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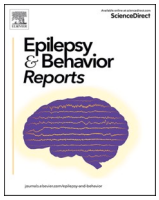

Comparison of neurological manifestation in children with and without coronavirus 2019 experiencing seizures with fever

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ABSTRACT

Whether neurologic symptoms due to SARS-CoV-2 differ from those of non-SARS-CoV-2 viral infection is unclear. We aimed to describe these neurological manifestations and compare the clinical characteristics and treatments in children with seizures and fever with or without COVID-19. We retrospectively analyzed data from 105 hospitalized children (<18 years) with clinical seizures and fever between September 2021 and August 2022. We compared the clinical characteristics and treatments between the COVID-19 (n = 20) and non-COVID-19 (n = 85) groups. Patients with COVID-19 were older than those without (32.5 [20–86] months vs. 20 [16–32] months, p = 0.029). Seizure type and duration and impaired consciousness duration did not differ between groups. Six and 32 patients experienced status epilepticus lasting 30 min in the COVID-19 and non-COVID-19 groups, respectively. Most treatments did not differ between groups; however, electroencephalography was used less frequently for COVID-19. Neurological sequelae occurred in one and four patients in the COVID-19 and non-COVID-19 groups, respectively. In conclusion, seizures with fever due to SARS-CoV-2 were more common in older children. Seizure characteristics and neurologic sequelae did not differ in children with and those without COVID-19. In general, electroencephalography was used less during COVID-19 for infection control measures.

1. Introduction

Most children with coronavirus disease 2019 (COVID-19) have a milder form than adults do [1]. However, neurological symptoms are diverse and include headache, impaired consciousness, and seizures [2]. In particular, during the Omicron strain of the COVID-19 epidemic, the number of pediatric patients presenting with seizures and fever increased [3,4]. Several pediatric case series have reported neurological symptoms associated with COVID-19 [5–8]. A few severe cases were reported in children [9,10]. However, whether the neurological symptoms due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are distinct or more severe than those associated with non-SARS-CoV-2 viral infections is unclear.

Febrile seizures are characterized by a fever at 6–60 months old [11]. However, seizures with fever have been reported in children older than five years [12,13]. Generally, the outcomes for these children are favorable. However, some cases of febrile status epilepticus are associated with subsequent neurological sequelae, including virus-associated acute encephalopathy [14,15], febrile infection-related epilepsy syndrome [15,16], and hippocampal abnormalities [17,18], which require appropriate treatment and management.

We hypothesized that children with febrile seizures due to SARS-CoV-2 would have different characteristics, such as onset age and neurological symptoms, compared with those without SARS-CoV-2. Therefore, this study aimed to describe the detailed clinical characteristics of children with COVID-19 during the Omicron variant era and compare them to those without COVID-19. We also hypothesized that treatment might be challenging and limited in children with COVID-19

Abbreviations: ASM, anti-seizure medication; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; EEG, electroencephalogram; PCPC, Pediatric Cerebral Performance Category; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WBC, white blood cell.

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due to infection isolation. Therefore, we compared the treatments in children with seizures and fever between COVID-19 and non-COVID-19 groups.

2. Materials and methods

2.1. Study design and patients

This study was conducted with the approval of the Ethics Committee of Kobe University Graduate School of Medicine, Kobe, Japan (number: 180011) and Kobe Children's Hospital, Kobe, Japan (number: 31–49), with a waiver for informed consent owing to the observational study design.

We retrospectively analyzed data collected from consecutive patients (aged < 18 years) admitted to Kobe Children's Hospital due to clinical seizures with fever between September 2021 and August 2022. Kobe Children's Hospital is a tertiary institution for severely ill children in the city of Kobe and the neighboring areas with a population of 1.5 million. Over 100 patients of seizures with fever were admitted to the hospital yearly before the COVID-19 epidemic. The indication for hospitalization of patients presenting with seizures was determined by a physician in the emergency department and a certified pediatric physician. Sometimes, these physicians consulted a pediatric neurologist before deciding on hospitalization. Patients with severe neurological symptoms, including prolonged seizures, seizure clusters, and prolonged impaired consciousness, were hospitalized. Conversely, COVID-19 did not affect the indication for hospitalization because the SARS-CoV-2 test was conducted after hospitalization.

Of the 144 patients, 38 with neurological histories (epilepsy, intellectual disability, developmental delay, or chromosomal abnormality) and one with symptomatic hypoglycemia were excluded from this study. In total, 105 patients were included in this study. We divided the cohort into two groups: (1) patients diagnosed with COVID-19 and (2) those not diagnosed with COVID-19. During the study period, all newly admitted patients underwent SARS-CoV-2 antigen assay using the Roche Diagnostics Cobas e 411 analyzer from a nasopharyngeal swab sample. Patients with a positive antigen assay result were diagnosed with COVID-19. However, patients with initial negative antigen assay results who were suspected of having COVID-19 underwent re-testing with the antigen assay or real-time polymerase chain reaction using the BioFire FilmArray Respiratory Panel 2.1, based on the infection control team's advice.

2.2. Outcomes and assessment items

Most data were obtained from our database, consisting of prospective demographic, clinical presentation, treatment, management, laboratory findings, and neurological sequelae. We also reviewed the medical charts, clinical presentations, and laboratory findings.

This was an exploratory study; thus, the primary outcome was not established. However, we described and compared the clinical characteristics of the COVID-19 and non-COVID-19 groups. The exploratory outcomes included age at seizure onset, neurological manifestations—such as convulsive seizure duration, impaired consciousness duration, seizure type, history of febrile seizures, examination findings, and neurological sequelae. Seizure onset was the onset of any neurological symptoms, including convulsions or eye deviation [19]. Seizure duration was the time between seizure onset, according to information from caregivers, and seizure cessation, as confirmed by physicians [19]. Convulsive seizure duration was the duration of a persistent convulsion or a sequence of intermittent convulsions without full recovery of consciousness between convulsions [20]. The seizure type was defined as focal, generalized, and unknown onset according to the International League Against Epilepsy classification [21]. Impaired consciousness was defined as a Glasgow Coma Scale score < 15. Neurological sequelae were assessed using the Pediatric Cerebral Performance Category (PCPC) scale, with a score of 1 representing normal performance; 2, mild disability; 3, moderate disability; 4, severe disability; 5, persistent vegetative state; and 6, death [22]. Neurological sequelae were defined as PCPC scores ≥ 2 at discharge. We assessed their treatment and management, including anticonvulsants and electroencephalogram (EEG) monitoring. Notably, EEG monitoring is a good indicator for patients with prolonged impaired consciousness. To assess the effect of COVID-19 on EEG monitoring, we compared the duration of impaired consciousness among patients, stratified by the presence or absence of EEG monitoring, in both the COVID-19 and non-COVID-19 groups.

2.3. Statistical analysis

Analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (version 3.1.2; The R Foundation for Statistical Computing, Vienna, Austria) [23]. Results were expressed as numbers (%) or medians (interquartile range [1st quartile–3rd quartile]). Numerical data were compared using the Mann–Whitney *U* test. Categorical data were compared using Fisher's exact test. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Patient demographics in the COVID-19 and non-COVID-19 groups

During the study period, approximately one-fifth of the cases were seizures associated with COVID-19. All patients with COVID-19 were admitted after February 2022, except one admitted on January 23 (Fig. 1). This occurred when the Omicron strain became predominant in Japan. Patient demographics of the COVID-19 (n = 20) and non-COVID-19 (n = 85) groups are presented in Table 1. The final diagnosis comprised acute encephalopathy/encephalitis in 1 patient (5.0 %), simple febrile seizure in 2 (10.0 %), and complex febrile seizure in 17 (85.0 %) in the COVID-19 group. In contrast, the final diagnosis in the non-COVID-19 group comprised acute encephalopathy/encephalitis in eight patients (9.4 %), simple febrile seizure in five (5.9 %), and complex febrile seizure in 72 (85.0 %).

The age at onset was higher in the COVID-19 versus non-COVID-19 group (32.5 [20–86] months vs. 20 [16–32] months, p = 0.029). Specifically, six (30.0 %) patients developed COVID-19 at over 5 years of age, with a bimodal onset age of 1 year and > 5 years (Fig. 2). Conversely, the non-COVID-19 group displayed a unimodal peak at 1 year of age. There was no significant difference in the medical history of febrile seizures. The temperature on admission or the time between fever and seizure onset did not differ between the COVID-19 and non-COVID-19 groups. Convulsive seizure duration did not significantly differ between the COVID-19 and non-COVID-19 groups at 15 (5–45) and 10 (4–50) minutes, respectively. Six patients (30.0 %) in the COVID-19 and 32 (37.6 %) in the non-COVID-19 group experienced status

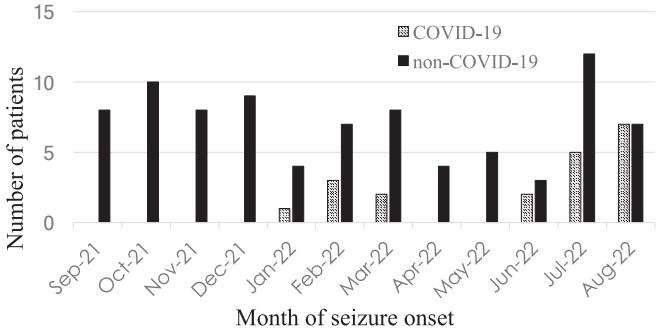

Fig. 1. Monthly hospitalization for seizures with fever. Abbreviations: COVID-19, coronavirus disease 2019.

Table 1
Clinical characteristics, examination findings, and outcomes in the COVID-19 (n = 20) and non-COVID-19 (n = 85) groups.

	COVID-19 group (n = 20)	Number of patients assessed	Non-COVID-19 group (n = 85)	Number of patients assessed	p-value
Age, months	32.5 (20–86)		20 (16–32)		0.029
Sex, Male	9 (45.0)		53 (62.4)		0.207
History of febrile seizure	7 (35.0)		26 (30.6)		0.790
Temperature on admission, ℃	39.3 (38.8–39.9)		39.4 (38.6–39.9)		0.906
Time from onset to arrival at hospital, min	57 (39–99)		45 (32–54)	76	0.024
Time between fever and seizure onset, h	8 (5–9)	15	7 (3–16)	27	0.837
Duration of convulsive seizure, min	15 (5–45)	17	10 (4–50)	81	0.944
Status epilepticus (≥30 min)	6 (30.0)		32 (37.6)		0.611
Refractory status epilepticus	1 (5.0)		5 (5.9)		1.000
Duration of impaired consciousness, min	102 (70–159)	19	179 (51–278)	78	0.360
Level of consciousness					
Incomplete recovery at 6 h	1 (5.0)		14 (16.5)		0.293
Incomplete recovery at 12 h	1 (5.0)		9 (10.6)		0.683
Incomplete recovery at 24 h	1 (5.0)		8 (9.5)		1.000
Type of seizure					0.098
Focal onset	2 (10.0)		11 (12.9)		
Generalized onset	9 (45.0)		56 (65.9)		
Unknown onset	9 (45.0)		18 (21.2)		
Recurrence within 24 h	10 (50.0)		38 (44.7)		0.804
Time from onset to initial blood test, min	76 (45–115)	17	80 (52–129)	76	0.728
Laboratory data					
WBC, $\times 10^6$/L	6700 (5000–8500)	16	11,400 (7800–17200)	78	<0.001
Hb, g/dL	12.1 (11.5–13.6)	16	11.9 (11.2–12.4)	78	0.099
PLT, $\times 10^9$/L	22.9 (20.4–27.3)	16	26.5 (21.9–31.9)	78	0.101
AST, U/L	40 (32–58)	16	36 (33–45)	78	0.392
ALT, U/L	15 (13–23)	16	15 (12–19)	78	0.555
CK, U/L	105 (62–156)	14	118 (87–188)	74	0.214
LDH, U/L	308 (261–327)	16	307 (270–341)	76	0.926
CRE, mg/dL	0.32 (0.25–0.48)	16	0.30 (0.14–0.53)	77	0.424
Na, mEq/L	135 (135–136)	16	135 (133–138)	78	0.574
Ca, mg/dL	9.7 (9.3–9.9)	11	9.4 (9.2–9.7)	49	0.309
GLU, mg/dL	120 (94–147)	15	127 (110–184)	74	0.169
CRP, mg/dL	0.27 (0.10–0.42)	16	0.53 (0.14–1.25)	76	0.049
NH_3, μg/dL	54 (49–65)	9	52 (44–62)	43	0.417
pH	7.38 (7.34–7.40)	16	7.37 (7.21–7.42)	72	0.307
BE, mEq/L	−3.8 (−6.1–−1.4)	16	−4.8 (−6.7–−2.4)	71	0.311
Lac, mmol/L	2.7 (1.5–4.2)	16	2.1 (1.4–2.9)	70	0.377
CT abnormality	1 (5.0)		1 (1.2)		1.000
MRI abnormality	0 (0)		3 (3.5)		1.000
Duration of hospital stay, days	3 (2–3)		3 (2–3)		0.509
Neurological sequelae	1 (5.0)		4 (4.7)		1.000
Final diagnosis					0.758
Acute encephalopathy/encephalitis	1 (5.0)		8 (9.4)		
Simple febrile seizure	2 (10.0)		5 (5.9)		
Complex febrile seizure	17 (85.0)		72 (84.7)		

Data are presented as the number of children (%) or median (IQR). Regarding the number of patients assessed, blank cells mean that all patients could be assessed. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BE, base excess; CK, creatine kinase; COVID-19, coronavirus disease 2019; CRE, creatinine; CRP, C-reactive protein; CT, computed tomography; GLU, glucose; Hb, hemoglobin; Lac, lactate; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging; PLT; platelet; WBC, white blood cell count.

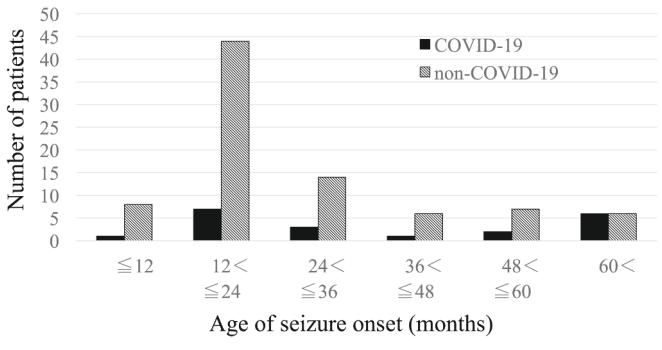

Fig. 2. Age distribution of seizure onset. Abbreviations: COVID-19, coronavirus disease 2019.

epilepticus lasting 30 min. Despite the lack of significance, the COVID-19 group had fewer focal-onset seizures. The duration of impaired consciousness and distribution of incomplete recovery of consciousness did not differ between the groups. Specifically, one patient (5.0 %) in the COVID-19 group and nine (10.6 %) in the non-COVID-19 group experienced prolonged impaired consciousness for over 12 h. Ten (50.0 %) patients had seizure recurrence within 24 h, indicating common recurrence of seizures; however, this was not significantly different between the COVID-19 and non-COVID-19 groups.

Blood investigations did not differ except for the white blood cell (WBC) and C-reactive protein (CRP). WBC and CRP levels were lower in the COVID-19 than those in the non-COVID-19 group, indicating a lower inflammatory reaction. One fatality occurred in the COVID-19 group with abnormal computed tomography findings; however, magnetic resonance imaging could not be performed. One patient (5.0 %) in the COVID-19 group and four (4.7 %) in the non-COVID-19 group had neurological sequelae at discharge. The duration of hospital stay did not differ between the groups.

3.2. Treatment and management in the COVID-19 and non-COVID-19 groups (Table 2)

The number or types of anti-seizure medications (ASMs) were not different between the COVID-19 and non-COVID-19 groups. EEG monitoring was performed less frequently in the COVID-19 group than in the non-COVID-19 group (5 [25.0 %] vs. 43 [50.6 %] patients, $p = 0.047$). Duration of impaired consciousness was longer in patients with EEG monitoring than in those without in the non-COVID-19 group (patients with EEG monitoring, 235 [172–309] minutes; patients without EEG monitoring, 57 [41–200] minutes; $p < 0.001$). In contrast, the duration of impaired consciousness was not different between patients with EEG monitoring and those without EEG monitoring in the COVID-19 group (patients with EEG monitoring, 184 [153–226] minutes; patients without EEG monitoring; 100 [65–130] minutes, $p < 0.121$). The proportions of mechanical ventilation, targeted temperature management, and intravenous methylprednisolone did not differ between groups.

3.3. Detailed clinical characteristics in the COVID-19 group (Table 3)

We excluded patients with a neurological history; therefore, no patient had a history of epilepsy. However, seven patients had a history of febrile seizures. The patients were aged 12 months to 13 years, including six patients > 5 years. Thirteen patients (65 %) experienced status epilepticus, that is, a seizure lasting at least 5 min. Six (30 %) patients presented with seizures longer than 30 min. Of the six older patients (cases 15–20), two had no convulsive seizures, and one required ASM. Time from onset to arrival at the hospital was 19–460 min, except for three patients who presented with seizures when they visited the hospital due to non-neurological symptoms. EEG monitoring was conducted in patients with impaired consciousness; however, a few patients with impaired consciousness for over 4 h did not undergo EEG monitoring (cases 3 and 20). One female patient aged 36 months (case 11) died. She had convulsive seizures for 93 min. Thereafter, EEG monitoring displayed electrographic seizures, and she required continuous midazolam administration and mechanical ventilation. She never regained consciousness and died from severe brain edema.

Table 2
Treatment and management in the COVID-19 (n = 20) and non-COVID-19 (n = 85) groups.

	COVID-19 group (n = 20)	Non-COVID-19 group (n = 85)	p-value
Number of ASM			
None	12 (60.0)	38 (44.7)	0.320
One	3 (15.0)	25 (29.4)	0.264
Two or more	5 (25.0)	22 (25.9)	1.000
Types of ASM			
DZP iv	0 (0)	7 (8.2)	0.342
MDL iv	6 (30.0)	37 (43.5)	0.319
fPHT iv	6 (30.0)	24 (28.2)	1.000
LEV iv	0 (0)	5 (5.9)	0.581
PB iv	0 (0)	4 (4.7)	1.000
MDL civ	1 (5.0)	1 (1.2)	0.346
Thiamylal civ	0 (0)	6 (7.1)	0.592
EEG monitoring	5 (25.0)	43 (50.6)	0.047
Mechanical ventilation	1 (5.0)	7 (8.2)	1.000
TTM	0 (0)	5 (5.9)	0.581
IVMP	1 (5.0)	7 (8.2)	1.000

Data are presented as the number of children (%).
Abbreviations: ASM, anti-seizure medication; civ, continuous infusion in vein; COVID-19, coronavirus disease 2019; DZP, diazepam; EEG, electroencephalogram; fPHT, fosphenytoin; iv, intravenous; IVMP, intravenous methylprednisolone; LEV, levetiracetam; MDL, midazolam; PB, phenobarbital; TTM, targeted temperature management.

4. Discussion

In this study, we describe the clinical characteristics of children with fever caused by SARS-CoV-2 infection. This is the first study to compare patient age, severity, neurological symptoms, laboratory findings, and treatment of seizures with fever associated with COVID-19 with those without COVID-19 using a consecutive cohort of patients hospitalized for neurological symptoms.

Our findings revealed that seizures associated with COVID-19 accounted for 19 % of all seizure with fever hospitalizations between September 2021 and August 2022. Nearly all COVID-19 cases were admitted after February 2022, when the Omicron strain became predominant in Japan. During this period, COVID-19 cases accounted for 29 % of all hospitalizations for seizures with fever. Previous studies have reported that, compared to that of previous strains, the proportion of neurological symptoms among all COVID-19-infected patients increased during Omicron strain epidemics [3,24]. The seizure rate in children before the Omicron strain epidemic was 1.7 %; however, it increased to 14.6 % during the Omicron strain epidemic [3]. In the other multicenter observational study, 19 of 61 (31 %) hospitalized patients with COVID-19 experienced seizures [24]. While previous reports have revealed an increased occurrence of neurological symptoms in all patients with COVID-19, our results indicate that COVID-19 accounts for a high proportion of all febrile seizures.

The onset age in the COVID-19 group was > 5 years in 30 % of the cases. In the non-COVID-19 group, 7 % of patients had febrile seizures at > 5 years. Considering the previously reported frequency of febrile seizures in patients > 5 years old (5.4 %) [25]. SARS-CoV-2 is more likely to cause febrile seizures after school age. Furthermore, susceptibility to neurological symptoms depends on the pathogen. In a prospective cohort study of 225 participants aged < 6 years, the viruses most likely to produce febrile seizures were respiratory-associated viruses, including influenza, parainfluenza, coronaviruses, and enteroviruses [26]. Among those participants, seasonal coronaviruses (OC45, 229E, and NL63) were associated with a greater risk of seizure in children aged 3–6 years compared to other viruses. In contrast, influenza was associated with febrile seizures in children aged 6 months to 3 years [26]. SARS-CoV-2 is an unconventional virus, and the absence of antibodies in older children may also contribute to the high occurrence of seizures in older children. Previously, H1N1 influenza, which was an unconventional virus at the time of the 2009 pandemic, has caused many cases of encephalopathy in older children [27].

Inflammation accelerates seizures [15]; therefore, severe inflammation and elevated body temperature affect neurological symptoms. The mean body temperature was high in both the COVID-19 group and non-COVID-19 group in this study; however, the inflammatory response as indicated by WBC and CRP levels, was mild in the COVID-19 group. The lower leukocyte and inflammatory responses in the COVID-19 group than in the non-COVID-19 group suggest that even mild inflammation may induce seizures, indicating that SARS-CoV-2 may have a higher neuroaffinity than that of other viruses. However, leukocyte and CRP are only examples of inflammatory responses. This study could not examine other inflammatory responses such as cytokines and chemokines. Therefore, this limitation should be addressed in future research.

Neurological symptoms associated with COVID-19 in children have been reported previously [5–8]. However, whether neurological symptoms caused by SARS-CoV-2 are more severe than those caused by other viral infections is unclear. Our results revealed that the incidence of neurological symptoms, such as seizure duration, impaired consciousness, seizure type, and neurological sequelae, did not differ between the COVID-19 and non-COVID-19 groups. However, both situations were associated with severe symptoms, such as status epilepticus, encephalopathy, or seizure recurrence, suggesting the need for appropriate treatment and management.

In our study, most treatments and management were not different; however, EEG monitoring was conducted less frequently in the COVID-

Table 3
Detailed clinical characteristics of patients with seizure and fever in the COVID-19 group (n = 20).

Case	Age, months	Sex	Temperature on admission, ℃	History of febrile seizure	Neurological sequelae	Time between fever and seizure onset, hours	Time from onset to arrival at hospital, minutes	Duration of convulsive seizure, minutes	Type of seizure	Seizure pattern	Duration of impaired consciousness, minutes	Recurrence within 24 h	EEG monitoring	Electrographic seizure	Mechanical ventilation	ASM
Case 1	12	Female	39.7	Yes	No	5	57	3	Generalized onset	Tonic-clonic seizure	64	Yes	No	No	No	None
Case 2	13	Male	38.9	No	No	4	0	19	Generalized onset	Clonic seizure	94	No	No	No	No	MDL iv
Case 3	13	Female	39.2	No	No	nd	44	8	Unknown onset	Unknown	249	Yes	No	No	No	MDL iv, fPHT iv
Case 4	15	Male	40.4	No	No	8	0	8	Generalized onset	Tonic-clonic seizure	102	Yes	No	No	No	None
Case 5	18	Female	39.7	No	No	nd	52	1	Generalized onset	Unknown	76	Yes	No	No	No	None
Case 6	21	Male	38.6	No	No	8	101	20	Unknown onset	Tonic seizure	100	Yes	No	No	No	MDL in ib, fPHT iv
Case 7	22	Male	40.2	No	No	9	460	5	Generalized onset	Tonic-clonic seizure	180	No	Yes	No	No	None
Case 8	23	Male	39.3	Yes	No	nd	62	Non-convulsive seizure only	Unknown onset	Unknown	64	No	No	No	No	None
Case 9	25	Male	39.9	No	No	7.5	38	52	Unknown onset	Tonic seizure	188	No	Yes	No	No	MDL iv, fPHT iv
Case 10	29	Male	39.0	Yes	No	9.5	57	15	Focal Onset	Tonic-clonic seizure	65	No	No	No	No	None
Case 11	36	Female	40.2	No	Yes, death	17	60	93	Unknown onset	Tonic seizure	Unrecovered	Yes	Yes	Yes	Yes	MDL iv, fPHT iv, MDL civ
Case 12	40	Male	39.3	No	No	5	99	145	Generalized onset	Tonic seizure	341	No	Yes	No	No	MDL iv, fPHT iv
Case 13	49	Female	39.5	No	No	6	78	1	Unknown onset	Tonic seizure	58	Yes	No	No	No	None
Case 14	51	Female	38.1	Yes	No	1.5	139	39	Generalized onset	Tonic seizure	139	Yes	No	No	No	fPHT iv
Case 15	82	Female	38.3	No	No	13	53	5	Focal Onset	Tonic seizure	63	Yes	No	No	No	None
Case 16	99	Female	39.3	Yes	No	0.5	18	Non-convulsive seizure only	Unknown onset	Unknown	123	No	No	No	No	None
Case 17	100	Female	39.9	Yes	No	12	0	74	Generalized onset	Tonic seizure	74	Yes	Yes	No	No	MDL iv
Case 18	115	Female	38.1	Yes	No	nd	40	Non-convulsive seizure only	Unknown onset	Unknown	130	No	No	No	No	None
Case 19	147	Female	39.9	No	No	20	181	45	Unknown onset	Tonic-clonic seizure	130	No	No	No	No	None
Case 20	159	Male	38.3	No	No	nd	188	1	Generalized onset	Clonic seizure	300	No	No	No	No	None

Abbreviations: ASM, anti-seizure medication; civ, continuous infusion in vein; COVID-19, coronavirus disease 2019; EEG, electroencephalogram; fPHT, fosphenytoin; iv, intravenous; MDL, midazolam; nd, not detected.

19 group than in the non-COVID-19 group. EEG monitoring is essential for detecting electrographic seizures [28]. Continuous EEG monitoring detected electrographic seizures in 26–57 % of pediatric patients following convulsive status epilepticus [29]. Moreover, electrographic seizures have been associated with poor neurologic outcomes [30,31]. Therefore, EEG monitoring is recommended in patients with prolonged impaired consciousness following a seizure [29]. The low rate of EEG monitoring in COVID-19 patients might be caused by infection isolation. Infection control measures for patients with COVID-19 are important; however, they may restrict appropriate treatment and management.

This study's strength is that it involved consecutive hospitalized patients with seizures and fever. Since the SARS-CoV-2 test was performed after the decision to hospitalize, COVID-19 did not influence the indication for hospitalization. Therefore, we could compare the COVID-19 and non-COVID-19 cases under the same conditions. However, this study had some limitations. First, the study data were based on cases from a single institution and were retrospectively analyzed. Clinical information was extracted from the medical charts; however, the seizure type may be inaccurate. Second, the COVID-19 cases were in the epidemic period of the Omicron strain; however, we could not identify the viral strain. Finally, we excluded cases with neurological histories to reduce the influence of background disease; therefore, the results cannot be applied to patients with a neurological history. Eight (21.1 %) of 38 patients with neurological histories had seizures associated with COVID-19.

5. Conclusions

Seizures with fever due to SARS-CoV-2 were more common in older children compared with seizures due to other viruses. Seizure characteristics and neurologic sequelae do not differ in children with and those without COVID-19. In general, EEG monitoring was used less during COVID-19 for infection control measures. The neurological manifestations of COVID-19 in this study will contribute to the appropriate treatment and management of COVID-19 in the future.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data statement

Data not available/The data that has been used is confidential.

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