (0.59)*	0.45 (0.59)
Middle-risk area	6.05 (0.96)*	0.22 (0.09)*	-7.72 (1.10)*	-0.11 (0.13)	1.40 (0.80)	0.80 (0.67)	0.07 (0.68)
Low-risk area	3.66 (0.80)*	0.13 (0.07)	-4.40 (0.91)*	-0.01 (0.11)	1.25 (0.66)	1.23 (0.56)*	0.67 (0.56)

In parenthesis are standard errors.
* p-value < 0.05 by interrupted time series.

Table 3
Results of the interrupted time series analysis of the monthly incidence of epilepsy.

	Intercept (SE)	Baseline trend	Level change	Trend change	Season 1	Season 2	Season 3
All patients	7.13 (0.44)*	0.05 (0.04)	-0.89 (0.51)	0.03 (0.06)	0.14 (0.37)	0.21 (0.31)	0.24 (0.31)
< 1 y	3.50 (0.38)*	-0.01 (0.04)	-0.83 (0.43)	0.08 (0.05)	0.16 (0.32)	0.08 (0.27)	-0.03 (0.27)
1 y	3.83 (0.43)*	0.11 (0.04)*	-0.87 (0.49)	-0.15 (0.06)*	0.23 (0.36)	-0.09 (0.30)	-0.11 (0.30)
2 y	3.96 (0.35)*	0.05 (0.03)	-0.58 (0.40)	0.04 (0.05)	0.33 (0.29)	0.14 (0.25)	-0.06 (0.25)
3 y	4.86 (0.47)*	0.04 (0.04)	-1.10 (0.53)	0.09 (0.06)	0.29 (0.39)	-0.19 (0.33)	-0.16 (0.33)
4 y	5.78 (0.49)*	0.03 (0.05)	-0.26 (0.57)	0.03 (0.07)	0.15 (0.41)	-0.06 (0.35)	-0.16 (0.35)
5 y	7.72 (0.51)*	-0.02 (0.05)	-0.50 (0.58)	0.11 (0.07)	-0.08 (0.42)	-0.10 (0.36)	-0.08 (0.36)
6–9 y	9.77 (0.68)*	0.06 (0.06)	-1.15 (0.77)	0.03 (0.09)	0.11 (0.56)	0.52 (0.47)	0.67 (0.48)
High-risk area	8.08 (0.54)*	0.06 (0.05)	-1.19 (0.62)	0.05 (0.07)	0.13 (0.45)	0.24 (0.38)	0.34 (0.38)
Middle-risk area	4.94 (0.43)*	0.11 (0.04)*	-0.70 (0.49)	-0.06 (0.06)	0.36 (0.36)	0.37 (0.30)	0.29 (0.30)
Low-risk area	6.34 (0.38)*	0.00 (0.04)	-0.26 (0.44)	0.05 (0.05)	0.03 (0.32)	0.02 (0.27)	-0.05 (0.27)

In parenthesis are standard errors.
* p-value < 0.05 by interrupted time series.

to pandemic-related fears, other characteristics of health service use for chronic diseases are thought to have not changed.

Our study has several limitations. There are inherent limitations in all studies that use insurance claims data. FS and epilepsy are diseases in which evaluations of clinical symptoms are important; however, patients were identified using ICD codes. Nevertheless, the corresponding ICD codes and definitions have been used widely in previous studies [16]. Second, we only examined the immediate short-term effects of the COVID-19 pandemic. Strict social distancing and vigilance against coronaviruses began immediately after the pandemic started. It remains to be seen whether the effects persist even if the policy on social distancing and the coronavirus type change over time.

Despite these limitations, to the best of our knowledge, this is the first study to observe the incidence by comparing acute and chronic diseases. This nationwide study found important differences between acute and chronic neurological conditions in children in a pandemic situation. These findings suggest that clinicians and researchers need to establish different disease management strategies for acute and chronic diseases during the pandemic and formulation of infection control measures. Also, virus suppression policies and the consequent reduction in FS have brought them closer to identifying the role of viral infection in the cause of febrile seizure. For patients, it is significant that simple life-style modifications such as wearing a mask or using hand sanitizers can help control acute febrile seizures.

In conclusion, the COVID-19 outbreak and resulting social distancing measures reduced the incidence of febrile seizure(FS) immediately rather than gradually. Unlike in the case of acute FS, the COVID-19 pandemic had no effect on the incidence of chronic epilepsy. While chronic epilepsy was unaffected by the pandemic and non-pharmaceutical interventions, the pandemic was a significant factor contributing to the occurrence and treatment of FS. Further studies are needed to elucidate whether the effects of the COVID-19 pandemic on FS and epilepsy continue over the long term.

Ethical approval

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. This study was approved by the Institutional Review Board of Yonsei University Gangnam Severance Hospital (IRB No. 3-2021-0374), and the requirement for informed consent was waived by the Yonsei University IRB since the analysis was based on secondary data with anonymized patient identification numbers.

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CRediT authorship contribution statement

AYK: data curation, analysis, visualization, writing original draft, and reviewing and editing. **JHN:** conceptualization. **HYK:** supervision and reviewing and editing. **HKL:** conceptualization, data curation, supervision and reviewing and editing. **YML:** conceptualization, supervision, project administration, and final approval.

Data availability

The authors confirm that the data supporting the findings of this study are available within the article. The raw data used and analyzed during the current study are not publicly available due to our

IRB policy, but are available from the authors upon reasonable request.

Declaration of Competing Interest

The authors declare that they have no financial or non-financial competing interests.

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