Impact of the Omicron strain on febrile convulsions in children: A single-center observational study

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Research Article

Keywords: febrile convulsion, respiratory virus, multiplex PCR, COVID-19, SARS-CoV-2, Omicron strain

Posted Date: June 6th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2984493/v1

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Abstract

<Purpose>
The emergence of the Omicron strain of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at the end of December 2021 has drastically increased the number of infected children in Japan, along with the number of children with febrile convulsions. However, impact of the Omicron strain on the febrile convulsions in children is not clear.

<Methods>
We compared the frequency of SARS-CoV-2 infection in children hospitalized with febrile convulsions with the frequency of SARS-CoV-2 infection in children with fever and respiratory symptoms without convulsions.

<Results>
In 2021 and 2022, 49 and 58 children, respectively, required emergency hospitalization for febrile convulsions (FC group), in which 24 and 38 children underwent a Filmarray respiratory panel ® test (FA test) and quantitative antigen test for SARS-CoV-2, respectively. In 2022, only six patients tested positive for SARS-CoV-2 (10.3%, 6/58). As a reference group, 655 children aged < 10 years who underwent the FA test for fever and respiratory symptoms during the same period were investigated, and 4 (1.8%, 4/223) and 42 (9.7%, 42/432) tested positive for SARS-CoV-2 in 2021 and 2022, respectively. Rhinovirus/enterovirus (RV/EV) was the most frequently detected virus, followed by respiratory syncytial virus (RSV) and parainfluenza virus 3 (PI3); no significant difference in the trend of detected viruses was observed between the two groups.

<Conclusions>
The frequency of febrile convulsions associated with SARS-CoV-2 infection of the Omicron strain in children may be similar to that of other common respiratory viruses.

Highlights

What is known:
The emergence of the Omicron strain has drastically increased the number of infected children with febrile convulsions.

What is new:
The frequency of febrile convulsions associated with SARS-CoV-2 infection of the Omicron strain in children may be similar to that of other common respiratory viruses.

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has had a huge impact worldwide.[1; 2] In Japan, the pandemic has greatly influenced socio-economic activities. Moreover, a strong impact on trends in acute epidemics other than COVID-19 was also observed, with a decline in invasive pneumococcal infections and the disappearance of seasonal influenza epidemics.[3–5] Japan had experienced eight waves of COVID-19 epidemics by March 2023, and the number of infected children had increased drastically, especially after the sixth wave caused by the Omicron strain, which began at the end of December 2021. As presented in Fig. 1, the number of infected children aged < 10 years in Tokyo increased by 26-fold in 2022 compared to that in 2021, while the number for all ages increased by 11-fold in 2022 compared to that in 2021. Similar to reports from overseas[6; 7], the symptoms of pediatric patients with COVID-19 in Japan were generally milder than those of adults; however, with the rapid increase in the number of pediatric patients, a certain number of severe cases and even deaths have been reported among them.[8–10] In pediatric emergency care facilities, a surge in pediatric patients with COVID-19-related convulsions has been observed, and cases of encephalopathy have also been recorded.[11; 12] Convulsions associated with acute viral illnesses are a common neurological complication in children.[13–15] Previous studies have reported that the recently introduced multiplex polymerase chain reaction (PCR) method can simultaneously analyze multiple types of respiratory viruses and detect viruses at a higher rate than conventional methods.[16; 17] However, few reports to date have compared the frequency of COVID-19-related convulsions with that of other viral diseases. Hence, we examined the results of the Filmarray respiratory panel® (FA test) (ver. 2.1), a multiplex PCR test, and a quantitative antigen assay for SARS-CoV-2 in patients hospitalized with febrile convulsions and compared them to those in whom the FA test was performed for respiratory symptoms in 2021–2022 at our institution.

2. Materials and methods

2.1. Patients

Our institution is a tertiary emergency general care hospital located in the Tokyo metropolitan area, adjacent to western central Tokyo.

Patients aged < 10 years who were admitted urgently to our hospital because of status epilepticus or cluster spasms associated with fever (≥ 38 °C) between January 2021 and December 2022 were included in the study as the febrile convolution group (FC group). Status epilepticus was defined as seizures lasting more than 30 minutes or recurrent seizures with no recovery of consciousness between attacks for more than 30 minutes.[18] Patients diagnosed with epilepsy and those taking antiepileptic medication were excluded. Meanwhile, patients aged < 10 years with fever and/or respiratory symptoms
who required hospitalization and underwent an FA test (BioMerieux Japan, Tokyo) at admission during the same period were included as the reference group.

### 2.2. Multiplex PCR test

The FA test (BioMerieux Japan, Tokyo) was used to detect respiratory viruses from nasopharyngeal swab samples from patients at the discretion of the physicians. The panel test can detect 18 viruses as follows: adenovirus (AdV); coronaviruses HKU1, 229E, OC43, and NL63; SARS-CoV-2; influenza A, A/H1, A/H1 2009, A/H3, and B; parainfluenza virus (PIV)-1, -2, -3, and -4; respiratory syncytial virus (RSV); rhinovirus/enterovirus (RV/EV); human metapneumovirus (hMPV); and four other microorganisms including *Bordetella pertussis*, *Bordetella parapertussis*, *Chlamydia pneumonia*, and *Mycoplasma pneumoniae*. Point-of-care antigen detection tests for influenza A/B (flu A/B), AdV, RSV, and hMPV were applied based on the physician’s discretion for patients who did not undergo an FA test.

### 2.3. Quantitative antigen assay for SARS-CoV-2

For all the hospitalized patients who did not undergo an FA test, a SARS-CoV-2 quantitative antigen test was performed at admission as part of the infection control strategy of our hospital. The HISCL™ SARS-CoV-2 Ag kit (Sysmex, Kobe) was used for quantitative assay for the SARS-CoV-2 antigen until July 2022 and has been replaced with the Elecsys® SARS-CoV-2 antigen kit (Roche Diagnostics Japan, Tokyo) since August 2022. According to an in-house validation study, the two assays had no significant differences in terms of sensitivity and specificity for detecting the SARS-CoV-2 antigen (data not shown).

### 2.4. Statistical analysis

Fisher’s exact test and Wilcoxon rank sum test were performed for statistical analysis, and p < 0.05 was considered significant. Statistical analyses were carried out using JMP 14 (SAS Institute, Cary, NC, USA).

### 3. Results

In 2021 and 2022, 49 and 58 children, respectively, required emergency hospitalization for febrile convulsions (designated as the febrile convulsions [FC] group). Their average ages were 31.5 ± 20.7 months (5–112 months old) and 35.9 ± 29.8 months (7–165 months old), respectively. No significant difference in the length of the average hospital stay was observed between the two groups (4.17 ± 4.17 days vs 4.35 ± 2.35 days) (Table 1).

In 2021, 24 of the 49 patients underwent FA tests, and the virus was detected in 18 patients (75.0%). None of the patients tested positive for SARS-CoV-2 using the FA or quantitative antigen tests. Seven other patients underwent the AdV antigen test, and three underwent the RSV antigen test, all of whom tested negative. In 2022, 38 of 58 patients underwent FA tests, and the virus was detected in 24 patients (63.2%). Additionally, one AdV antigen test and one RSV antigen test were performed, both of which yielded negative results. The SARS-CoV-2 antigen quantitative test was performed in all the patients who did not undergo the FA test, and only in 2022, four patients tested positive in the quantitative antigen test. In 2022, two patients tested positive for SARS-CoV-2 in the FA test. By contrast, 655 children aged < 10
years (average age: 34.7 ± 27.5 months, 0–4 years old: 536, and 5–9 years: 119) with fever and respiratory symptoms during the same period underwent the FA test (designated as the reference group), and 4 and 42 children were positive for SARS-CoV-2 in 2021 and 2022, respectively. One or more viruses were detected in 74.0% (165/223) and 69.7% (301/432) of the patients, respectively.

The trends in the number of newly registered pediatric patients with COVID-19 aged < 10 years in Tokyo and the detected viruses in the reference group are presented in Figs. 1 and 2, respectively. RV/EV was the most frequently detected virus in both groups, followed by RSV and PIV3 (Table 2). Multiple viruses were detected in 12.9% (8/62) of the patients in the FC group and in 15.1% (99/655) of the patients in the reference group, which was not significantly different. Biphasic encephalopathy was reported in a patient who tested positive for PIV3 in 2021, and in another patient who tested positive for PIV1 and RV/EV in 2022. No significant difference in the frequency of viruses detected was observed between the FC and reference groups in 2021 and 2022 (Table 2). We performed quantitative antigen testing for SARS-CoV-2 in all inpatients who had not undergone FA testing at admission and outpatients with mild respiratory symptoms and fever as needed. The proportion of positive outpatients aged < 10 years was 19.1% (205/1701) in 2022 (Table 3).

4. Discussion

This study had some limitations. First, it focused on patients with relatively severe symptoms who visited an emergency center, whereas pediatric patients with mild symptoms were not included in the FA test targets. Second, this was a single-center study with a small sample. Lastly, the indications for FA testing were determined by the physician. In general, FA testing tends to be applied to severely ill patients in the reference group, and patients without severe symptoms are subjected to quantitative antigen testing for SARS-CoV-2.

Quantitative antigen testing for SARS-CoV-2 was performed in outpatients with mild respiratory symptoms and fever and in inpatients who had not undergone FA testing at admission. The proportion of outpatients aged < 10 years was 19.1% (205/1701) in 2022 (Table 3), which was significantly higher (p < 0.001) than that of patients who underwent FA testing in the same period. According to the official monitoring data available in Tokyo[20], the average positive ratio of PCR or antigen testing for SARS-CoV-2 in 2022 was 32.3% (2 181 707/3 615 475), and the total number of positive cases accounted for 60.3% of the officially registered patient number. Epidemiological data demonstrate that children aged < 10 years in Tokyo account for 7.4% of the total population, and the number of patients of the same age infected with SARS-CoV2 and registered accounts for 12.1% of all registered patients in Tokyo in 2022, indicating that the actual number of children infected with SARS-CoV-2 among febrile children could be higher than that observed in our institution.[21]

5. Conclusion
In conclusion, SARS-CoV-2 infection may not be more likely to significantly induce convulsions requiring hospitalization than other common respiratory viral infections in our study. Further, the frequency of febrile convulsions associated with the Omicron strain of SARS-CoV-2 infection in children may be less or almost the same as that of RV/EV, RSV, PIV3, and other viruses.

References


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Declarations

Data availability statement

Data are available upon request because of privacy/ethical restrictions.

Funding statement

The authors received no funding in relation to this work.

Conflict of interest disclosure

The authors declare no conflicts of interests.

Ethics approval statement

This study was performed in compliance with the ethical treatment policy of human and animal research participants and the Declaration of Helsinki, and was approved by the Clinical Research Ethical Committee of Musashino Red Cross Hospital (no. 4046).

Patient consent statement

Informed consent was secured by opt-out method.

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Author contributions

All the authors met the ICMJE authorship criteria. M.N. conceptualized and designed the study, supervised the study, and drafted and revised the manuscript. M.O. and R.N. helped with the data analysis. T.S., S.H., H.Y., T.U., and A.O. contributed to data collection. All the authors contributed to the writing of the manuscript and agreed to its content.

Tables

Tables 1-3 are available in the supplementary files section.

Figures
Figure 1: Trend of SARS-CoV-2 infected patient number under 10 years old in Tokyo.

See above image for figure legend.
Figure 2: Trend of four major respiratory viruses detected by Filmarray respiratory panel® (ver2.1) test in children under 10 years old in the reference group.

Figure 2

See above image for figure legend.

Supplementary Files

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