

Household Secondary Transmission of the Severe Acute Respiratory Syndrome Coronavirus 2 Alpha Variant From a Community Cluster in a Nursery in Japan

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Background: Spread of variants of concerns (VOCs) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to an increase in children with coronavirus disease 2019 (COVID-19). In February 2021, clusters of the Alpha variant of SARS-CoV-2 started to be reported in Niigata, Japan, including a large nursery cluster. We investigated the transmission routes and household secondary attack rates (SARs) in this cluster.

Methods: Epidemiologic data related to a nursery cluster in Niigata, Japan, particularly child-origin and adult-origin SARs, were analyzed. VOCs were confirmed by whole-genome sequencing of virus from patients.

Results: In total, 42 persons (22 children and 20 adults) in the cluster were infected with the Alpha variant. In the nursery, 13 of 81 children (16.0%) and 4 of 24 teachers (16.7%) were infected. SARS-CoV-2 later spread to 25 persons (10 children and 15 adults) outside the nursery. Child-origin and adult-origin household SARs were 27.7% (13/47) and 47.0% (8/17) ($P = 0.11$), respectively, which were higher than rates attributable to non-VOCs in previous studies.

Conclusions: As compared with non-VOCs, the Alpha variant of SARS-CoV-2 exhibited high transmissibility among children and adults and may pose a high risk for household secondary transmission from SARS-CoV-2-infected children. Increased transmissibility of current or future VOCs could lead to greater transmission from children to adults or other children.

Key Words: Alpha variant, children, household transmission, severe acute respiratory syndrome coronavirus 2, variants of concern

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During the pandemic of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), children present with less severe diseases, and are sometimes asymptomatic, and transmissibility is lower than in

adults.^{1–4} Children are usually infected with SARS-CoV-2 at home in households, rather than in the community.⁵ The spread of SARS-CoV-2 in nurseries and schools, which leads to cluster formation of COVID-19 among children, had been uncommon. When clusters did occur, they began in adults rather than in children.^{1,6–8}

The transmissibility of SARS-CoV-2 variants was recently reported to have increased, which could facilitate cluster formation. SARS-CoV-2 continues to undergo genetic changes, and variants of concerns (VOCs) have been identified since the circulation of SARS-CoV-2. As of November 2021, there are 5 VOCs (Alpha through Delta and Omicron) and 5 variants of interests (VOIs; Eta to Mu), classified by World Health Organization.⁹ In December 2020, the SARS-CoV-2 Alpha variant (B.1.1.7, N501Y.V1) began to circulate in Europe and rapidly spread worldwide.¹⁰ Because transmissibility may be higher for the Alpha variant than for non-VOCs/VOIs,¹¹ we estimated that the emergence of the Alpha variant has caused an increase in pediatric COVID-19 cases.¹²

The Alpha variant was first sporadically detected in Japan in January 2021, and circulated in large cities in February 2021 and began to spread nationwide on March 2021.¹³ In Niigata Prefecture, in the north of the main island, COVID-19, including the Alpha variant, was sporadically detected. We observed the first cluster formations by the Alpha variant in Japan in early February 2021, in Niigata, Japan.

We identified a large community cluster of the Alpha variant among children and adults in a nursery and noted secondary transmission to household members. To our knowledge, previous reports of nursery clusters caused by the Alpha variant lacked detailed epidemiologic information on the clusters. Herein, we describe the transmission routes and household secondary attack rates (SARs) of a nursery cluster, to determine if children are a major driver of SARS-CoV-2.

MATERIALS AND METHODS

Data Collection

Because COVID-19 has been identified as a designated infectious disease by the Infectious Disease Control Law of Japan, public health centers are responsible for investigating individual COVID-19 cases and clusters and conducting contact tracing as part of notifiable disease surveillance. The Department of Health and Welfare of Niigata Prefecture collects data on COVID-19 cases and contact tracing from all public health centers in Niigata. Using these data, we analyzed a nursery-related COVID-19 cluster involving children and adults. The age, sex, symptoms and family composition were obtained from the children and teachers of the nursery, their family members and others related to the cluster from the public information. We also ascertained the date when SARS-CoV-2 polymerase chain reaction (PCR) was tested, the PCR test results and the date of symptom onset. After data collection, we created an

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epi-curve of the COVID-19 in the cluster and COVID-19 transmission routes inside and outside the nursery.

Additionally, using national data from the Japanese Ministry of Health, Labour and Welfare,¹⁴ we analyzed rates of COVID-19 pediatric cases in January 2021 through October 2021 in Japan to determine if the rates changed because of the effects of VOCs/VOIs. We compared rates of newly SARS-CoV-2–positive children younger than 10 years in the period of non-VOCs/VOIs circulation (January 2021), the period of Alpha variant predominance (May 2021) and the period of Delta variant predominance (September 2021).

Definitions

A COVID-19 case was defined as a person with a positive PCR result for SARS-CoV-2 under national surveillance. The index case was defined as the first documented person in the COVID-19 cluster who spread SARS-CoV-2 and thus formed the cluster.¹⁵ A COVID-19 close contact was defined as a person who had close contact (distance of ≤ 6 feet for a total of ≥ 15 minutes) with a SARS-CoV-2–infected person. In addition to analysis of close contacts, all children and teachers in the nursery where the cluster occurred underwent PCR testing for SARS-CoV-2 as part of contact tracing. A case of secondary transmission was defined as a person with COVID-19 who had close contact with COVID-19 and had a confirmed positive SARS-CoV-2 PCR result within 14 days of the close contact. Household transmission was defined as secondary transmission from the first confirmed COVID-19 case in the family. SAR was defined as the number of COVID-19 patients with close contact divided by the total number of people with close contact.

Molecular and Phylogenetic Analyses

A reverse transcription PCR assay for SARS-CoV-2¹⁶ that used saliva or a nasopharyngeal swab was performed at the Niigata Prefectural Institute of Public Health and Environmental Sciences. Whole-genome sequencing of positive PCR samples was performed at the National Institute of Infectious Diseases in Japan. We used PANGO Lineage (Ver: 2022.3.8) to classify viral sequences. A phylogenetic tree was constructed based on the whole-genome sequence (29,809 nucleotides) of virus strains obtained in Niigata Prefecture between February 1, 2021, and February 28, 2021, using Nextclade version 1.13.2 (<https://clades.nextstrain.org/>).

Ethical Considerations

Because we used publicly available anonymous data, informed consent was not required according to the ethical guidelines for human research in Japan. The epidemiologic study of the cluster was approved by the Ethics Committee of Niigata University (2020-0499).

Statistical Analysis

The χ^2 test was used to compare rates of asymptomatic disease between children and adults and SAR of child origin and adult origin. The χ^2 test was used to compare rates of new SARS-CoV-2 positivity in children younger than 10 years during the period of non-VOCs/VOIs circulation (January 2021), the period of Alpha variant predominance (May 2021) and the period of Delta variant predominance (September 2021). All statistical analyses were performed with Stata version 16.1 (Stata Corp., College Station, TX). A *P* value of <0.05 was considered to indicate statistical significance.

RESULTS

Overview of the Nursery Cluster

The index case (number 1) was a 38-year-old man whose symptoms started on January 31, 2021. He had worked outside

Niigata Prefecture between January 21, 2021, and January 30, 2021 (Figs. 1 and 2) and had transmitted the infection to his 9-year-old daughter (number 2) and 5-year-old daughter (number 3), who attended the nursery (Fig. 3). There were 24 teachers and 81 children from 1- to 6-year-old in 4 classes (classes A, B, C and D) divided by their age. Each classroom was spatially separated. Daily activities typically took place in 1 room for each class; however, there was a mixture of the children outside of each class during break. At lunchtime, the children usually sit side-by-side and were asked to be quiet not spread the fomites during eating. The typical day is approximately 8 hours from 9 AM to 5 PM; however, an extension of nursing time was available at the family's request. Each class had a designated teacher; however, some teachers were assigned multiple classes for assistance. The teachers harbored the teachers' room, sharing the limited number of tables and chairs. During the study period, enhanced social distancing, masking, ventilation measures and routine cleaning of the facilities after hours were performed in the nursery to reduce potential virus transmission; however, strict social distancing and appropriate face masks wearing among children, especially small children were difficult to achieve. The child-index case (number 3) belonged to class A. After PCR testing confirmed a positive result for SARS-CoV-2 in this child, on February 5, 2021 (Fig. 1), the nursery closed on February 6, 2021. PCR results were positive for 3 teachers (numbers 6 to 8) on February 8 (Fig. 1), and SARS-CoV-2 was later transmitted to other teachers and children in the nursery and to their family members outside the nursery. In total, 16% (13/81) of children and 16.7% (4/24) of teachers were infected with SARS-CoV-2. Of the 13 infected children in the nursery, 8, 2 and 3 children belonged to class A, B and C, respectively. Although the index children (number 3) belonged to class A, SARS-CoV-2 spread to outside of class A, including classes B and C. Contact tracing revealed that the infection spread to an additional 25 persons (10 children and 15 adults) outside the nursery (Fig. 3). The last PCR-positive case in the cluster was on February 22. In total, 42 persons (22 children and 20 adults) were infected with SARS-CoV-2; asymptomatic disease was more common in children (72.7%) than in adults (40.0%) (*P* = 0.03; Table 1), and the transmission route for 21 patients (50.0%) was household secondary infection. None of the investigated persons had received a COVID-19 vaccine, because no such vaccine was available in Japan during this period.

Household SAR

Because the infection spread among individuals who had close contact with infected children and teachers in the nursery, the secondary attack of COVID-19 was critical in spreading the cluster outside the nursery. Secondary transmission in the household was frequent (21/42 cases, 50%); 19 infected persons (13 children and 6 adults) had a close contact in their household, and transmission originated from children in 53.8% (7/13) of these cases and from adults in 50% (3/6) of these cases. The median number of households were 3.9 households with the child-index cases and 2.8 with the adult-index cases, respectively. The child-origin and adult-origin household SARs were 27.7% (13/47) and 47.0% (8/17), respectively (*P* = 0.11) (Fig. 3).

Phylogenetic Analysis of SARS-CoV-2 Lineage

Among the 42 cases, whole-genome sequences were successfully obtained from 31 cases. Genetic analysis was not possible for the remaining 11 cases because of insufficient RNA concentration or quantity. We constructed a phylogenetic tree that included the 31 samples from the nursery cluster. All the samples collected were classified as Alpha variant, with an amino acid mutation of N501Y, and they were genetically identical between adults and children (Fig. 4).

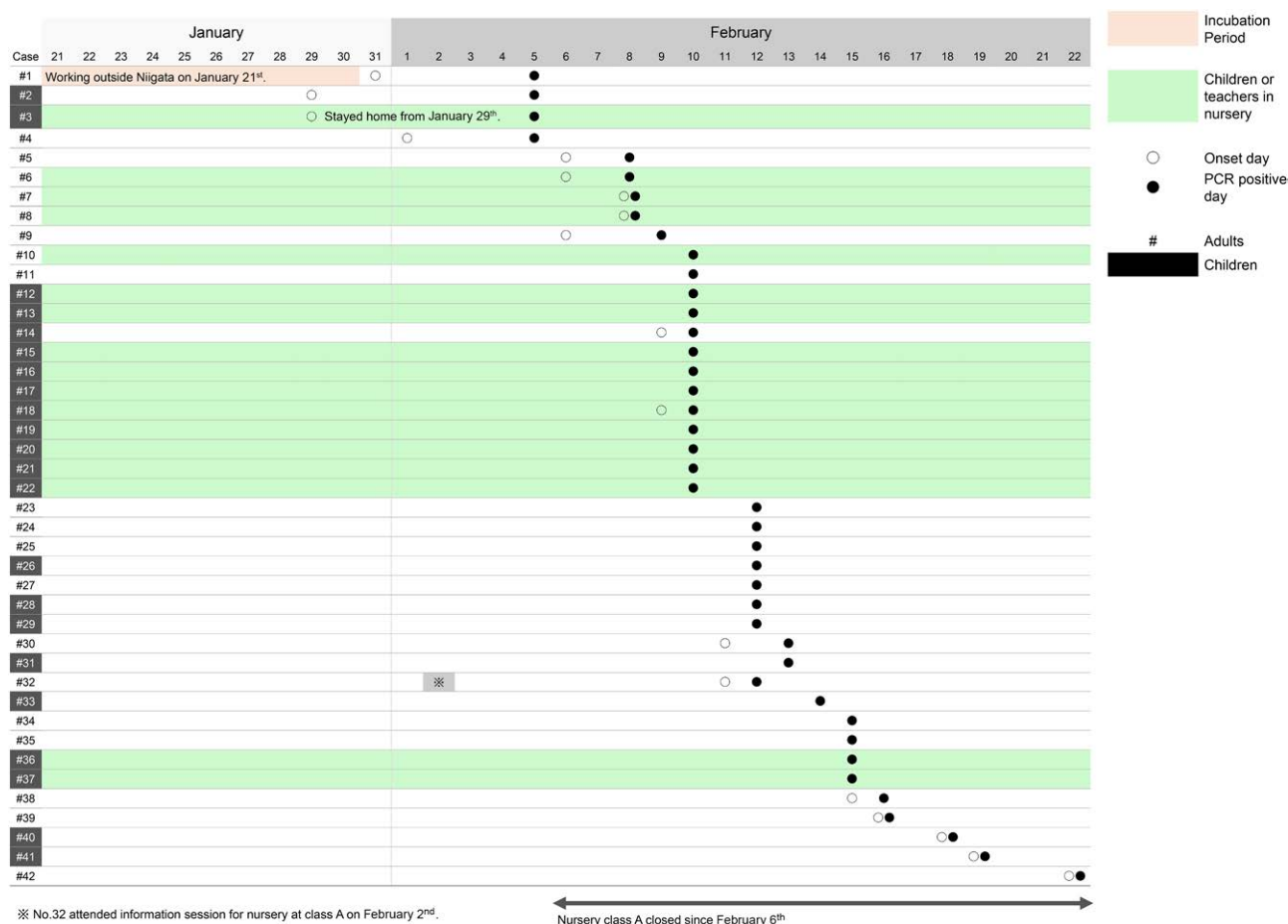


FIGURE 1. Time course of symptoms and laboratory diagnosis of patients with COVID-19 in a nursery cluster in Niigata, Japan. The index cases (numbers 1–3) were confirmed as COVID-19 on February 5, 2021, and the nursery was closed on February 6, 2021. White circles indicate the day of onset of symptoms, and black circles indicate the day of the positive PCR test result for SARS-CoV-2.

Effects of VOC on Pediatric SARS-CoV-2-infected Cases in Japan

During the study period, SARS-CoV-2 testing has been performed on only symptomatic persons and contact persons to ensure accurate contact tracing. Between January 2021 and October 2021, a total of 1,512,279 individuals were infected with SARS-CoV-2 in Japan, and 5.9% (88,515/1,512,279) were children younger than 10 years (5.9%). The rate was 2.8% (3826/136,709) in January, when non-VOCs/VOIs circulated; however, the rate increased to 4.1% (5867/143,749) in May ($P < 0.001$) when the Alpha variant became predominant. The rate further increased to 9.1% (32,440/354,739) in September ($P < 0.001$), when the Delta variant became predominant (see Supplementary Table 1, <http://links.lww.com/INF/E755>).

DISCUSSION

This study describes a nursery cluster of the SARS-CoV-2 Alpha variant and household SARs originating from children and adults. Compared with previous reports on non-VOCs,^{17,18} the present Alpha variant child-origin household SAR was higher for children and adults, indicating that these variants are more efficient in transmitting the virus to children, as well as to adults, thus leading to more pediatric cases.

Household transmission, especially from parents, is one of the most common routes by which children are infected with

SARS-CoV-2.⁵ Because infected parents may transmit SARS-CoV-2 to their children, secondary transmission in the household is important. However, it is difficult to keep physical distance from and avoid close contact with family members and to wear masks during conversation or meals at home, where space is often limited. Children tend to remain near their parents and siblings. Thus, protecting children from family members in their home is difficult for the entire family. Before the Alpha variant emerged, household infection was mainly from adults to children; transmission from children to adults or children was relatively rare.¹⁷ A South Korean study of COVID-19 contact tracing conducted before the emergence of VOCs reported that the household SAR was lower for child-index patients (age, 0–9 years) than for adult-index patients (age, >20 years) (5.3% vs. 11.7%, respectively).¹⁸ In the present study, although the child-index SAR (27.7%) was lower than the adult-index SAR (47.0%), both adult and child-index household SARs were higher than those in previous reports of non-VOCs/VOIs infection.¹⁸ The increased transmissibility attributable to the emergence of VOCs affected the higher household SARs for children and adults.

The Alpha variant was first reported in the United Kingdom, in late 2020, and spread worldwide.¹⁹ The clinical manifestations of Alpha variant infections in children have not been well characterized. In adults, the Alpha variant resulted in higher viral loads in saliva and nasopharyngeal excretions of COVID-19 patients.²⁰

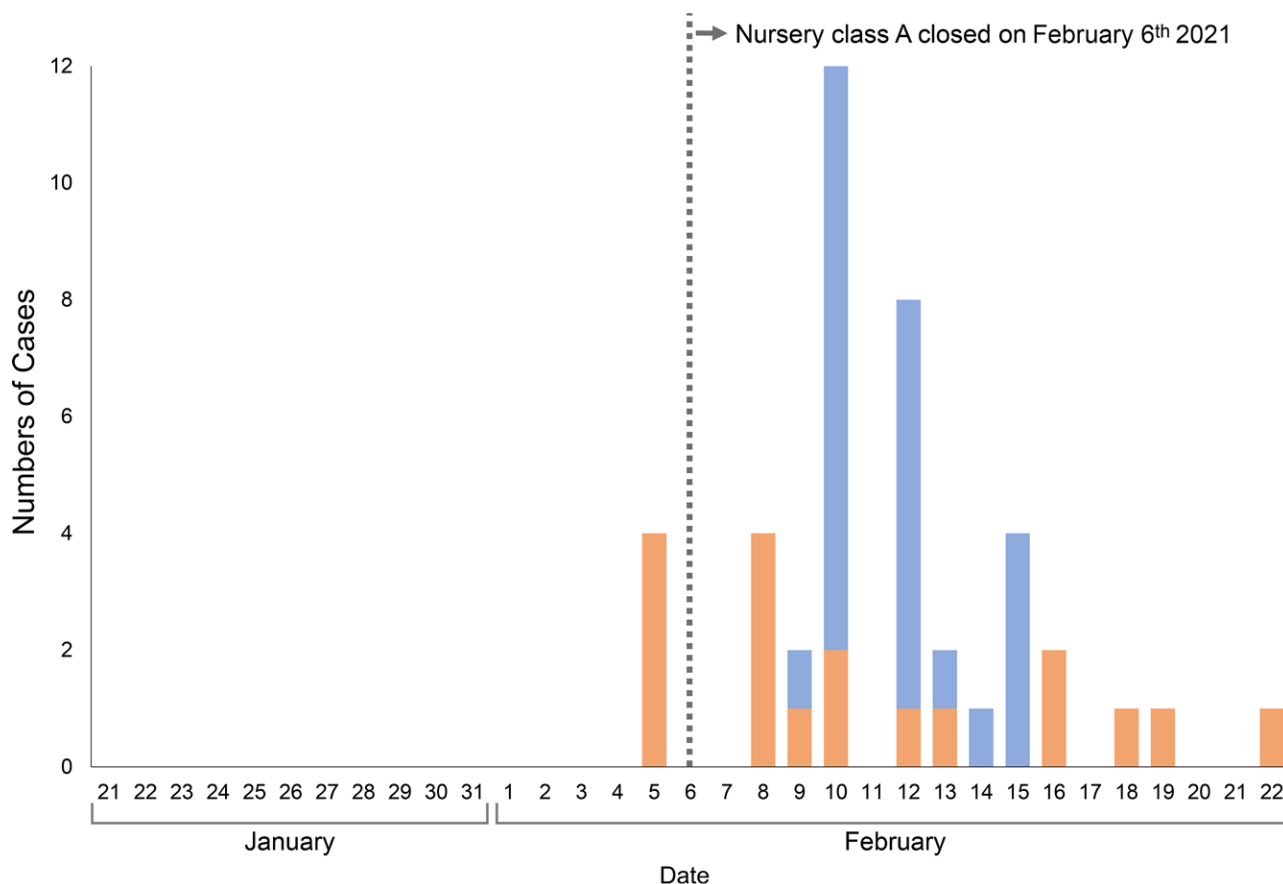


FIGURE 2. Numbers of cases with COVID-19, by day of positive PCR test result. Numbers of COVID-19 patients in relation to the day of the positive PCR test result, in patients with and without symptoms. The epi-curve shows the numbers of COVID-19 patients on the day of diagnosis. Light blue bars indicate asymptomatic cases, and light orange bars indicate symptomatic cases.

Additionally, transmissibility was higher for the Alpha variant than for non-VOCs/VOIs,¹¹ and secondary transmission rates were also higher for the Alpha variant than for non-VOCs/VOIs.²¹ Nursery clusters due to the Alpha variant were merely reported and not carefully described; only 1 report, in Germany, actually described nursery clusters due to the Alpha variant.²² In that report, the child-origin SAR was similar to the adult-origin SAR (23% vs. 30%; $P = 0.15$). In addition, child-origin and adult-origin household transmission rates were similar (32% vs. 39%, respectively; $P = 0.27$). In adults, the Alpha variant caused more-severe disease^{23,24}; however, the severity of pediatric COVID-19 was similar for the Alpha variant and non-VOCs/VOIs.¹² To date, as compared with non-VOCs/VOIs, the Alpha variant has higher transmissibility and similar severity among children.

The emergence of SARS-CoV-2 variants with higher transmissibility affects the risk of local community clusters, especially in nurseries and schools. Among the 5 VOCs (Alpha through Delta and Omicron), the Alpha variant (B.1.1.7), the first dominant variant with 1.29 times higher transmissibility than the non-VOCs/VOIs,¹¹ has circulated worldwide and caused over 1 million cases.²⁵ In Japan, the Alpha variant was replaced by the Delta variant, with 1.97 times higher transmissibility than non-VOCs/VOIs,¹¹ in July 2021. Subsequently, the Delta variant was replaced by the Omicron variant, which has been the predominant variant in Japan since January 2022. We believe that the number of local community clusters in children will increase if these

significant VOCs/VOIs with higher transmissibility continue to circulate worldwide.

The emergence of VOCs may increase the rate of infected children in an infected population. In Japan, the rate of infected children increased from 2.8% to 4.1% when Alpha variants were predominant and to 9.1% when Delta variants were predominant (see Supplementary Table 1, <http://links.lww.com/INF/E755>). The vaccination coverage in the adult population in February 2021 was 0% because the BNT162b2 messenger RNA (mRNA) COVID-19 vaccine to health care workers started on February 17, 2021. Later, the mRNA-1273 vaccine was introduced on May 24, 2021, in Japan. The vaccine target was gradually expanded to include adults over 65 years, in late April/early May 2021. In November 2021, nearly 80% of Japanese had received 2 doses of mRNA vaccines. This high immunization rate may affect the relative increase in pediatric cases during the period of Delta variant predominance. Thus, the impact of the Delta variant on the increase in pediatric cases during the period might be overestimated. In contrast, COVID-19 vaccination was limited when the Alpha variants predominated in Japan and it was estimated that only 0.04% (911/2,185,626 persons) of the population in Niigata prefecture had the COVID-19 by the end of January 2021 (Supplementary Table 2, <http://links.lww.com/INF/E755>); therefore, the increased rate of pediatric cases during the period was little affected by immunization. As of November 2021, majorities of populations in developed countries have been vaccinated. Our current data are thus particularly important

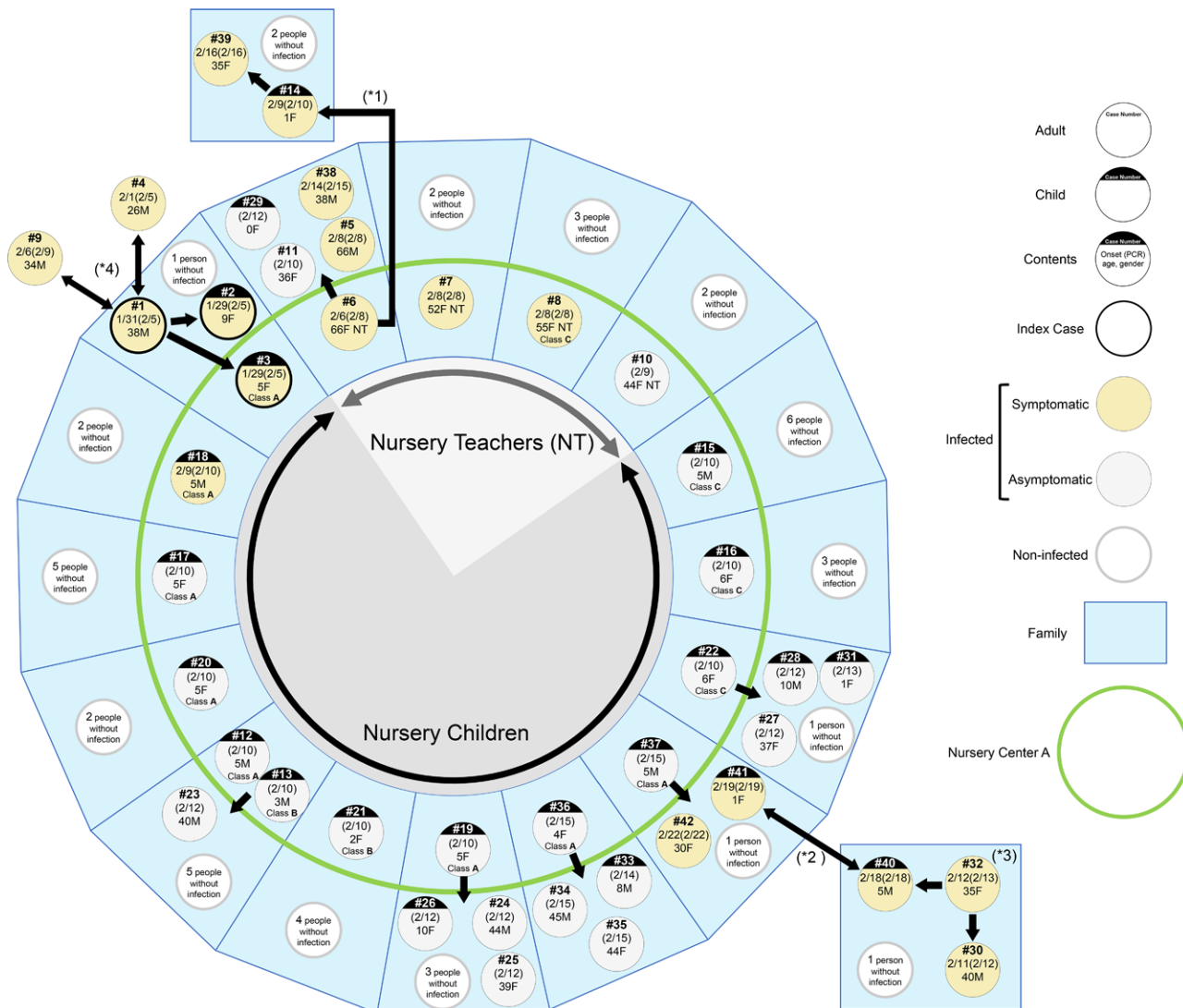


FIGURE 3. Transmission routes of severe acute respiratory syndrome coronavirus 2 at the nursery and in families. Each blue trapezoid shows a family living in the same home, and green circles show the nursery. The black arrows show the estimated transmission routes. Intra-nursery center transmission rates were similar, 16.0% (13/81) and 16.7% (4/24) in children and adults, respectively. Child-origin and adult-origin household secondary transmission rates were 27.7% (13/47) and 47.0% (8/17) in children and adults, respectively. *1 #6 (adult) was working in a different temporary nursery center. *2 #41 (child) was also using nursery center B. *3 #32 (adult) attended an information session at nursery center A with her 3-year-old daughter; however, the daughter did not have COVID-19; thus, the route of transmission to the family was through #40 who attended nursery center B. *4 #4 and #9 were working at the same place with #1.

because SARs for VOCs/VOIs not affected by immunization will not be available in the future.

Host immunity has changed because of worldwide COVID-19 immunization. COVID-19 vaccines, especially the mRNA vaccines, are highly effective against non-VOCs/VOIs and VOCs/VOIs.^{24,26–30} Effectiveness was similar against the Alpha variant and non-VOCs/VOIs²⁷ but lower against the Delta and Omicron variant than against the other VOCs.^{29–31} A study of non-VOCs/VOIs showed that vaccination decreased secondary transmission;³² however, effectiveness against secondary transmission of VOCs is unknown. Vaccination might prevent secondary transmission of the Alpha and Delta variants, because SARS-CoV-2 infections by these variants, including asymptomatic infections, were prevented by vaccination.^{28,30} Although the potential emergence of new, more

transmissible VOCs could result in nursery clusters, vaccination of teachers and staff members involved in child care would decrease secondary transmission and could prevent further spread to the community.

Some VOCs/VOIs are resistant to existing immunity by natural infection or immunization, as indicated by the higher neutralization titers for VOCs/VOIs than for non-VOCs/VOIs.³³ As compared with non-VOCs/VOIs, the Beta and Mu variants were 6.3-fold and 7.6-fold as resistant to sera from mRNA vaccine (BNT162b2) recipients, respectively, whereas the Alpha and Delta variants were 1.7-fold and 2.6-fold as resistant to them, respectively.³³ Although the Beta and Mu variants had the highest resistance among VOCs/VOIs, these 2 VOCs have caused less spread worldwide than the Alpha and Delta variants. Notably, viral excretion from respiratory

TABLE 1. Characteristics of Children and Adults With Coronavirus Disease 2019 in the Investigated Nursery Cluster

Characteristics	Children (n = 22)	Adults (n = 20)
Age, median, yr (range)	5.0 (0–10)	39.5 (26–66)
Sex, male, n (%)	8 (36.4)	9 (45.0)
Asymptomatic, n (%)	16 (72.7)	8 (40.0)
Numbers of cases diagnosed in nursery, n (%)	13 (59.1)	4 (20.0)
Household close contacts, n (%)	13 (59.1)	6 (30.0)
Index case of household transmission	7 (58.4)	3 (50.0)
Numbers of cases transmitted from household, n (%)	9 (40.9)	12 (60.0)

samples was higher in persons infected with the Alpha and Delta variants than with other VOCs/VOIs and non-VOCs/VOIs.^{20,34–36} Higher viral loads in respiratory samples were found to be associated with efficient transmissibility,³⁷ which could be reduced by wearing face masks.³⁸ In contrast to older children and adults, younger children are not able to wear face masks or maintain appropriate masking. Moreover, use of COVID-19 vaccines is limited in young children. Thus, to protect this vulnerable population from VOCs, older children and adults near young children need to be vaccinated and should adhere to appropriate infection control measures such as wearing face masks and strict hand hygiene, when needed.

In the present study, the exact transmission routes in the nursery were difficult to identify. Nursery teachers were in close contact with children, and some cared for children in multiple classes,

which explains infection spread to classes without direct contact with the adult-index case (number 1) or child-index case (number 3). The teacher infected by the child-index case might have spread SARS-CoV-2 to other teachers, who subsequently spread the infection to other classes. The teachers’ room—a possible area for virus transmission among teachers when infection control measures are inadequate³⁹—could contribute to transmission by teachers.

We acknowledge a few study limitations. First, this report originated from a single nursery in Niigata, Japan. Further investigation of different regions of Japan and other countries will yield more information on the effect of the Alpha variant on transmission among children in nurseries and schools. Second, the comparison of child-origin and adult-origin household SAR did not differ significantly. This could be related to the beta error due to the small population size. Third, detailed clinical information on patients was not available because of the nature of the study design; however, no severe or fatal pediatric cases were reported in Japan during the study period. Last, the Delta variant became the predominant strain in the world as of November 2021; thus, the Alpha variant is now less important. However, the present findings provide us further data on the effect of VOCs on SARS-CoV-2 transmission. Under the current situation when Omicron dominates, too many clusters have occurred to investigate details of each cluster, and it is difficult to investigate in detail how the clusters among children begin and spread to households. Therefore, this observation is important how the first VOC, Alpha variant, spread among children and adults in nurseries and schools, even the VOC differs from the one currently spreading. In addition, this information will be useful if new VOCs harbor mutations or characteristics of the Alpha variants.

As compared with previous findings for non-VOCs, the SARS-CoV-2 Alpha variant had higher transmissibility among

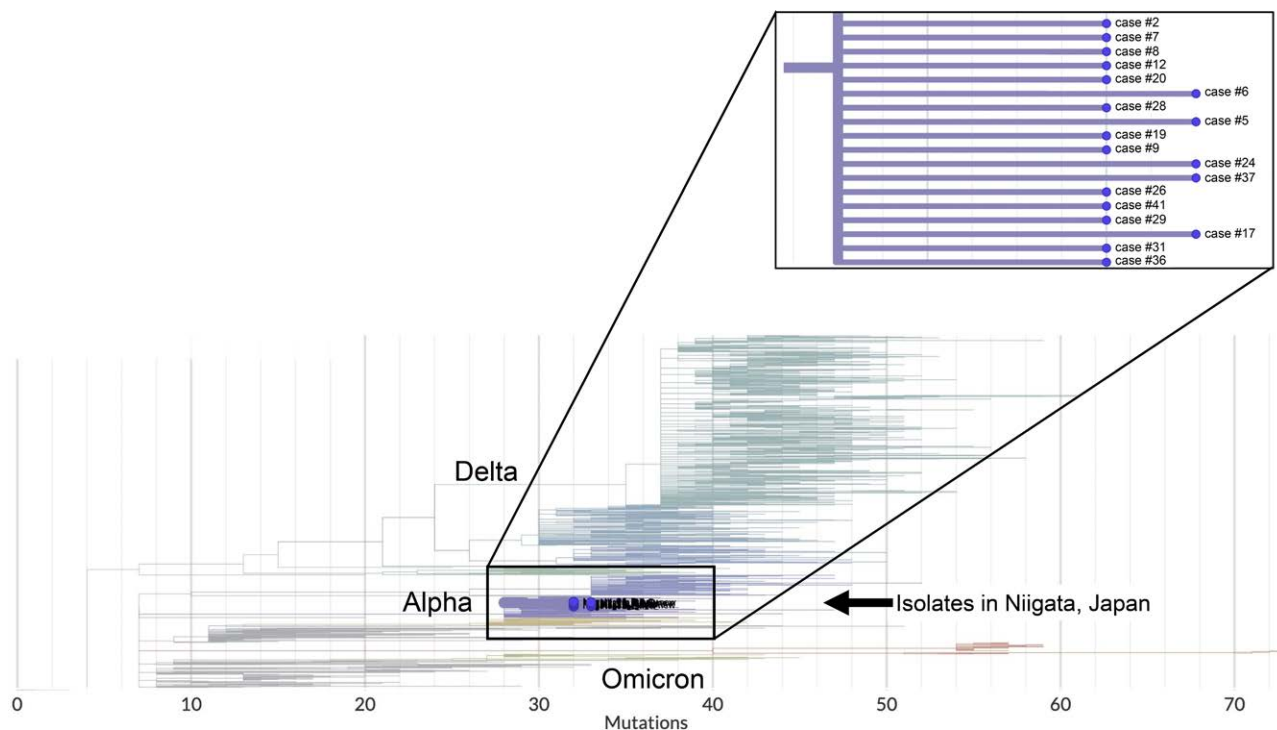


FIGURE 4. Phylogenetic tree of severe acute respiratory syndrome coronavirus 2 isolated in the nursery cluster. Among the 42 cases, whole-genome sequences were successfully obtained from 18 cases. The phylogenetic tree was constructed with Nextclade version 1.13.2 and was based on the whole-genome sequence (29,809 nucleotides) of virus strains obtained in Niigata Prefecture between February 1, 2021, and February 28, 2021. The arrow shows the sequences obtained from the nursery cluster, and phylogenetic tree in the magnified rectangle demonstrates genetically identical viruses between adults and children.

children and a higher risk for household secondary infection from SARS-CoV-2-infected children. Before the spread of the Alpha variant, the household SAR originating from children was much lower than that originating from adults; however, the household SAR from children with the Alpha variant was similar to that from adults. A potential increase in transmissibility in current or future VOCs could play a role in secondary household transmission from both children and adults.

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