J Korean Med Sci. 2024 May 20;39(19):e171
https://doi.org/10.3346/jkms.2024.39.e171
eISSN 1598-6357·pISSN 1011-8934

JKMS

Original Article
Infectious Diseases

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Epidemiology of Respiratory Viruses in Korean Children Before and After the COVID-19 Pandemic: A Prospective Study From National Surveillance System

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OPEN ACCESS

Received: Jan 23, 2024
Accepted: Apr 23, 2024
Published online: May 14, 2024

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ABSTRACT

Background: The coronavirus disease 2019 (COVID-19) pandemic led to a decrease in the seasonal incidence of many respiratory viruses worldwide due to the impact of nonpharmaceutical interventions (NPIs). However, as NPI measures were relaxed, respiratory viral infections re-emerged. We aimed to characterize the epidemiology of respiratory viruses in Korean children during post-COVID-19 pandemic years compared to that before the pandemic.
Methods: A nationwide prospective ongoing surveillance study has been conducted for detection of respiratory viruses between January 2017 and June 2023. We included data on adenovirus (AdV), human bocavirus (HBoV), human coronavirus (HCoV), human metapneumovirus (HMPV), human rhinovirus (HRV), influenza virus (IFV), parainfluenza virus (PIV), and respiratory syncytial virus (RSV), which were detected in children and adolescents younger than 20 years. We analyzed the weekly detection frequency of individual viruses and the age distribution of the affected children. The study period was divided into prepandemic (2017–2019) and postpandemic (2021–2023) periods.
Results: A total of 19,589 and 14,068 samples were collected in the pre- and postpandemic periods, respectively. The overall detection rate of any virus throughout the study period was 63.1%, with the lowest occurring in the 2nd half of 2020 (50.6%) and the highest occurring in the 2nd half of 2021 (72.3%). Enveloped viruses (HCoV, HMPV, IFV, PIV, and RSV) almost disappeared, but nonenveloped viruses (AdV, HBoV, and HRV) were detected even during the peak of the COVID-19 pandemic. The codetection rate increased from 15.0% prepandemic to 19.1% postpandemic ($P < 0.001$). During the postpandemic period, a large out-of-season PIV and HMPV epidemic occurred, but the usual seasonality began to be restored in 2023. The mean age of children with each virus detected in 2023 was significantly greater than that in prepandemic years ($P = 0.003$ and 0.007 for AdV and HCoV, respectively; $P < 0.001$ for others). The mean age of children with IFV increased in 2022 (11.1 ± 5.2 years) from prepandemic years (7.9 ± 4.6 years) but decreased to 8.7 ± 4.1 years in 2023.
Conclusion: With the relaxation of NPI measures, several seasonal respiratory viruses cocirculated with unusual seasonal epidemic patterns and were associated with increasing age of infected children.

Keywords: Respiratory Viruses; Epidemic; Children; COVID-19 Pandemic; Korea

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Funding
This study was supported by a grant from the Korea Disease Control and Prevention Agency (grant No. 6300-6332-304).

Disclosure
The authors have no potential conflicts of interest to disclose.

Data Sharing Statement
The data that support the findings of this study are available on request from the corresponding author, Yun KW.

Author Contributions
Conceptualization: Choi EH, Kim EJ. Data curation: Rhee JE, Lee NJ, Woo S, Lee J, Lee SW. Formal analysis: Yun KW. Methodology: Cho HJ. Software: Cho HJ, Kang D. Validation: Rhee JE, Choi EH, Kim EJ. Investigation: Cho HJ, Kang D, Yun KW. Writing - original draft: Cho HJ, Rhee JE, Yun KW. Writing - review & editing: Choi EH, Lee NJ, Woo S, Lee J, Lee SW, Kim EJ, Yun KW.

INTRODUCTION

Along with its impact on public health, the global economy, and environmental health, the coronavirus disease 2019 (COVID-19) pandemic has altered the epidemiology of respiratory viruses.[1,2] While minimal changes have been noted in the yearly trends of nonenveloped viruses such as human rhinovirus (HRV), human bocavirus (HBoV), and adenovirus (AdV), enveloped viruses such as respiratory syncytial virus (RSV), parainfluenza virus (PIV), human metapneumovirus (HMPV), and influenza virus (IFV), which typically cause seasonal epidemics, were minimally detected during the COVID-19 pandemic.[3] The difference is explained by the susceptibility of enveloped viruses to hand hygiene measures compared to non-enveloped viruses, primarily transmitted through contact, thereby directly influencing the effectiveness of nonpharmaceutical interventions (NPIs), such as social distancing and mask wearing.[4,5] In South Korea, social distancing was implemented in February 2020, and the national NPI strategy with regulation started in June 2020, was partially lifted in November 2021, and fully lifted in April 2022. As NPI measures were lifted, the detection rates of enveloped viruses started to increase, with epidemiological patterns that differed from those before the pandemic.[6,7]

This study aimed to characterize the nationwide epidemiological trends of respiratory viruses in South Korea after the COVID-19 pandemic compared with those before the pandemic using national surveillance data. This study could provide an opportunity to better understand the transmission mechanisms of respiratory viruses by analyzing the epidemiological changes resulting from nationwide NPIs.

METHODS

Study design and data sources

We conducted a prospective surveillance study to compare the epidemiological characteristics of respiratory viral infections in Korean children before and after the COVID-19 pandemic using Korea Respiratory Virus Integrated Surveillance System (K-RISS) data from January 2017 to June 2023. The K-RISS contains data from 150 clinics nationwide, including 77 hospitals for pathogen sentinel surveillance, and was originally expanded from the Korea Influenza and Respiratory Virus Surveillance System (KINRESS) in July 2022. Samples were collected in viral transport medium (BD, Franklin Lakes, NJ, USA) from patients with upper respiratory symptoms at 77 sentinel surveillance agencies and transported to 18 regional public health and environmental research institutes to establish a respiratory virus detection system with six commercial real-time reverse transcription–polymerase chain reaction kits (Kogene Bio, Seoul, Korea). A total of 8 respiratory viruses (AdV, HBoV, human coronavirus [HCoV], HMPV, HRV, IFV, PIV, and RSV) were tested in the KINRESS, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was added to the K-RISS. The surveillance program was maintained, and practices remained unchanged during the COVID-19 pandemic.

Using K-RISS data, we analyzed the overall detection rate, number, and seasonality of each virus and the demographic information of the children from whom the corresponding virus samples were collected. K-RISS data on the detection of SARS-CoV-2 were excluded to maintain consistency in comparisons during the overall study period.

Definition

This study used K-RISS data from children and adolescents younger than 20 years. The detection rate was calculated as the number of detected viruses divided by the total number of tests collected for each time period. The codetection rate was calculated as the number of tests for two or more viruses divided by the total number of any virus-detected tests. The prepandemic and postpandemic periods were defined as 2017–2019 and 2021–2023, respectively.

Statistical analysis

We used descriptive statistics, including means, medians, interquartile ranges, counts, and proportions. Categorical variables were compared by Fisher's exact test and the χ^2 test. Continuous variables were compared by Student's *t*-test, the Mann-Whitney *U* test or the Kruskal-Wallis test. The mean age of the children with detected viruses was compared between the prepandemic period (2017–2019) and individual postpandemic years (2021, 2022, and 2023). Two-sided *P* values < 0.05 were considered to indicate statistical significance. The data were analyzed using SPSS version 25.0 (SPSS, Inc., Chicago, IL, USA) and PRISM 9.3.1 (GraphPad Software, Inc., San Diego, CA, USA).

Ethics statement

This study was reviewed and approved by the Institutional Review Board of the Korea Disease Control and Prevention Agency (Ethics number: 2016-05-02-C-A, 2022-02-05-C-A). Informed consent was submitted by all subjects when they were enrolled for this study.

RESULTS

Half-annual detection rate of respiratory viruses before and after the COVID-19 pandemic

Approximately 3,000 respiratory samples were collected, and tests were performed on samples from children and adolescents during each half of the year from 2017 to 2019. However, between 2020 and the 1st half of 2022, samples were collected at levels ranging from 40% to 70% of the amount during the prepandemic period. Although more than 4,000 samples from the K-RISS were collected in the 2nd half of 2022, the average number of samples per institute remained lower than that in the prepandemic period (**Table 1**). While there were minimal differences in the overall detection rate of any respiratory virus throughout the study period, the 2nd half of 2020 had the lowest rate (50.6%), whereas the 2nd half of 2021 had the highest rate (72.3%). In terms of virus-specific data, nonenveloped viruses exhibited relatively consistent detection throughout the study period. However, HRV and HBoV had markedly greater rates in the 2nd half of 2020 and 1st half of 2021 (38.0–45.3% and 10.8–17.5%, respectively) than in the prepandemic period (17.7–26.3% and 0.7–4.1%, respectively), although the actual case numbers of HRV and HBoV detected were comparable to those in pre- and postpandemic periods.

On the other hand, the detection rate of enveloped viruses decreased greatly during the peak pandemic years of 2020–2021, occasionally with zero reported cases. However, the detection rates of PIV, RSV, HCoV, IFV, and HMPV started to increase after the 2nd half of 2021 in that order. In particular, PIV, RSV, and HMPV had significantly greater detection rates (30.5%, 24.2%, and 18.0%, respectively) in the postpandemic years than in the prepandemic years (5.3–10.5%, 2.0–10.7%, 0.5–10.9%, respectively; **Table 1**).

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Table 1. Number of samples and proportion of viruses detected

Periods	2017		2018		2019		2020		2021		2022		2023	Total
	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	2nd	1st	
Total samples	3,408	3,048	3,320	3,112	3,278	3,423	1,865	1,469	1,769	1,839	1,956	4,173	4,331	36,991
Samples/Institutes	44.3	39.6	43.1	40.4	42.6	44.5	24.2	19.1	23.0	23.9	25.4	27.8	28.9	32.3
Any virus	2,053 (60.2)	1,731 (56.8)	2,294 (69.1)	1,934 (62.1)	2,263 (69.0)	2,032 (59.4)	999 (53.6)	743 (50.6)	1,070 (60.5)	1,330 (72.3)	1,106 (56.5)	2,914 (69.8)	2,879 (66.5)	23,348 (63.1)
HRV	684 (20.1)	801 (26.3)	702 (21.1)	552 (17.7)	648 (19.8)	673 (19.7)	364 (19.5)	558 (38.0)	801 (45.3)	630 (34.3)	465 (23.8)	751 (18.0)	726 (16.8)	8,355 (22.6)
HBoV	191 (5.6)	22 (0.7)	110 (3.3)	78 (2.5)	190 (5.8)	140 (4.1)	50 (2.7)	158 (10.8)	310 (17.5)	102 (5.5)	108 (5.5)	443 (10.6)	313 (7.2)	2,215 (6.0)
AdV	210 (6.2)	200 (6.6)	252 (7.6)	512 (16.5)	370 (11.3)	531 (15.5)	214 (11.5)	133 (9.1)	181 (10.2)	110 (6.0)	110 (5.6)	240 (5.8)	546 (12.6)	3,609 (9.8)
PIV	339 (9.9)	195 (6.4)	348 (10.5)	165 (5.3)	286 (8.7)	201 (5.9)	13 (0.7)	0 (0)	0 (0)	560 (30.5)	4 (0.2)	468 (11.2)	472 (10.9)	3,051 (8.2)
RSV	83 (2.4)	356 (11.7)	91 (2.7)	332 (10.7)	67 (2.0)	288 (8.4)	89 (4.8)	3 (0.2)	1 (0.1)	154 (8.4)	473 (24.2)	416 (10.0)	514 (11.9)	2,867 (7.8)
HMPV	373 (10.9)	17 (0.6)	361 (10.9)	16 (0.5)	317 (9.7)	62 (1.8)	46 (2.5)	0 (0)	0 (0)	0 (0)	0 (0)	753 (18.0)	265 (6.1)	2,210 (6.0)
IFV	354 (10.4)	297 (9.7)	624 (18.8)	368 (11.8)	734 (22.4)	401 (11.7)	271 (14.5)	2 (0.1)	0 (0)	0 (0)	0 (0)	317 (7.6)	440 (10.2)	3,808 (10.3)
HCoV	168 (4.9)	75 (2.5)	184 (5.5)	206 (6.6)	96 (2.9)	98 (2.9)	91 (4.9)	1 (0.1)	5 (0.3)	5 (0.3)	115 (5.9)	212 (5.1)	313 (7.2)	1,569 (4.2)

HRV = human rhinovirus, HBoV = human bocavirus, AdV = adenovirus, PIV = parainfluenza virus, RSV = respiratory syncytial virus, HMPV = human metapneumovirus, IFV = influenza virus, HCoV = human coronavirus.

Seasonal variation in the detection of respiratory viruses during the postpandemic period

There were no significant changes in the seasonal epidemic patterns of the three nonenveloped viruses or HCoV, except for the occasional high detection rates of HRV and/or HBoV in the spring-summer and winter of 2020 and 2021 (**Fig. 1**). RSV showed one month of delayed re-emergence and peaked in the 2021/2022 season, and there was an earlier peak in the fall of the 2022/2023 season. IFV re-emerged with its usual seasonality in the 2022/2023 season. However, these two viruses continued to circulate in low amounts throughout the 1st half of 2023 (**Fig. 1**). PIV and HMPV re-emerged with unusual seasonal patterns and higher rates than usual. In 2021, PIV had the highest peak between September and November, and in 2022, it had a lower peak between November and December. Like RSV and IFV, PIV also circulated in low amounts throughout the 1st half of 2023. There were very few cases of HMPV detected after the pandemic until the fall of 2022 (between August and November). In 2023, the seasonal pattern of HMPV detection was almost restored, although it was still delayed by 1–3 months compared to that before the pandemic (**Fig. 1**).

Codetection rates and viruses

The overall codetection rate was 16.5%, with the lowest rate occurring in the 2nd half of 2017 (12.1%) and the highest rate occurring in the 1st half of 2023 (21.2%). Soon after the relaxation of national NPI measures, the codetection rates were also high, at 19.9% in the 1st half of 2021 and 20.5% in the 2nd half of 2022 (**Fig. 2**). Compared with that in the prepandemic period, the codetection rate was significantly greater in the postpandemic period (15.0% vs. 19.1%, $P < 0.001$). HRV (40–70%), AdV (30–70%), and HBoV (20–60%) were the most frequently codetected viruses annually. There was no significant difference in the codetected viral distribution before or after the COVID-19 pandemic.

Trends in the mean age of children with detected viruses

After the COVID-19 pandemic, most viruses were detected at an older mean age than before the pandemic (**Fig. 3**). For HRV, AdV, HCoV, and PIV, the mean ages of the children with

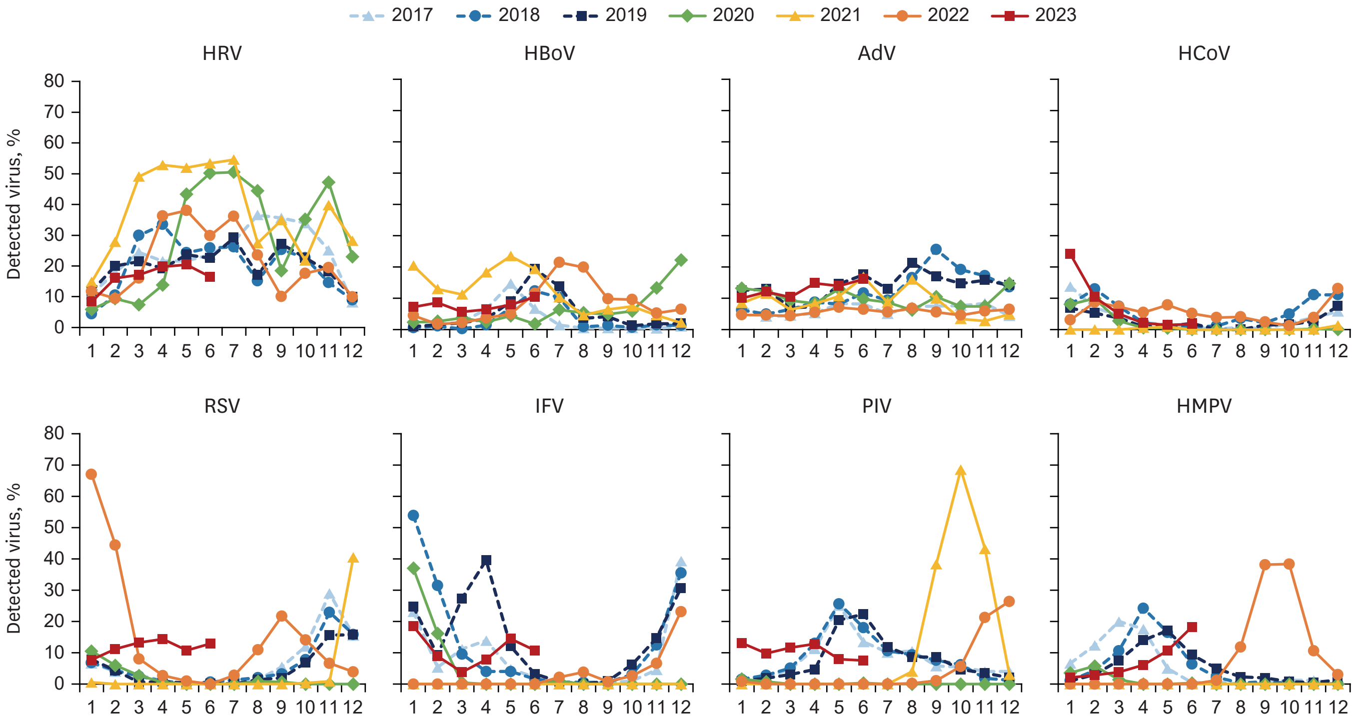

Fig. 1. Seasonal variation in the detection of respiratory viruses in Korean children, January 2017–June 2023.
HRV = human rhinovirus, HBoV = human bocavirus, AdV = adenovirus, HCoV = human coronavirus, RSV = respiratory syncytial virus, IFV = influenza virus, PIV = parainfluenza virus, HMPV = human metapneumovirus.

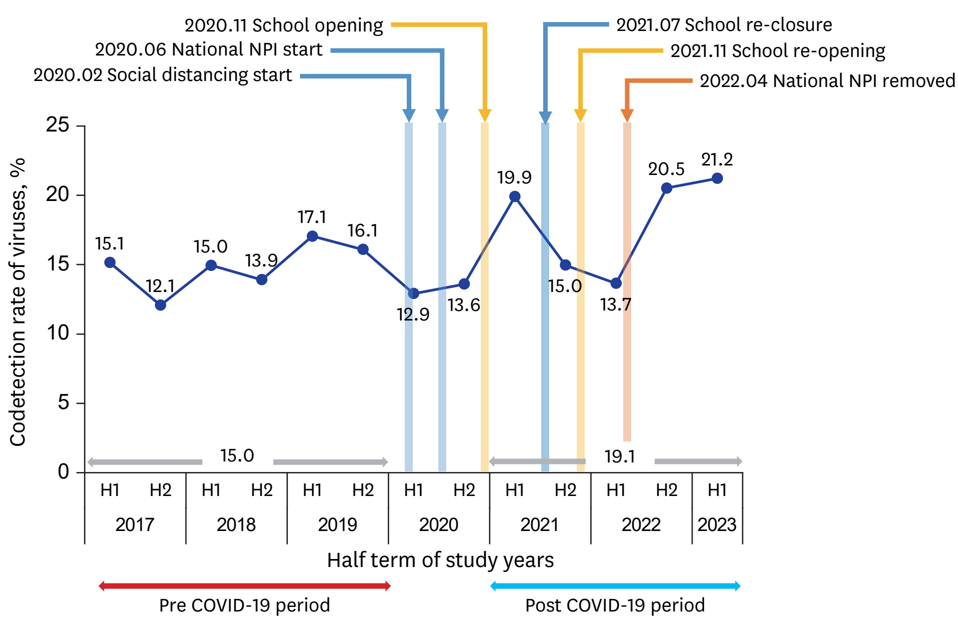

Fig. 2. Half-annual rate of viral codetection among Korean children, January 2017–June 2023.
NPI = nonpharmaceutical intervention, COVID-19 = coronavirus disease 2019.

these viruses significantly decreased in 2021 (4.3 ± 3.7, 3.0 ± 2.5, 1.7 ± 0.7, and 2.6 ± 1.9 years of age, respectively) compared to those in the prepandemic period (4.7 ± 4.7, 3.7 ± 3.0, 4.1 ± 4.2, and 3.3 ± 3.3 years, respectively; $P < 0.001$ for all) and then increased from 2022–2023. In 2023, the mean ages of the children with HRV (5.3 ± 4.5 years), AdV (4.1 ± 3.1 years), HCoV

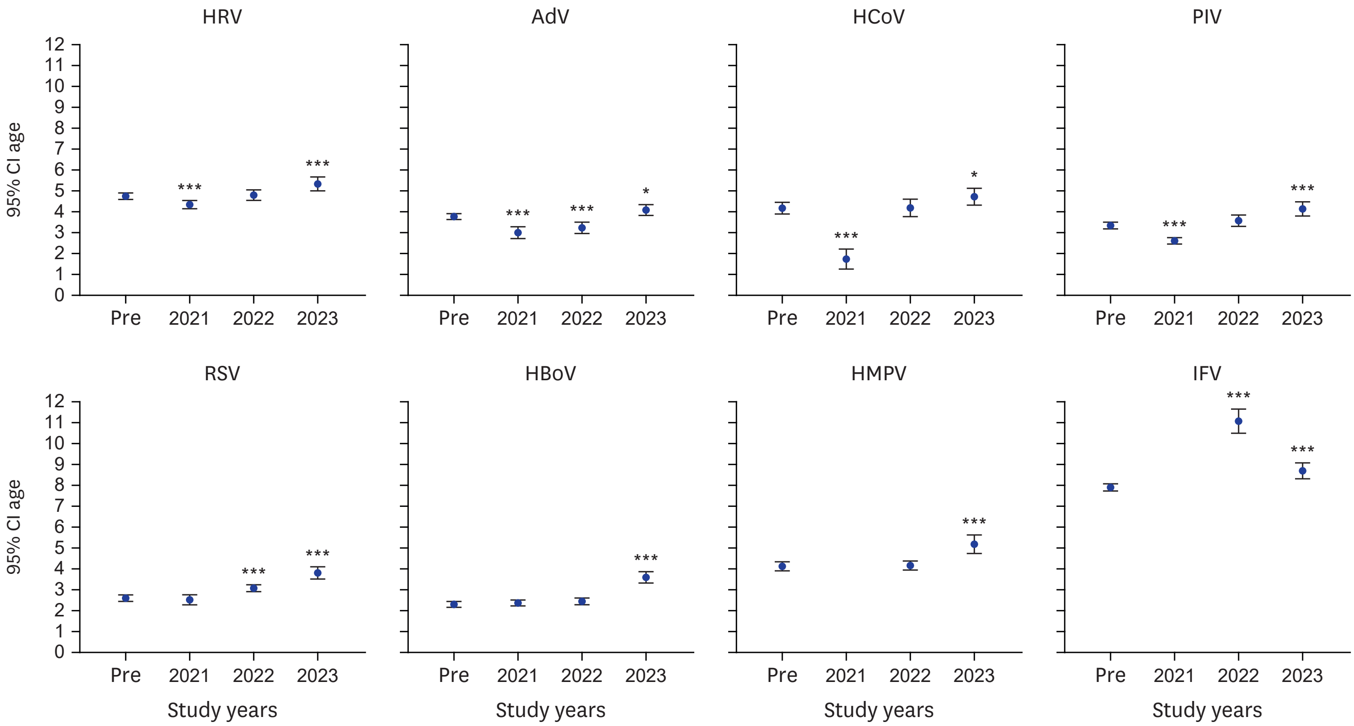

Fig. 3. Mean age of Korean children with each virus detected, January 2017–June 2023.
HRV = human rhinovirus, HBoV = human bocavirus, AdV = adenovirus, PIV = parainfluenza virus, RSV = respiratory syncytial virus, HMPV = human metapneumovirus, HCoV = human coronavirus, IFV = influenza virus.
The blue dot represents the mean age within 2 standard deviations. Above the values, the *** represents results with $P < 0.001$ and * represents those with $P < 0.05$.

(4.7 ± 3.7 years), and PIV (4.1 ± 3.8 years) were significantly greater than the prepandemic values. Although there was no decrease in the mean age of children with RSV or HBoV and no cases of HMPV were detected in 2021, the mean ages of the children in the 2023 cohort (3.8 ± 3.4, 5.2 ± 3.6, and 3.6 ± 2.5 years of age, respectively) were significantly greater than the prepandemic values for these three viruses (2.6 ± 3.0, 4.1 ± 3.7, and 2.3 ± 2.0 years of age, respectively; $P < 0.001$ for all). However, the mean age of the children with IFV significantly increased in 2022 compared with before the pandemic (11.1 ± 5.2 vs. 7.9 ± 4.6 years of age; $P < 0.001$) and then decreased markedly in 2023 (8.7 ± 4.1 years of age; $P < 0.001$).

DISCUSSION

This study analyzed national surveillance data on the detection of respiratory viruses in Korean children before and after the COVID-19 pandemic. During the peak period of the pandemic in 2020, few respiratory viruses were detected overall, particularly enveloped viruses. However, when the national NPI strategy began to be relaxed, the incidence of respiratory viral infections started to increase, with an unusual seasonal pattern. During the postpandemic years, virus codetection rates increased, and the mean age of children with detected viruses increased compared with that in the prepandemic years.

Several studies have demonstrated that COVID-19 has contributed to a change in the epidemiology of respiratory viral illnesses. In 2020–2021, many countries lost the typical winter seasonal wave of RSV and IFV infections.[5,8,9] In addition, minimal cases of PIV and HMPV, which are typically highest in the spring, were reported over the two years.[10-12] The situation was similar in South Korea. As shown in the present and previous studies,[2,10,13-15] there was no evident outbreak of seasonal respiratory viral infections until one year after the start of the COVID-19 pandemic. This is likely due to the widespread implementation of NPIs, resulting in reduced respiratory virus transmission via contact and droplets.[3-5] However, the reduction in healthcare facility utilization itself during the COVID-19 pandemic may have acted as a contributing factor to the even lower detection rates of respiratory viruses.[16]

In the current study, the circulation of different respiratory viruses varied during the COVID-19 pandemic. The most distinct difference was between enveloped and nonenveloped viruses. Enveloped viruses were more susceptible to hand hygiene measures compared to non-enveloped viruses, thereby directly influencing the effectiveness of NPIs.[4,5] The presence of an envelope along with the characteristics of each virus, such as their main transmission routes, environmental stability, infectious periods, and reproduction numbers, could have influenced the extent and magnitude to which the epidemiology of these viruses was affected by NPIs during the COVID-19 period.[7,17] This aspect may require further in-depth research for each individual virus.

As countries started to relax quarantine rules and other NPI measures, the resurgence of seasonal respiratory viruses tended to show unusual seasonal patterns during and after the pandemic.[8,12,18] In particular, the reopening of schools was closely associated with increased RSV activity in the community.[19,20] In the current study, alongside the school reopenings in November 2020, codetection rates of non-enveloped viruses increased and sequential reappearances of enveloped viruses occurred from 2021 onwards. RSV exhibited delayed and earlier peaks in the 2021/2022 and 2022/2023 seasons, respectively. In addition, PIV and HMPV exhibited large peaks in the falls of 2021 and 2022, respectively. Following the lifting of NPIs in the 1st half of 2022, extended circulation of RSV, Flu, and PIV occurred, leading to a further increase in the codetection rates. Researchers have suggested that interruption of the circulation of respiratory viruses during the COVID-19 pandemic might result in reduced infection-induced immunity at the population level, which could have contributed to increased susceptibility and more severe disease after the re-emergence of respiratory viruses in postpandemic years. These factors could have counteracted the effect of environmental factors such as high temperatures, which suppressed the increase in out-of-season cases of the corresponding viruses.[9,20,21]

A previous US study performed during 2019–2021 reported that there was no increasing trend of virus codetection during the COVID-19 pandemic and that HRV was the most frequently detected virus in patients with codetected viruses.[12] However, in the present study, as multiple viruses started to re-emerge in South Korea in the fall of 2022 and spring of 2023, codetection rates increased compared to those in prior years, although HRV, AdV, and HBoV had the highest proportion of codetections. A higher number of children infected with nonenveloped viruses with a longer period of shedding might have codetected RSV, PIV, and HMPV in 2022–2023 than before. Additionally, children with codetected viruses might have more severe clinical presentations and thus tend to visit hospitals and to be tested. Although previous studies have not shown a consistent association between coinfection and increased disease severity,[22,23] future studies are necessary to better understand the clinical impact and severity of increased virus codetection.

Australian studies demonstrated an increased number of RSV infections in children aged 2 to 4 years during the postpandemic years. The authors explained this as the existence of an RSV-susceptible population of older children due to disrupted circulation during the COVID-19 pandemic.[18,24] Other researchers also indicated that the median age of children admitted for RSV infection increased during the resurgence of the virus during the postpandemic period.[25,26] In the present study, most viruses, including nonenveloped viruses (HRV, AdV, and HBoV), as well as RSV, exhibited a significant increase in the mean age of patients during the postpandemic years compared with the prepandemic years. One possible explanation is that more severe infections might have occurred in older children after the COVID-19 pandemic due to the reduced natural immunity to the corresponding viruses and the increased virus coinfection rate. This could have made older children need medical care more often than before. In addition, it is possible that respiratory viral testing capacity and behavior has increased because COVID-19 has raised global community concern and awareness about respiratory infections.[25] Viral testing could have increased for older children after the pandemic compared with before. However, the age distribution of patients with IFV during the postpandemic years is unique. It is speculated that natural immunity to IFV rapidly made up among school-aged children after the schools opened, and then the target population age might have decreased.

This study has several limitations. First, the number of collected specimens greatly decreased during the COVID-19 pandemic because most patients with respiratory symptoms visited screening clinics instead of local community hospitals, which may have influenced the viral detection rates. We ultimately controlled for these variables by using rates proportional to the increase in the number of cases and focused more on observing temporal patterns of viruses. In addition, this study targeted patients who visited surveillance institutions and had respiratory specimens collected. It is possible that during the COVID-19 pandemic, many patients who actually had respiratory virus infections might not have visited hospitals as part of social distancing measures. Consequently, the frequency and types of viruses detected in these patients remain unknown and the virus detection rate during the COVID-19 period is likely underestimated. However, considering that the detection rates of non-enveloped viruses did not significantly decrease, it is evident that the detection rate of enveloped viruses decreased during the COVID-19 period. Second, understanding the change in the clinical impact of the COVID-19 pandemic on viral epidemiology is difficult due to the lack of clinical information. Third, test results for SARS-CoV-2 were eliminated from this study to maintain consistency in comparisons before and after the pandemic. As a result, we were unable to analyze the interactions between SARS-CoV-2 and other viruses. Lastly, factors other than NPIs and viral structure such as vaccination levels in populations, seasonality, differing levels of pre-existing herd immunity for each virus, and global transmission spread through traveling likely influenced epidemic patterns. Despite these limitations, this study performed an in-depth evaluation of the nationwide epidemiological trends of respiratory viral infections in Korean children before and after the COVID-19 pandemic.

In conclusion, NPIs during the COVID-19 pandemic help curb the spread of seasonal respiratory viruses. However, when the natural immunity of the community to viruses is not established, it is possible that the seasonality, severity, and target population of the virus could change. Thus, it is important to construct community-level immunity for the target population by decreasing the severity of natural infection and/or increasing immunization. This is the reason why vaccine development and implementation against major respiratory viral pathogens, such as RSV, PIV, and HMPV, should be promoted. Achieving herd immunity at the community level will aid in mitigating the spread and severity of respiratory viral infections. In addition, the epidemiological trends of respiratory viruses should be monitored to understand viral pathophysiology and utilize it to inform vaccine development as well as public health interventions in homes and schools.

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