

ORIGINAL ARTICLE

The effects of COVID-19 measures on the hospitalization of patients with epilepsy and status epilepticus in Thailand: An interrupted time series analysis

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Abstract

Objective: To investigate the effect of Coronavirus disease 2019 (COVID-19) measures on the hospitalization of patients with epilepsy and status epilepticus (SE).

Methods: This interrupted time series design included data from the Thai Universal Coverage Scheme electronic database between January 2017 and September 2020. The monthly hospitalization rate of epilepsy and SE was calculated by the number of hospitalizations divided by the midyear population. Segmented regression fitted by ordinary least squares (OLS) was used to detect the immediate and overtime effects of COVID-19 measures on the hospitalization rate.

Results: During January 2017 and September 2020, the numbers of epilepsy and SE patients admitted to the hospital were 129 402 and 15 547 episodes, respectively. The monthly trend of the hospitalization rate in epilepsy decreased immediately after the COVID-19 measure (0.739 per 100 000 population [95% CI: 0.219 to 1.260]). In particular, the number of children declined to 1.178 per 100 000 population, and the number of elderly individuals dropped to 0.467 per 100 000 population, while there was a nonstatistically significant change in SE.

Significance: COVID-19 measures reduced the hospital rate in epilepsy, particularly in children and adults. However, there was no change in SE patients.

KEYWORDS

coronavirus disease, hospital admission, noncommunicable diseases, public measures, seizure

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an emergency respiratory infection that rapidly spreads from person to person and becomes pandemic in a short time.¹ The continuously increasing number of COVID-19 cases impacts the system of public health, economy, or education

worldwide. Various public health measures have been implemented to limit the spread of disease (e.g., lockdown, social distancing, or wearing a face mask).²⁻⁴

Thailand first reported the COVID-19 cases in January 2020. Since the first COVID-19 cases were found, the newly cases gradually increased until early March, the number of cases rapidly rose because of the local transmission

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cluster in Bangkok that mostly tract to boxing stadium and nightclubs. Thus, the public places were closed (e.g., mall, market, and school), and the partial lockdown was implemented in and outside Bangkok. However, the cases spread widely throughout the country within March due to the workers in Bangkok returned to their hometowns. Then, a curfew, restriction of movement, and active case finding were implemented in April across the country.^{5,6}

The measures not only slowed down COVID-19 cases⁷⁻⁹ but also affected the number of other public health issues, such as drug overdose,¹⁰⁻¹² accidents,^{13,14} respiratory diseases,¹⁵⁻¹⁷ respiratory tract infection,^{18,19} and mental health.^{20,21} Moreover, as a consequence of the growing number of COVID-19 cases and established measures, health care resources have been conserved for COVID-19 patients. Thus, hospitals have restricted or delayed treatment for nonessential cases, causing the hospitalization of inpatients with noncommunicable diseases to decrease.²²⁻²⁴

Epilepsy and status epilepticus (SE) are neurological disorders that affect disability and mortality. The discontinuation of antiseizures medications in epilepsy patients is a common etiology of SE; continuous therapy is required to reduce the frequency and severity of the seizure.²⁵ Given the consequences of the COVID-19 outbreak and implemented measures, patients ranging from 4% to 35% had worse seizure control because of sleep problems, depression, and anxiety factors. In addition, 14.5% to 61.0% of those were postponed neurological tests.²⁶ Previous studies have shown that COVID-19 decreased the number of seizure-related admissions in children,²⁷ while there was no change in adult SE patients.²⁸ However, previous reports have studied children and adults. Therefore, this study aimed to investigate the effect of COVID-19 measures on the hospitalization of all patients with epilepsy and SE.

2 | MATERIALS AND METHODS

2.1 | Design and setting

This study was an interrupted time series (ITS) design and conducted the data on the Thai Universal Coverage Scheme electronic database, which is an insurance of Thai citizens and covers over 75% of the Thai population.

2.2 | Participants

Patients who were admitted to the hospital and had a primary diagnosis of epilepsy and SE from January 2017 to September 2020 were included. The database search was performed by using guidelines described in the International Statistical Classification of Diseases and

Key points

- The COVID-19 measures impacted the hospitalization rate differently in each age group.
- The hospitalization of epilepsy decreased after COVID-19 measure implementation in children and elderly
- There was a nonstatistically significant change of hospitalization rate after COVID-19 measure implementation in SE

Related Health Problems – 10th Revision (ICD-10) with codes G40 (epilepsy) and G41 (SE). Epilepsy and SE diagnosis were followed by the guideline of the International League Against Epilepsy.^{29,30} There were no restrictions on age, sex, or epilepsy and SE type. Patients with missing date of admission were also excluded.

2.3 | The COVID-19 transmission and public health measures in Thailand

The COVID-19 outbreak in Thailand began in January 2020 and the number of newly cases peaked in March which were mainly cause form local transmission cluster in Bangkok. Thus, the state of emergency announced on 26 March to impose the partial lockdown which was a nighttime curfew and a ban on gatherings of more than five people in and around Bangkok. As a result of state of emergency announcement, the public venues were closed and working from home was encouraged. However, the cases continuously rose and widely spread throughout the country because the workers migrated to countryside. Then, a nationwide curfew was implemented on April 3, 2020. In addition, restriction of movement, and active case finding were established in several provinces.⁵

2.4 | Outcome

The monthly hospitalization rate of epilepsy and SE was calculated by the number of hospitalizations divided by the midyear population.

2.5 | Sample size

We used the monthly hospitalization rate during January 2017 to September 2020 to perform an ITS analysis for

evaluating the impact of COVID-19 measures. Thus, there were 36-time points before and nine points after established measures which had an adequate sample size for ITS analysis.³¹

2.6 | Statistical analysis

Segmented regression fitted by ordinary least squares (OLS) was used to detect the immediate and overtime effect of COVID-19 measures in April 2020 (curfew, movement restriction, and active case finding) on the hospitalization rate. The equation of segmented regression model was represented as follows:

$$Y_t = \beta_0 + \beta_1 \times \text{time}_t + \beta_2 \times \text{intervention}_t + \beta_3 \times \text{time after intervention}_t + e_t$$

When Y_t is the hospitalization rate at time t , time indicate time in month from the start (January 2017) to end (September 2020) of the observation, intervention is the indicator for time t occurring before (intervention = 0) or after (intervention = 1) the implementation of the COVID-19 measures, β_0 estimate the baseline level of hospitalization rate at t_0 , β_1 represent hospitalization trend before introducing the COVID-19 measures, β_2 is the level change of hospitalization rate immediately after measures implementation, β_3 show the trend change between before and after establishing the COVID-19 measures, and $\beta_1 + \beta_3$ estimate the trend of post-intervention. Autocorrelation was examined by the Cumby–Huizinga test, and the Newey–West standard error was used to account for autocorrelation. The seasonal effect was controlled by including it as a covariate in the model.^{32,33} All statistical analyses were performed by STATA 15.0. The study protocol was approved by the ethics committee in human research, Khon Kaen University, Khon Kaen, Thailand (HE641589).

3 | RESULTS

During January 2017 and September 2020, the numbers of epilepsy and SE patients admitted to the hospital were 129 402 and 15 547 episodes, respectively. Most of the patients were men, and the median age was 36 (interquartile range [IQR] = 35) for epilepsy and 42 (IQR = 45) for SE patients (Table 1). The hospitalization rate of epilepsy before the COVID-19 spread peaked in the early year and fluctuated over the year, the rate in 2020 presented dramatically dropped from January to April. While SE was high at early of the year and gradually decreased until it returned to high again in the midyear (Figure 1). Thus, the effect of seasonality was controlled to consider the effect

TABLE 1 Characteristics of admitted epilepsy and SE patients

Characteristics	Epilepsy (n = 129 402)		SE (n = 15 547)	
	n	(%)	n	(%)
Sex				
Male	83 831	(64.8)	9815	(63.1)
Female	45 571	(35.2)	5732	(36.9)
Age (years)				
<10	20 453	(15.8)	3249	(20.9)
10–19	15 822	(12.2)	1159	(7.4)
20–29	17 379	(13.4)	1355	(8.7)
30–39	18 423	(14.2)	1598	(10.3)
40–49	20 476	(15.8)	2048	(13.2)
50–59	16 398	(12.7)	2092	(13.5)
≥60	20 451	(15.8)	4046	(26.0)
Mean (SD)	35.60	(22.2)	39.3	(26.0)
Median (IQR)	36	(35)	42	(45)
Season ^a				
Summer	42 700	(33.0)	5133	(33.0)
Rainy	47 103	(36.4)	5685	(36.6)
Winter	39 599	(30.6)	4729	(30.4)

Abbreviations: IQR, interquartile range; SD, standard deviation; SE, status epilepticus.

^aSeason including summer (February to May), rainy (June to September), and winter (October to January).

of COVID-19 measures on the hospitalization of epilepsy and SE.

3.1 | Hospitalization rate for epilepsy

The trend of hospitalization rate for overall epilepsy before the implementation of the measures increased 0.010 per 100 000 population in each month and it dropped to 0.739 per 100 000 population immediately after the first month of the COVID-19 measure was implemented. In particular, the hospitalization rate in elderly individuals declined to 0.467 per 100 000 population, and that in children declined to 1.178 per 100 000 population. However, the monthly trend after measures increased in children (Table 2).

3.2 | Hospitalization rate for SE

The immediate and overtime effects of measures on the hospitalization rate of SE were not statistically significant for all age groups (Table 2).

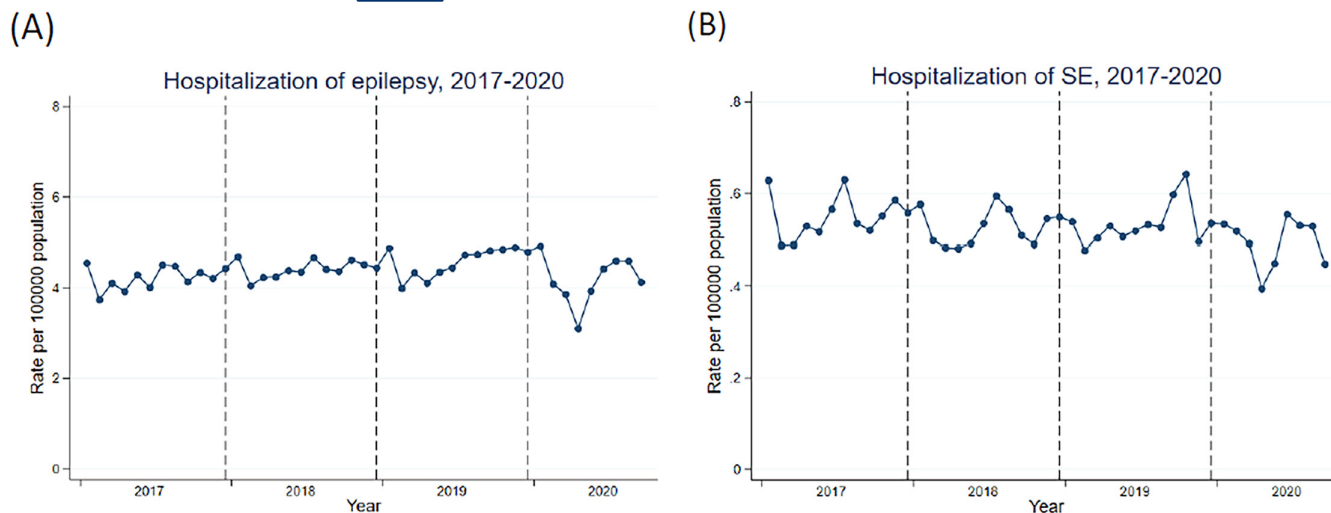


FIGURE 1 The hospitalization rate of epilepsy (A) and SE (B) patients during 2017 and 2020. SE, status epilepticus

4 | DISCUSSION

The first COVID-19 case in Thailand was reported in January 2020, and the number of cases rose continually. Thus, the curfew, movement restriction, and active case finding measures were established in April 2020 to control the spread of COVID-19. These measures affected the reduction in hospitalization of epilepsy in pediatric (0.129 per 100 000 population), which was similar to previous studies that reported a 59% decrease.²⁷ Moreover, our findings found that the hospitalization in the elderly also declined after the first month of measures (0.467 per 100 000 population). Due to concern about COVID-19 infection, medical appointments were canceled or postponed,³⁴ and the results found that increasing age was an important factor associated with experiencing a delay.³⁵ In particular, worry in caregivers or parents was a reason for delayed hospitalization in children.³⁶ Furthermore, the measures (e.g., lockdown and social isolation) were another cause for canceling appointments scheduled at medical care.^{37,38} Although the hospitalization rate of epilepsy in pediatric and elderly after the first month of implemented measures decreased, the overall trend after measures increased in pediatric patients because of therapy discontinuation in the early COVID-19 period and measure implementation.

In contrast to epilepsy, our SE results showed there was no change in the immediate and overtime effects of COVID-19 measures on the hospitalization rate, which was consistent with the latest study.²⁸ Because seizures are more severe in SE patients, patients require rapid treatment. Thus, the hospitalization rate of SE was not different between before and after establishing COVID-19 measures.

In addition, our study showed that the seasonal pattern increased the hospitalization of epilepsy (rainy: 0.379 per 100 000 population [95% CI: 0.200 to 0.558] and winter: 0.491 per 100 000 population [95% CI: 0.308 to 0.674]) and SE (rainy: 0.060 per 100 000 population [95% CI: 0.034 to 0.085] and winter: 0.061 per 100 000 population [95% CI: 0.035 to 0.087]), which was in accordance with previous research reporting that seasonality affected the number of epileptic seizures.^{39–41} Preferably in a country with a generally hot temperature, the turning from hot to cold weather is one of the triggers to increase the risk of seizures.

To our knowledge, this study reported the effect of COVID-19 measures on the hospitalization rate of epilepsy and SE and conducted data with a large sample size based on multicentre data collection. Additionally, we performed subgroup analysis by age, which was classified into children, adults, and elderly. These results provided information to plan for preventing the hospitalization of a specific age group, for instance, the physicians need to provide the information on continued medication intake to caregivers of pediatric and elderly patients in the outbreak situation because discontinuation of antiseizures medications leads to worse seizure control and eventually hospital admission. However, this study examined the effect of COVID-19 measures only in the first wave in Thailand because the time duration and measures in the first wave could obviously identify. Furthermore, living in different COVID-19 zoning areas, especially the red zone that is the area with the continued surge in cases and the maximum control, can impact decisions to go to the hospital. Moreover, the database did not contain information about anti-seizure medications which are the important factor associated with hospital admission in epilepsy and SE. Thus, further studies are needed to evaluate the effect

TABLE 2 Effect of COVID-19 measures on the hospitalization rate in epilepsy and SE patients

	Preintervention trend: β_1		Immediate level change: β_2		Trend change: β_3		Post-intervention trend: $\beta_1 + \beta_3$	
	Hospitalization rate (95% CI)	P-value	Hospitalization rate (95% CI)	P-value	Hospitalization rate (95% CI)	P-value	Hospitalization rate (95% CI)	P-value
Epilepsy								
Overall	0.010 (0.003 to 0.162)	.005	-0.739 (-1.260 to -0.219)	.007	0.112 (-0.073 to 0.298)	.228	0.122 (-0.062 to 0.306)	.188
Children ^a	0.015 (0.006 to 0.023)	.001	-1.178 (-1.478 to -0.879)	<.001	0.129 (0.020 to 0.239)	.022	0.144 (0.036 to 0.252)	.010
Adult ^b	0.008 (0.002 to 0.014)	.015	-0.603 (-1.342 to 0.136)	.107	0.125 (-0.115 to 0.366)	.297	0.133 (-0.106 to 0.373)	.267
Elderly people ^c	0.012 (-0.003 to 0.028)	.107	-0.467 (-0.908 to -0.025)	.039	0.122 (-0.079 to 0.323)	.288	0.134 (-0.071 to 0.339)	.193
SE								
Overall	-0.001 (-0.002 to 0.001)	.217	-0.039 (-0.113 to 0.036)	.298	0.001 (-0.023 to 0.024)	.947	0.0001 (-0.024 to 0.024)	.992
Children ^a	-0.002 (-0.004 to 0.001)	.136	-0.089 (-0.218 to 0.040)	.170	-0.030 (-0.075 to 0.016)	.193	-0.032 (-0.077 to 0.014)	.171
Adult ^b	-0.0002 (-0.002 to 0.001)	.794	-0.033 (-0.086 to 0.020)	.212	0.007 (-0.010 to 0.023)	.421	0.006 (-0.010 to 0.022)	.428
Elderly people ^c	-0.002 (-0.005 to 0.001)	.203	0.006 (-0.134 to 0.145)	.934	0.023 (-0.013 to 0.059)	.200	0.021 (-0.014 to 0.057)	.230

Abbreviation: SE, status epilepticus.

^aChildren, less than 20 years old.^bAdult, 20 to 59 years old.^cElderly people, 60 years old and above.

of COVID-19 measures on the hospitalization rate of epilepsy and SE in various COVID-19 zoning areas and performing subgroup analysis in with and without continuous antiseizure medications.

In conclusion, the COVID-19 measures impacted the reduced hospitalization rate in epilepsy, especially children and adults, but there was a nonsignificant decrease in SE patients.

CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose. 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.

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