

Shifts in patterns in influenza virus and RSV infections in Korea after the COVID-19 pandemic resulting from immunity debt

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Abstract

Background: Non-pharmaceutical interventions (NPIs) such as mask-wearing and social distancing during the COVID-19 pandemic significantly reduced the transmission of respiratory viruses. The "immunity debt" theory suggests that decreased exposure to pathogens during this period may have led to increased susceptibility and severity of these viruses once restrictions were lifted. However, the post-pandemic impact of NPIs on the burden of these viruses, particularly in young children, remains underexplored.

Objective: This study aimed to evaluate the impact of NPIs during the COVID-19 pandemic on the epidemiology and clinical burden of influenza and RSV in Korea, focusing on changes in incidence, timing, and severity of infections in children.

Methods: We analyzed weekly virologic, outpatient, and inpatient surveillance data for influenza and RSV from the Korea Disease Control and Prevention Agency (KDCA) from 2017 to 2024, covering pre-pandemic, pandemic, and post-pandemic periods. Time-series analyses were conducted to assess trends in incidence and clinical severity across age groups before and after the pandemic.

Results: Pre-pandemic seasons showed typical winter peaks for both influenza and RSV, with RSV epidemics occurring slightly earlier. Post-pandemic, RSV returned in 2021/22 with delayed and prolonged epidemic peaks, whereas influenza did not resurface until the 2022/23 season. The overall burden of both influenza and RSV was reduced in post-pandemic seasons, though the proportion of severe RSV cases increased among children aged 1-6 years, consistent with the "immunity debt" hypothesis. Hospitalization rates for influenza, however, increased in older children aged 7-18 years post-pandemic.

Conclusions: The patterns of influenza and RSV infections in Korea following the COVID-19 pandemic reveal distinct shifts in timing, severity, and affected age groups. Substantial increases in susceptibility among younger children for RSV and older children for influenza, potentially due to immunity gaps highlight the lasting impacts of pandemic-related disruptions on population immunity and respiratory disease transmission patterns. Ongoing surveillance and targeted public health measures remain critical to understanding and managing seasonal respiratory viruses in a post-pandemic context.

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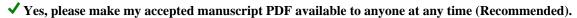
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pandemic resulting from immunity debt

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ABSTRACT

Background

Non-pharmaceutical interventions (NPIs) such as mask-wearing and social distancing during the COVID-19 pandemic significantly reduced the transmission of respiratory viruses. The "immunity debt" theory suggests that decreased exposure to pathogens during this period may have led to increased susceptibility and severity of these viruses once restrictions were lifted. However, the post-pandemic impact of NPIs on the burden of these viruses, particularly in young children, remains underexplored.

Objectives

This study aimed to evaluate the impact of NPIs during the COVID-19 pandemic on the epidemiology and clinical burden of influenza and RSV in Korea, focusing on changes in incidence, timing, and severity of infections in children.

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We analyzed weekly virologic, outpatient, and inpatient surveillance data for influenza and RSV from the Korea Disease Control and Prevention Agency (KDCA) from 2017 to 2024, covering prepandemic, pandemic, and post-pandemic periods. Time-series analyses were conducted to assess trends in incidence and clinical severity across age groups before and after the pandemic.

Results

Pre-pandemic seasons showed typical winter peaks for both influenza and RSV, with RSV epidemics occurring slightly earlier. Post-pandemic, RSV returned in 2021/22 with delayed and prolonged epidemic peaks, whereas influenza did not resurface until the 2022/23 season. The overall burden of

both influenza and RSV was reduced in post-pandemic seasons, though the proportion of severe RSV

cases increased among children aged 1-6 years, consistent with the "immunity debt" hypothesis.

Hospitalization rates for influenza, however, increased in older children aged 7-18 years post-

pandemic.

Conclusions

The patterns of influenza and RSV infections in Korea following the COVID-19 pandemic reveal

distinct shifts in timing, severity, and affected age groups. Substantial increases in susceptibility

among younger children for RSV and older children for influenza, potentially due to immunity gaps

highlight the lasting impacts of pandemic-related disruptions on population immunity and respiratory

disease transmission patterns. Ongoing surveillance and targeted public health measures remain

critical to understanding and managing seasonal respiratory viruses in a post-pandemic context.

Keywords: influenza; RSV; immunity debt; epidemiology; public health.

INTRODUCTION

Non-pharmaceutical interventions (NPIs) employed during the COVID-19 pandemic to mitigate the spread of SARS-CoV-2, including mask-wearing and social distancing led to an unprecedented decline in the incidence of respiratory viruses [1–3]. The concept of "immunity debt," which suggests that reduced exposure to common pathogens during the pandemic might result in heightened susceptibility and more severe disease outcomes when these viruses begin circulating again, has gained a great deal of attention from public health researchers, particularly in the context of influenza and respiratory syncytial virus (RSV) [1,4,5]. Young children, who typically build their immune defenses through early exposures, may be particularly more vulnerable to severe RSV, given that most children will be infected with RSV by the age of 2 [6].

Influenza virus and RSV are two of the most significant respiratory pathogens that cause substantial morbidity and mortality, particularly in infants, young children, and the elderly. The World Health Organization estimates that seasonal influenza affects approximately 1 billion people globally each year, with around 3 to 5 million cases of severe illness [7]. RSV is a leading cause of acute lower respiratory tract infections (LRTIs) particularly in children under the age of 5. It is estimated that RSV causes approximately 33 million new episodes of LRTI globally each year, leading to about 3.6 million hospitalizations [8]. However, the impact of NPIs on the burden of influenza and RSV in young children using real-world data in post-pandemic years remains underexplored.

This study aims to investigate the impact of the COVID-19 pandemic on the epidemiology and clinical burden of influenza and RSV using surveillance data in Korea. Specifically, we seek to elucidate the extent to which NPIs influenced the timing, incidence, and clinical severity associated with these infections, particularly in young children.

METHODS

Data Sources

We analyzed weekly virologic, outpatient, and inpatient surveillance data collected from August 2017 to July 2024 through the Influenza and Respiratory Viruses Surveillance System (KINRESS) by the Korea Disease Control and Prevention Agency (KDCA). Virologic and outpatient surveillance data were extracted from KDCA weekly reports, and inpatient surveillance data including the agespecific number of hospital admissions with confirmed influenza or RSV were obtained from the KDCA database.

Statistical Analysis

Each season was defined from epi-week 36 of one year to epi-week 35 of the following year, as per the KINRESS. We then categorized these seven seasons into three distinct periods as follows: prepandemic (2017/18 to 2019/20; 3 seasons), pandemic (2020/21; 1 season), and post-pandemic (2021/22 to 2023/24; 3 seasons). For the present analyses, we consider the 2021/22 season as post-pandemic since it followed the government's "Living with COVID-19" plan, a phased approach aimed at progressively lifting NPIs and returning to normal life, which began on Nov 1, 2021, although some control measures did continue through to mid-2022, and there was a period in early 2022 where some measures were temporarily re-introduced to manage a large surge in Omicron cases [9].

As with previous studies on influenza, we used the proportion of influenza-like illness (ILI) patients and the proportion of respiratory specimens testing positive for each influenza type and subtype or RSV to derive a weekly indicator of influenza or RSV incidence [10]. We conducted a time-series analysis using the proxies to describe trends and seasonal patterns of influenza and RSV over the past years. The weekly number of hospitalizations associated with influenza and RSV was collated

by age group for each season to compare the clinical severity across pre- and post-pandemic periods.

Analyses were conducted using R version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

In pre-pandemic seasons, influenza and RSV followed a similar seasonal pattern, both peaking in winter, with RSV epidemics typically occurring 3-4 weeks earlier than influenza (epi-week 49-50 for RSV and epi-week 52-2 for influenza), as illustrated in Figure 1.

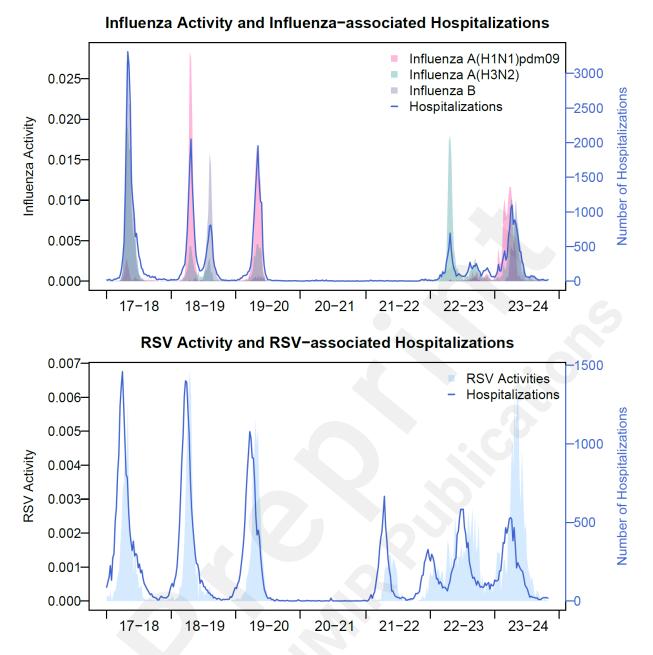


Figure 1. Virus activity and the number of hospitalizations: Influenza and RSV in South Korea, 2017/18 to 2023/24

Following the pandemic, RSV reappeared in the 2021/22 season with a delayed epidemic peak in epi-week 5, which occurred 7-8 weeks later than usual. In the 2022/23 season, RSV had two distinct peaks: an early peak in epi-week 41, 8-9 weeks ahead of the typical timing, and a second peak in epi-week 17 amid a prolonged epidemic. Influenza took one more season than RSV to reappear in the 2022/23 season with a typical winter peak in epi-week 1.

The number of influenza- and RSV-associated hospitalizations from 2017/18 to 2023/24 is shown in Supplementary Table 1. The overall burden was substantially reduced in post-pandemic seasons. Between the 2019/20 and 2020/21 seasons, there was a significant reduction in the number of hospital admissions associated with influenza (12,660 to 211; 98.3%) and RSV (11,969 to 80; 99.3%) across all age groups (Supplementary Table 1). In pre-pandemic seasons (2017/18 to 2019/20), influenza and RSV caused an average of 17,000 and 14,583 hospital admissions, respectively. In post-pandemic seasons (2021/22 to 2023/24), RSV caused an average of 8,728 hospital admissions, which is only about 60% of the admissions from pre-pandemic seasons.

A similar pattern was observed in influenza- and RSV-associated hospitalization rates (Table 1). The overall influenza-associated hospitalization rate significantly declined from 24.7 per 100,000 in the 2019/20 season to nearly zero in the pandemic and early post-pandemic years, but bounced back to 23.9 per 100,000 by the 2023/24 season, indicating a near full recovery to pre-pandemic levels. As for RSV, hospitalization rates dropped significantly across all age groups during the pandemic before rebounding to near pre-pandemic levels in the 2022/23 season. The overall RSV hospitalization rate substantially declined from 23.3 per 100,000 persons to just 0.2 then to 10.5 in the 2020/21 and 2021/22 seasons, respectively. By the 2022/23 season, the rate had recovered to 23.4 per 100,000, closely mirroring pre-pandemic levels.

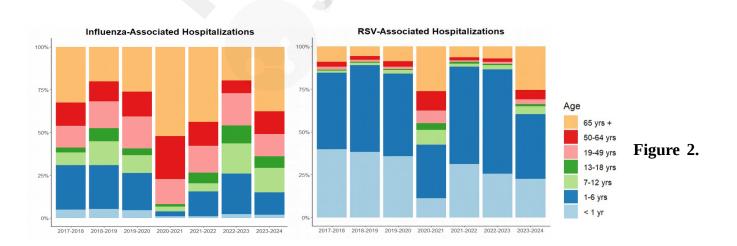
Season	Peak (wk)	All	< 1 y	1-6 y	7-12 y	13-18 y	19-64 y	≥65 y
Influenza								_
2017/18	1	42.2	287.5	205.6	57.5	18.6	16.3	99.4
2018/19	52	32.7	267.1	162.4	83.9	40.6	13.2	45.7
2019–20	2	24.7	189	109.5	46.8	16.4	12.0	42.9
2020/21	49	0.4	0.7	0.3	0.2	0.1	0.2	1.4
2021/22	33	0.6	1.2	1.9	0.5	0.6	0.3	1.5
2022/23	1	15.1	70.3	89.9	49.6	28.8	5.9	16.9
2023/24	50	23.9	102.5	84.7	63.2	29.9	9.4	48.7
RSV								
2017/18	49	32.8	1,811.4	275.2	8.0	2.5	2.2	21.3

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	2018/19	49	29.2	1,725.5	287.6	7.8	2.6	1.5	11.4
	2019/20	50	23.3	1,396.2	230.8	8.4	2.2	1.6	13.4
	2020/21	13	0.2	3.2	1.1	0.2	0.1	0.0	0.3
	2021/22	5	10.5	648.1	138.0	3.5	1.8	0.4	4.0
	2022/23	18	23.4	1,236.1	357.5	10.3	3.6	1.1	9.6
	2023/24	4	17.2	843.1	177.5	15.2	4.2	2.1	23.5

Table 1. Influenza- and RSV-associated hospitalization rates (per 100,000 persons)

Note: For influenza, the 2023-24 season includes data from week 36 of 2023 through to week 27 of 2024.

For influenza, more older children aged 7-12 years and 13-18 years suffered severe outcomes requiring hospitalization post-pandemic (Figure 2 and Supplementary Table 1). In the 2022/23 season, the proportion of children aged 7-12 years was 18%, a significant increase from 10% in the 2019/20 season. Similarly, the proportion for children aged 13-18 years increased from 4% in the 2019/20 to 10% in the 2022/23 season. Similarly, children aged 7-12 years and 13-18 years experienced the greatest increase in influenza-associated hospitalization rates post-pandemic. For children aged 7-12 years, the rate rose from 46.8 per 100,000 in the 2019/20 season to 63.2 per 100,000 in the 2023/24 season, while for those aged 13-18 years, it increased from 16.4 to 29.9 per 100,000. On the other hand, the hospitalization rates for infants (<1 year) and children aged 1-6 years declined (Table 1).



Influenza- and RSV-associated hospitalizations by age group (%)

For RSV, the proportion of young children aged 1-6 years among RSV-associated hospitalizations increased post-pandemic (Figure 2 and Supplementary Table 1). In the 2021/22 season, this age group accounted for 57% of RSV hospitalizations, up from 48% in the 2019/20 season. By the 2022/23 season, this figure rose further to 61%, This contrasts with all other age groups whose proportion either remained the same or decreased in post-pandemic seasons. Similarly, age-specific hospitalization rates show that the most significant increase in RSV-associated hospitalizations post-pandemic occurred in children aged 1-6 years (Table 1). This group saw their hospitalization rate rise from 231 per 100,000 in the 2019/20 season to 358 per 100,000 in the 2022/23 season, marking the greatest increase among all age groups. Meanwhile, infants under 1 year, who had the highest RSV burden pre-pandemic, experienced a considerable decline, with the rate dropping from 1,400 per 100,000 in the 2019/20 season to 1,240 per 100,000 in 2022/23.

DISCUSSION

The widespread implementation of NPIs during the COVID-19 pandemic led to substantial reductions in the transmission of influenza and RSV in Korea, as it did elsewhere [1–3]. As the NPIs were progressively relaxed in late 2021, RSV returned almost immediately, followed by influenza a year later. We identified substantial changes in RSV and influenza activity with both viruses having delayed and prolonged epidemics in post-pandemic seasons. However, this prolonged activity was not linked to an increased burden. In fact, our analysis revealed a lower overall epidemiological burden compared to previous years. This was contrary to the feared "triple-demic" [11]. The lessened impact could be due to a step-change in awareness of infectious disease prevention, such as more frequent hand-washing and mask-wearing after the pandemic.

An important observation in our study is the significantly increased proportion of young children aged 1-6 years among RSV-associated hospital admissions in the post-pandemic years. This may indicate that the susceptibility to severe infections, especially in young children, may be higher than in pre-pandemic seasons. This could be partly due to the accumulated "immunity debt," where more young children are susceptible to severe outcomes because they have not developed immunity through prior exposures during the pandemic [4,5]. In particular, our findings suggest that immunity debt was more significant for RSV, particularly in children aged 1-6 years. They were the only age group that experienced an increased severity, with an increased proportion among all RSV-related hospital admissions in the first two post-pandemic seasons. This is consistent with a recent US study [12], which found a significantly higher RSV burden in children aged 2-5 years, having almost 4.86 times as likely to be hospitalized in 2022 compared to pre-pandemic years, whereas younger children such as infants aged 0-5 months were only 1.77 times as likely. Primary RSV infections tend to be more severe than re-infections [13], and by delaying primary infections for one or two years, clinical severity may have become elevated in slightly older children who had avoided RSV infection during the COVID-19 pandemic.

Our analysis revealed that the proportion of older children aged 7-18 years increased among influenza-associated hospital admissions in the post-pandemic years. It may be partly due to the delayed exposure to influenza during the pandemic, which may have resulted in reduced immunity in these school-age children. School closures, remote learning, and reduced social interactions during the pandemic likely disrupted the usual circulation of influenza, leading to fewer infections in younger populations. As restrictions eased and normal social interactions resumed, these children who had lower pre-existing immunity, became more susceptible to the virus, contributing to higher hospitalization rates in this age group. Additionally, changes in vaccination coverage or the effectiveness of the influenza vaccine in these years may also have played a role in the observed

increase in hospitalizations.

Furthermore, while both influenza and RSV have returned as NPIs eased, the timing and clinical burden of these rebounds varied. RSV returning a year earlier than influenza might suggest that NPIs had less effect on RSV. RSV is thought to spread more through direct contact with contaminated surfaces and is more stable on these surfaces than influenza, allowing it to survive longer outside the human body [14]. This stability, combined with the virus's prolonged shedding in infected individuals, especially children, could make RSV transmission more resilient to NPIs focused on airborne spread, such as masking and social distancing. In contrast, influenza's shorter infectious period and reliance on airborne transmission make it more susceptible to these interventions, leading to a more effective reduction in its spread compared to RSV.

Limitations

Our study has several limitations. First, changes in the burden of severe influenza or RSV in postpandemic seasons could be partially associated with increases in testing after the pandemic linked to
increased laboratory capacity and attention to viral infections [15]. However, it is unlikely that
increased testing fully explains our observations, particularly for RSV. In Korea, RSV diagnostic
testing is generally less actively conducted than for influenza or COVID-19 due to the absence of a
standard antiviral treatment, though testing is more common in infants who are at higher risk of
severe illness. The diagnostic methods for RSV—such as rapid antigen tests, PCR, and viral culture
—have not significantly changed before or after the COVID-19 pandemic. Thus, despite the
pandemic's impact on healthcare, the frequency and methods of RSV testing in Korea likely
remained consistent. Second, changes in health-seeking behaviors after the pandemic must also be
accounted for when interpreting results from the study. The COVID-19 pandemic significantly
altered how individuals accessed healthcare services, often delaying or avoiding visits to hospitals or

clinics due to fear of exposure, public health restrictions, or overwhelmed healthcare systems. This shift may have resulted in the underreporting of cases in the surveillance data, affecting the comparability of pre- and post-pandemic disease burden. Finally, increased awareness of respiratory infections could also artificially inflate case detection in post-pandemic years compared to pre-pandemic seasons.

Conclusions

The patterns of influenza and RSV infections in Korea following the COVID-19 pandemic reveal distinct shifts in timing, severity, and affected age groups. While the resurgence of RSV and influenza was anticipated with the relaxation of NPIs, the delayed and prolonged epidemic patterns observed in the post-pandemic seasons did not correspond with an increased overall disease burden. Instead, we found specific increases in susceptibility among younger children for RSV and older children for influenza, potentially due to immunity gaps arising from limited exposure during the pandemic. These findings highlight the lasting impacts of pandemic-related disruptions on population immunity and respiratory disease transmission patterns. Ongoing surveillance and targeted public health measures remain critical to understanding and managing seasonal respiratory viruses in a post-pandemic context.

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Conflicts of Interest

MP reports no potential conflicts of interest. WSC has consulted for Moderna, Sanofi Pasteur, and

CSL, and has been an investigator in clinical trials sponsored by SK Bioscience, GlaxoSmithKline, Pfizer, Moderna, Sanofi Pasteur, and Janssen. BJC has consulted for AstraZeneca, Fosun Pharma, GlaxoSmithKline, Haleon, Moderna, Novavax, Pfizer, Roche, and Sanofi Pasteur.

Authors' Contributions

MP, WSC, and BJC designed the study. MP collected and conducted all statistical analyses. MP and BJC wrote the first draft. WSC reviewed and commented on the manuscript. All authors reviewed the final manuscript.

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