Seizure Incidence among Children Hospitalized with COVID-19 during the Omicron Wave

Sze Pei Eow, MRCPCH¹, Ker Yang Chua, MMedPaeds¹, Karuthan Chinna, PhD², Sitti Sulhoon Mohamed, MMedPaeds¹, Ahmad Rithauddin Mohamed, FRCPCH¹

¹Pediatric Department, Hospital Tunku Azizah, Ministry of Health, Malaysia, Kuala Lumpur, Malaysia
²Faculty of Business and Management, UCSI University, Kuala Lumpur, Malaysia

Purpose: Since late 2019, coronavirus disease 2019 (COVID-19) has rapidly spread worldwide. Some children with COVID-19 present with seizures; in particular, studies have reported an increase in seizure episodes during the Omicron wave of the pandemic. This study was performed to describe the clinical characteristics of seizures among children hospitalized with COVID-19 before and during the Omicron wave.

Methods: A retrospective cross-sectional study was conducted on all pediatric admissions for COVID-19 at Hospital Tunku Azizah from June 2021 to May 2022.

Results: During this period, 1,586 children were admitted with COVID-19, of whom 111 (7.0%) experienced seizures. Patients with seizures were more likely to have a history of seizure (odds ratio [OR], 71.4; 95% confidence interval [CI], 23.7 to 215.2; P<0.001) and prior antiseizure medication use (OR, 55.1; 95% CI, 6.1 to 497.4; P<0.001). Most seizures (55.0%) occurred on the first day of illness, with 86.5% lasting less than 5 minutes. None of the children required intubation or admission to the pediatric intensive care unit, and all were discharged without complications. Between June 2021 and January 2022, the seizure rate varied from 1.3% to 3.4%; however, it increased to 18% in April 2022, coinciding with the period of Omicron variant predominance in Malaysia. Children admitted during the Omicron wave had significantly higher odds of experiencing seizures (OR, 7.89; 95% CI, 2.07 to 13.07; P<0.001) than children hospitalized prior to this wave.

Conclusion: In conclusion, the study revealed a marked increase in seizures associated with pediatric COVID-19 cases during the Omicron wave.

Keywords: COVID-19; Pediatrics; Seizures, febrile; SARS-CoV-2 variants; Prevalence

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to a global pandemic [1]. In addition to respiratory symptoms, some patients exhibit neurological manifestations, including headaches, paresthesia, vertigo, delirium, encephalitis, and seizures [2]. Early studies from China indicated that between 0.47% and 0.66% of adult patients with COVID-19 experience seizures [3,4]. In children, seizure is an early and primary manifestation of acute COVID-19; in one study, 6% of pediatric patients diagnosed with SARS-CoV-2 infection in the emergency department presented...
with seizures [5]. In Malaysia, a study conducted in Negeri Sembilan revealed that 57.9% of children with COVID-19 were asymptomatic upon presentation, and only 1.5% reported headache [6]. Meanwhile, a separate study in Selangor found that only 5.8% of pediatric patients with SARS-CoV-2 infection exhibited neurological symptoms [7].

The Omicron variant first appeared in Malaysia in December 2021, and by January 2022, it accounted for 80% of all sequenced SARS-CoV-2 genomes [8]. Recent studies have identified seizures as an early sign of acute SARS-CoV-2 infection in children during the spread of the Omicron variant [9]. Furthermore, a study from South Africa indicated that convulsions were present in 20% of pediatric patients during the Omicron wave [10].

This study was performed to describe the clinical manifestations of seizure among children hospitalized for COVID-19 before and during the Omicron wave.

### Materials and Methods

A retrospective cross-sectional study was conducted on all pediatric patients admitted with COVID-19 to Hospital Tunku Azizah (HTA) in Malaysia between June 1, 2021, and May 31, 2022. The study received approval with a waiver of consent from the Medical Research and Ethics Committee of the Ministry of Health, Malaysia (ID NMRR ID-22-02322-T6L [IIR]) on December 22, 2022. The authors declared no conflicts of interest.

This study included all pediatric patients aged 1 month to 12 years who tested positive for COVID-19 via polymerase chain reaction or antigen rapid test kit and were admitted to HTA. These participants were identified using the institution’s COVID-19 database, which the pediatric department of HTA created and maintains. The database, established in April 2020, includes records of all children admitted to HTA with confirmed or suspected COVID-19. The information retrieved from the database encompassed demographic characteristics, dates of admission and discharge, comorbidities, and presenting symptoms. For cases involving seizures, electronic health records were examined for details regarding seizure characteristics, laboratory results, and medications administered. Seizure diagnosis was categorized as simple (lasting less than 15 minutes with no recurrence within 24 hours) or complex (lasting more than 15 minutes, recurring within 24 hours, and/or accompanied by focal neurological deficits) febrile seizure, if occurring between 6 months and 6 years of age; fever-provoked seizure (outside the typical age range for febrile seizure or affecting individuals with underlying neurological abnormalities); breakthrough seizure (in persons with epilepsy who are taking antiseizure medication); meningoencephalitis; or afebrile seizure.

### 1. Statistical analysis

Data were analyzed using IBM SPSS Statistics version 27 (IBM Corp., Armonk, NY, USA). Descriptive statistics were employed to summarize quantitative variables, presented as median (minimum to maximum), while qualitative variables were expressed as frequency (percentage). Statistical analysis was conducted using the chi-square test and Fisher exact test for categorical data, along with the Mann-Whitney U test for continuous data. A $P$ value of less than 0.05 was considered to indicate statistical significance.

### Results

During the study period, a total of 1,586 pediatric patients were admitted to HTA with COVID-19 infection. Of these individuals, 111 (7.0%) presented with seizures, either at onset or during the course of the infection. The remaining 1,475 children were admitted with a diagnosis of COVID-19 but did not experience seizures.

Patients with seizures were more likely to have a history of seizure (odds ratio [OR], 71.4; 95% confidence interval [CI], 23.7 to 215.2; $P<0.001$) and prior antiseizure medication use (OR, 55.1; 95% CI, 6.1 to 497.4; $P<0.001$) (Table 1).

The seizure rate among COVID-19 admissions ranged from 1.3% to 3.4% between June 2021 and January 2022 (Fig. 1). Starting in January 2022, the seizure rate began to increase, peaking at 18.0% in April 2022. The following month, the rate declined to 3.6%. Children admitted for COVID-19 from February 2022 to May 2022 had significantly higher odds of experiencing seizures compared to those admitted between June 2021 and January 2022.

### Table 1. Characteristics of COVID-19 patients with and without seizures

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>With seizures (n=111)</th>
<th>Without seizures (n=1,475)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mo)</td>
<td>21 (1.2–133)</td>
<td>18 (1–144)</td>
<td>0.160</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>66 (59.5)</td>
<td>818 (55.5)</td>
<td>0.413</td>
</tr>
<tr>
<td>Female</td>
<td>45 (40.5)</td>
<td>657 (44.5)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td>0.147</td>
</tr>
<tr>
<td>Malay</td>
<td>95 (85.6)</td>
<td>1,356 (91.9)</td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>7 (6.3)</td>
<td>50 (3.4)</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>7 (6.3)</td>
<td>54 (3.7)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>2 (1.8)</td>
<td>15 (1.0)</td>
<td></td>
</tr>
<tr>
<td>History of seizure</td>
<td>18 (16.2)</td>
<td>4 (0.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous antiseizure medication</td>
<td>4 (3.6)</td>
<td>1 (0.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of hospitalization</td>
<td>8 (1–37)</td>
<td>7 (1–40)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are presented as median (range) or number (%).


$^*$Mann–Whitney U test; $^\dagger$Chi-square test; $^\ddagger$Fisher exact test.
Among children admitted with seizures, 55.0% experienced seizures on the first day of illness, and the majority (86.5%) had seizures that lasted no longer than 5 minutes (Table 2). None of the patients experienced neurological complications such as Guillain-Barré syndrome or encephalopathy. Five patients underwent lumbar puncture, and all cerebrospinal fluid results were normal. One patient had a computed tomography scan of the brain, which also yielded normal findings.

Electroencephalography was not performed on any of the children because the seizures were considered provoked. None of the children with seizures required intubation or admission to the pediatric intensive care unit. All children were discharged in good health, regardless of whether they had experienced seizures. Four patients who were discharged on antiseizure medications had been on these medications prior to their admission for COVID-19.

**Discussion**

This study revealed that seizures occurred in 7.0% of all COVID-19 admissions across the study period, with a peak of 18.0% in April 2022. Although genomic surveillance was not routinely conducted at the hospital, the temporal trend from February 2022 onwards aligned with the period during which the Omicron variant was predominant in Malaysia.

Our findings indicated higher odds of seizures among children hospitalized with COVID-19 during the Omicron wave relative to the prior period. This finding aligns with numerous reports indi-
cating a higher prevalence of seizures in children infected with the Omicron variant [9–17]. Infection with the Omicron variant has been suggested to trigger particularly robust innate immune responses, leading to a greater incidence of febrile seizures than was observed during the pre-Omicron period [17].

Among patients admitted for COVID-19 infection, those who experienced seizures were more likely to have a history of seizures and to have previously been on antiseizure medication. This finding is consistent with other research indicating that patients with COVID-19 who have seizures are comparatively likely to have a history of seizures or an underlying condition, most commonly epileptic disorders [13,14].

In this study, none of the children with COVID-19 and seizures required intubation or intensive care. This suggests that seizures associated with COVID-19 in children are generally not severe. Supporting our observation, a study by Kurd et al. [5] found that seizures, including status epilepticus, during COVID-19 infection were not associated with disease severity. However, a report from the Pediatric Neurology Unit of HTA (the same center as our study) indicated an uptick in referrals with severe neurological manifestations during the period when the Omicron variant was predominant [18]. One possible explanation for this discrepancy is that severe cases in the Klang Valley were referred to a dedicated COVID-19 hospital. In contrast, those from outside the Klang Valley were initially managed at the referring hospital before being seen later in the neurology clinic.

The limitations of this study include its retrospective nature and reliance on hospital records, which had the potential to introduce biases. Additionally, the variant strains were not directly detected, and the classification of patients as having the Omicron variant was thus based solely on epidemiological data. Nevertheless, given the national monitoring of SARS-CoV-2 circulation, this approach likely yielded a reasonably accurate estimate.

Future studies could explore the incidence and long-term prognosis of COVID-19–related seizures, as well as the reasons behind the differing symptoms caused by individual variants.

In conclusion, this study demonstrated that the Omicron wave was associated with a relatively high rate of seizures among children infected with COVID-19.

Conflicts of interest
No potential conflict of interest relevant to this article was reported.

ORCID
Sze Pei Eow, https://orcid.org/0009-0005-9060-8558
Ker Yang Chua, https://orcid.org/0000-0003-1568-2609

Author contribution
Conceptualization: SPE, KYC, SSM, and ARM. Data curation: SPE, KYC, and SSM. Formal analysis: KYC and KC. Methodology: SPE, KYC, and KC. Visualization: SPE, KYC, KC, and ARM. Writing - original draft: SPE. Writing - review & editing: SPE, KYC, KC, SSM, and ARM.

Acknowledgements
The authors would like to thank the Director General of Health Malaysia for granting permission to publish this article.

References
8. Ministry of Health Malaysia. Perkembangan semasa varian baharu Omicron (B.1.1.529) dan langkah-langkah kawalan serta pencegahan di Malaysia [Current developments regarding the new Omicron variant (B.1.1.529) as well as control...


