

นิพนธ์ต้นฉบับ

การเปลี่ยนแปลงทางระบาดวิทยาของการติดเชื้อ respiratory syncytial virus

ในเด็กก่อนและหลังการระบาดของ COVID-19 ในโรงพยาบาลกลาง กรุงเทพมหานคร

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บทคัดย่อ

ความเป็นมา: Respiratory Syncytial Virus (RSV) เป็นสาเหตุสำคัญของการติดเชื้อทางเดินหายใจส่วนล่างในเด็กทั่วโลก การระบาดของโรค COVID-19 ส่งผลให้รูปแบบทางระบาดวิทยาของ RSV เปลี่ยนแปลงอย่างมีนัยสำคัญ ในหลายพื้นที่

วัตถุประสงค์: เพื่อประเมินแนวโน้ม ลักษณะทางคลินิก และความรุนแรงของการติดเชื้อ RSV ในเด็กก่อนและหลังการระบาดของ COVID-19 ในกรุงเทพมหานคร

วิธีการศึกษา: การศึกษาย้อนหลังจากเวชระเบียนอิเล็กทรอนิกส์ของผู้ป่วยเด็กอายุน้อยกว่า 15 ปี ที่ได้รับการวินิจฉัยว่าติดเชื้อ RSV ในโรงพยาบาลกลาง ระหว่างเดือนมกราคม พ.ศ. 2561 ถึงเดือนธันวาคม พ.ศ. 2566 โดยเปรียบเทียบข้อมูลระหว่างช่วงก่อนการระบาด (พ.ศ. 2561–2563) และหลังการระบาด (พ.ศ. 2564–2566) ได้แก่ ข้อมูลประชากร ลักษณะทางคลินิก การให้ออกซิเจน ระยะเวลาอนโรพยาบาล ค่าใช้จ่ายในการรักษา และการใช้ยาปฏิชีวนะ วิเคราะห์โดยใช้ Mann-Whitney U test และ chi-square test

ผลการศึกษา: พบผู้ป่วย RSV ทั้งหมด 137 ราย จำนวนผู้ป่วยติดเชื้อ RSV ค่อย ๆ ลดลงจนเป็นศูนย์ในปี พ.ศ. 2564 และเพิ่มขึ้นอีกครั้งในช่วงปี พ.ศ. 2565–2566 อายุมัธยฐานของผู้ป่วยเพิ่มขึ้นอย่างมีนัยสำคัญจาก 12 เดือนในช่วงก่อนการระบาด เป็น 18 เดือนในช่วงหลังการระบาด (p value 0.042) ไม่พบความแตกต่างอย่างมีนัยสำคัญในด้านการให้ออกซิเจน ระยะเวลาอนโรพยาบาล และค่าใช้จ่ายในการรักษา อย่างไรก็ตาม สัดส่วนของผู้ป่วยที่ต้องได้รับการช่วยหายใจขั้นสูงมีแนวโน้มเพิ่มขึ้น (ร้อยละ 19.1 เทียบกับร้อยละ 5.8) ขณะที่การใช้ยาปฏิชีวนะลดลงอย่างมีนัยสำคัญ (ร้อยละ 26.5 เทียบกับร้อยละ 50.7, p value < 0.05)

สรุป: ภายหลังการระบาดของ COVID-19 พบการเปลี่ยนแปลงของระบาดวิทยา RSV ในเด็ก โดยพบมีการกลับมาระบาดในลักษณะที่ผิดไปจากเดิม และผู้ป่วยมีอายุนั้นเข้ารับการรักษาสูงขึ้นในช่วงหลังการระบาด ขณะที่ผลลัพธ์ทางคลินิกที่สำคัญโดยรวมไม่เปลี่ยนแปลงอย่างชัดเจน การเฝ้าระวังอย่างต่อเนื่อง และมาตรการการป้องกันที่มีประสิทธิภาพ จึงมีความสำคัญในการลดภาระของโรคปอดอักเสบจากการติดเชื้อ RSV ในเด็ก

คำสำคัญ: ไวรัสอาร์เอสวี, การติดเชื้อทางเดินหายใจส่วนล่างในเด็ก, การระบาดของโควิด-19, ความรุนแรงของโรค, การใช้ยาต้านจุลชีพอย่างสมเหตุสมผล

**Changes in the epidemiology of respiratory syncytial virus infection
in children before and after the COVID-19 pandemic at Klang Hospital, Bangkok**

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Abstract

Background: Respiratory Syncytial Virus (RSV) remains a leading cause of pediatric lower respiratory tract infections (LRTIs) worldwide. The COVID-19 pandemic has substantially altered the epidemiology of RSV in many regions.

Objective: To evaluate temporal trends, clinical characteristics, and disease severity of pediatric RSV infections before and after the COVID-19 pandemic in Bangkok, Thailand.

Methods: We conducted a retrospective study using electronic health records of children younger than 15 years old diagnosed with RSV infection at Klang Hospital from January 2018 to December 2023. Demographic and clinical characteristics, oxygen therapy, hospital length of stay (LOS), treatment costs, and antibiotic prescribing patterns were compared between the pre-pandemic (2018-2020) and post-pandemic (2021-2023) periods. Statistical analyses were performed using the Mann-Whitney U test and chi-square test.

Results: A total of 137 pediatric RSV cases were identified. Number of RSV cases declined to zero in 2021 and subsequently rebounded during 2022-2023. The median age of affected children increased significantly from 12 months in the pre-pandemic period to 18 months in the post-pandemic period (p value 0.042). No significant differences were found in oxygen therapy requirements, LOS, or treatment costs between the two periods. The proportion of severe cases requiring advanced respiratory support showed a numerical increase in the post-pandemic period (19.1% vs. 5.8%). Antibiotic prescribing decreased significantly after the pandemic (26.5% vs. 50.7%, p value < 0.05).

Conclusion: The epidemiology of pediatric RSV pneumonia in Bangkok changed substantially following the COVID-19 pandemic, with an atypical resurgence and an older age at presentation in the post-pandemic period. However, major clinical outcomes remained largely unchanged, highlighting the need for continued RSV surveillance and effective preventive strategies to reduce the burden of RSV pneumonia in children.

Keywords: Respiratory syncytial virus, Pediatric lower respiratory tract infections, COVID-19 pandemic, Disease severity, Antimicrobial stewardship

Introduction

Respiratory Syncytial Virus (RSV) is a major respiratory pathogen that predominantly affects young children, particularly those under five years of age, as well as older adults and immunocompromised individuals. RSV circulates worldwide and causes annual epidemics, typically peaking during the winter months in temperate regions and lasting approximately four to five months.¹ In Thailand, RSV activity demonstrates a distinct seasonal pattern, with outbreaks occurring mainly during the rainy season and extending into early winter (July to January).

Certain pediatric populations are at increased risk for severe RSV infection, including infants—especially those younger than one year of age—preterm infants, children with underlying conditions such as chronic lung disease, congenital heart disease, and immunocompromising conditions.² RSV infection may present as either an upper respiratory tract infection (URTI) or a lower respiratory tract infection (LRTI). Common clinical manifestations include rhinorrhea, nasal congestion, sneezing, and cough, whereas hoarseness and laryngitis are less frequently observed.³ Importantly, RSV is recognized as one of the leading causes of LRTIs, particularly bronchiolitis and pneumonia, among children under five years of age.⁴ Nearly all children experience at least one RSV infection by two years of age.⁵

Although the exact pathophysiological mechanisms of RSV infection are not fully elucidated, current evidence suggests that direct viral cytopathic effects on the respiratory epithelium lead to epithelial necrosis and increased mucus production. These processes contribute to bronchiolar obstruction, resulting in air trapping, hyperinflation, and atelectasis.

In Thailand, national surveillance conducted by the Ministry of Public Health (MoPH) in collaboration with the Centers for Disease Control and Prevention (CDC) has identified RSV as the leading viral cause of LRTIs among hospitalized children, accounting for 19.5% of cases, followed by influenza virus at 8.2%.⁶ Management of RSV infection remains largely supportive, with prevention relying primarily on standard infection control measures, including proper hand hygiene and patient isolation.⁷ In infants younger than six months, maternally derived antibodies—particularly those acquired through breastfeeding—may provide partial protection against RSV infection.

Passive immunization with the monoclonal antibody palivizumab is recommended for selected high-risk pediatric populations to prevent severe RSV disease and associated mortality.⁸ More recently, the long-acting monoclonal antibody nirsevimab has been developed to provide season-long protection and was

approved for use in the United States in July 2023.⁹⁻¹¹ In addition, a maternal RSV vaccine—the bivalent prefusion F protein vaccine (Abrysvo)—was approved in 2023 for use during pregnancy, enabling transplacental transfer of RSV-specific antibodies and providing passive protection to infants during the first six months of life. Ongoing advances in longer-acting monoclonal antibodies and vaccine development are expected to further strengthen RSV prevention strategies in pediatric populations.

The COVID-19 pandemic has substantially altered the epidemiology of respiratory infections, including RSV.^{12,13} Public health and social measures (PHSMs) implemented during the pandemic led to a marked reduction in RSV circulation. However, following the initial pandemic period, atypical RSV resurgences have been observed globally.¹⁴ Reduced viral exposure during the pandemic may have resulted in an expanded pool of immunologically naïve children, increasing susceptibility to infection in younger age groups.^{15,16}

Objective

This study aimed to evaluate changes in epidemiological trends and clinical severity of RSV infection in children by comparing the pre- and post-COVID-19 pandemic periods.

Methods

This retrospective study was conducted using electronic health records from Klang Hospital, a tertiary care center in Bangkok, Thailand. The study population included pediatric patients presenting with respiratory symptoms who underwent rapid diagnostic testing for respiratory syncytial virus (RSV) and human metapneumovirus (hMPV) using the Quick Chaser[®] RSV test kit. Data were collected over a six-year period from January 1, 2018, to December 31, 2023. The study period was divided into two phases: the pre-COVID-19 era (2018-2020) and the post-COVID-19 era (2021-2023).

To evaluate post-infection respiratory outcomes, caregivers were interviewed by telephone regarding recurrent wheezing, a clinical manifestation of airway hyperresponsiveness (AHR). Additional data included bronchodilator use during healthcare visits, hospitalizations due to physician-diagnosed dyspnea, and subsequent physician-diagnosed asthma following RSV infection. These outcomes were assessed primarily within the first year after the initial infection.

The inclusion criteria were as follows: (1) children aged < 15 years; and (2) laboratory-confirmed RSV infection with clinical features consistent with upper and/or lower respiratory tract infection. Eligible cases were identified from inpatient and outpatient medical records using the International Classification of Diseases, Tenth Revision (ICD-10) code J12.1 (RSV pneumonia). In addition, patients with laboratory-confirmed RSV infection and the following clinical diagnoses were included J21.8 (acute bronchiolitis due to other specific organisms), J20.9 (acute pharyngitis, unspecified), and J00 (acute nasopharyngitis). Presenting symptoms at initial evaluation included fever, cough, rhinorrhea, nasal congestion, sore throat, conjunctival injection, tachypnea, cyanosis, apnea, nausea, vomiting, diarrhea, decreased appetite, and seizures.

Data collection and statistical analysis

Data collected for analysis included patient demographics (age and sex), underlying medical conditions, clinical manifestations at presentation, laboratory-confirmed RSV infection, requirement for oxygen therapy, length of hospital stay, treatment costs, and the development of airway hyperresponsiveness within one year following infection. Demographic characteristics and disease severity were compared between the pre- and post-COVID-19 periods. Patients with negative RSV test results or identified alternative respiratory pathogens were excluded.

Data distribution was assessed using the Kolmogorov-Smirnov test and was found to be non-normal (p value < 0.05). Accordingly, nonparametric methods were applied. Continuous variables were compared using the Mann-Whitney U test, and categorical variables were analyzed using the chi-square test. A p value < 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA).

Ethical approval

The study protocol was reviewed and approved by the Bangkok Metropolitan Administration Human Research Ethics Committee (BMAHREC) (Approval No. So29hc/67_EXP) and conducted in accordance with internationally accepted ethical principles for research involving human subjects.

Results

A total of 137 pediatric patients were diagnosed with RSV infection at Klang Hospital between January 2018 and December 2023. The number of cases was comparable between the pre-COVID-19 period (2018-2020; $n = 69$), and the post-pandemic period (2021-2023; $n = 68$). Marked year-to-year variation was observed, with a peak in 2018 ($n = 43$), followed by a decline in 2019 ($n = 12$) and 2020 ($n = 14$). No cases were reported in 2021. RSV activity reemerged in 2022 ($n = 28$) and increased further in 2023 ($n = 40$). Temporal trends are shown in Figure 1, and baseline characteristics are summarized in Table 1.

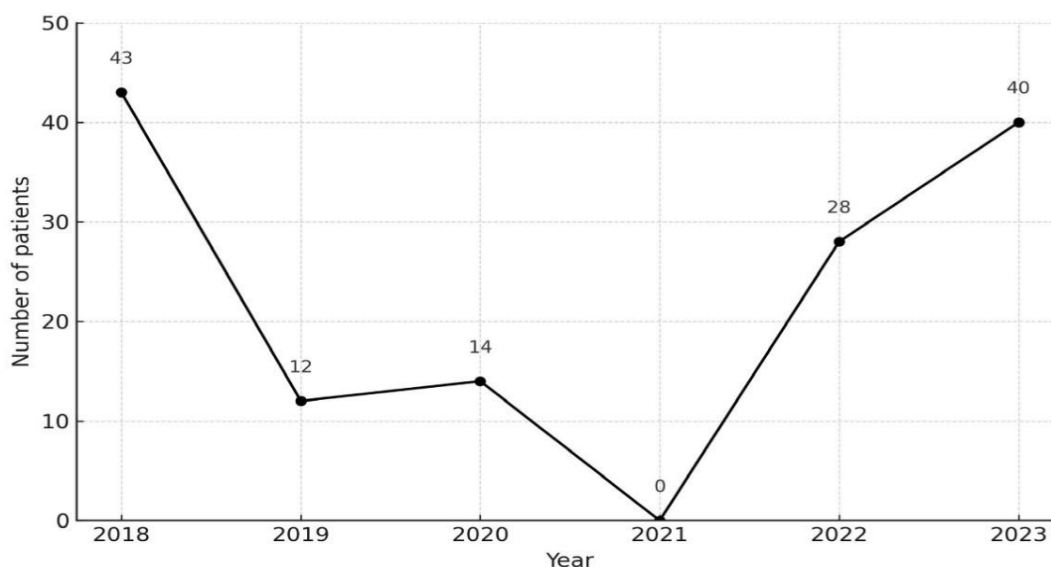


Figure 1 Annual number of pediatric patients with RSV infection from 2018 to 2023.

Underlying medical conditions included prematurity, asthma and congenital heart disease. Prematurity was the most common condition, occurring in 2, 2, 2, 3, and 4 patients in 2018, 2019, 2020, 2022 and 2023, respectively. Asthma was reported in 2 patients in 2018 and 1 patient each in 2022 and 2023, while congenital heart disease was reported in 1 patient in 2018.

The median age was 14 months (IQR 6.5-32.0). A significant increase in median age was observed in the post-pandemic period (18 months, IQR 6.3-43.5) compared with the pre-pandemic period (12 months, IQR 6.5-24.5; p value 0.042). Median length of stay (LOS) decreased from 5 to 4 days (p value 0.112), and median treatment costs declined from USD 115.9 to 102.2 (p value 0.35), although these differences were not statistically significant. No significant differences were observed in BMI, duration of oxygen therapy, LOS, or

total treatment costs between periods. Disease severity was generally comparable between periods, with no significant differences in clinical severity scores, oxygen requirements, or need for advanced respiratory support. However, a higher proportion of severe cases requiring high-flow nasal cannula (HFNC) or endotracheal intubation was observed in the post-pandemic period (19.1% vs. 5.8%). Among the 17 patients with severe disease, age distribution is shown in Figure 2. Most patients had no underlying medical conditions (70.6%), while prematurity and asthma were present in 23.5% and 5.9%, respectively.

Antibiotic use declined significantly from 50.7% in the pre-pandemic period to 26.5% in the post-pandemic period (p value < 0.05). Antibiotic prescribing was associated with disease severity, with higher use in patients requiring more intensive oxygen support. Among severe cases, antibiotic use increased from 8.9% in the pre-COVID-19 era to 27.3% in the post-COVID-19 era (p value 0.029).

Table 1. Characteristics of children with RSV infection before and after the COVID-19 pandemic

Characteristic	Pre-COVID-19 (n=69)	Post-COVID-19 (n=68)	p value
Age at time of diagnosis (months), median (IQR)	12.0 (6.5 to 24.5)	18.0 (6.3 to 43.5)	0.042
Underlying disease (%)	13 (18.8)	14 (20.6)	0.833
Length of hospital stay (days), median (IQR)	5.0 (3.0 to 6.5)	4.0 (3.0 to 6.0)	0.112
Cost of treatment (USD), median (IQR)	115.9 (73.5 to 159.8)	102.2 (63.1 to 158.2)	0.350
Need oxygen therapy (%)	45 (65.2)	44 (64.7)	1.000
Severe cases requiring HFNC and ET tube (%)	4 (5.8)	13 (19.1)	0.053
Antibiotic use (%)	35 (50.7)	18 (26.5)	0.005

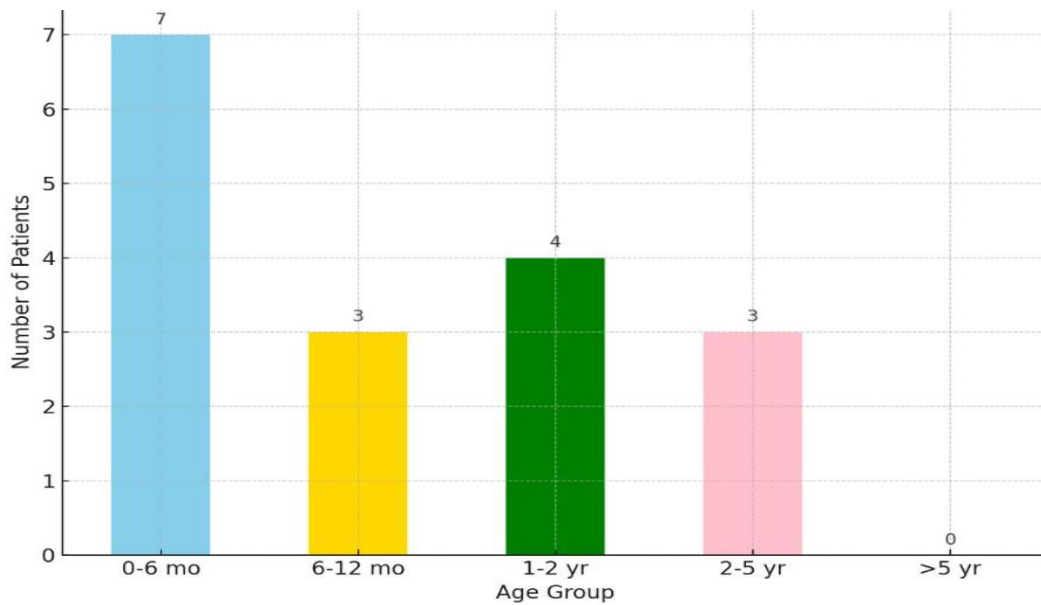


Figure 2 Age distribution of children with severe RSV infection requiring HFNC therapy or endotracheal

Pneumonia was the predominant diagnosis (121 cases, 88.3%), followed by acute bronchiolitis (8.0%), acute nasopharyngitis (2.9%), and acute pharyngitis (0.7%) (Figure 3). Annual distribution of RSV diagnoses in children were presented in Table 2. These findings highlighted the substantial burden of RSV-associated lower respiratory tract infections (LRTIs) and were consistent with global epidemiological patterns. Age-specific distribution were shown in Figure 4.

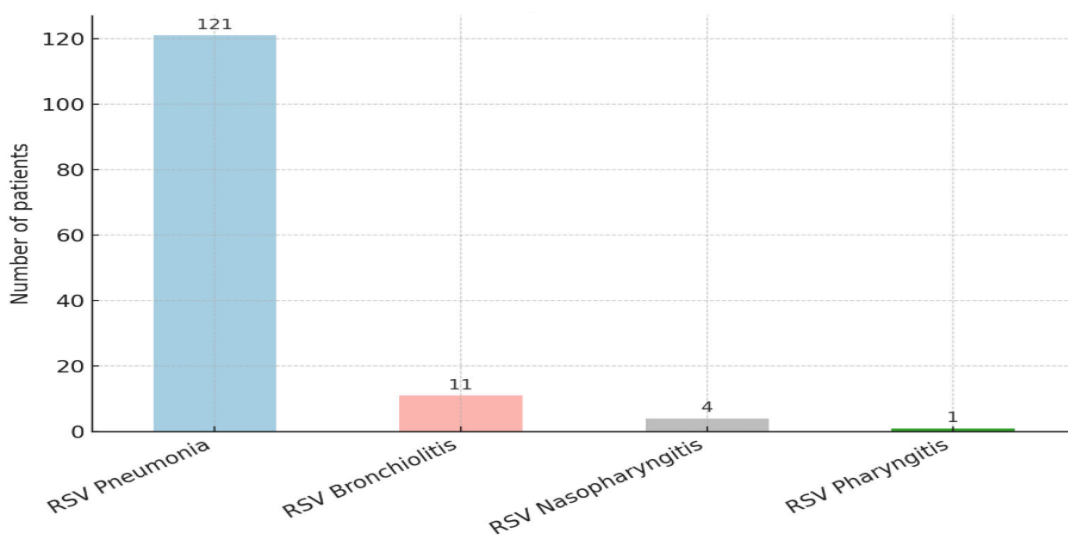
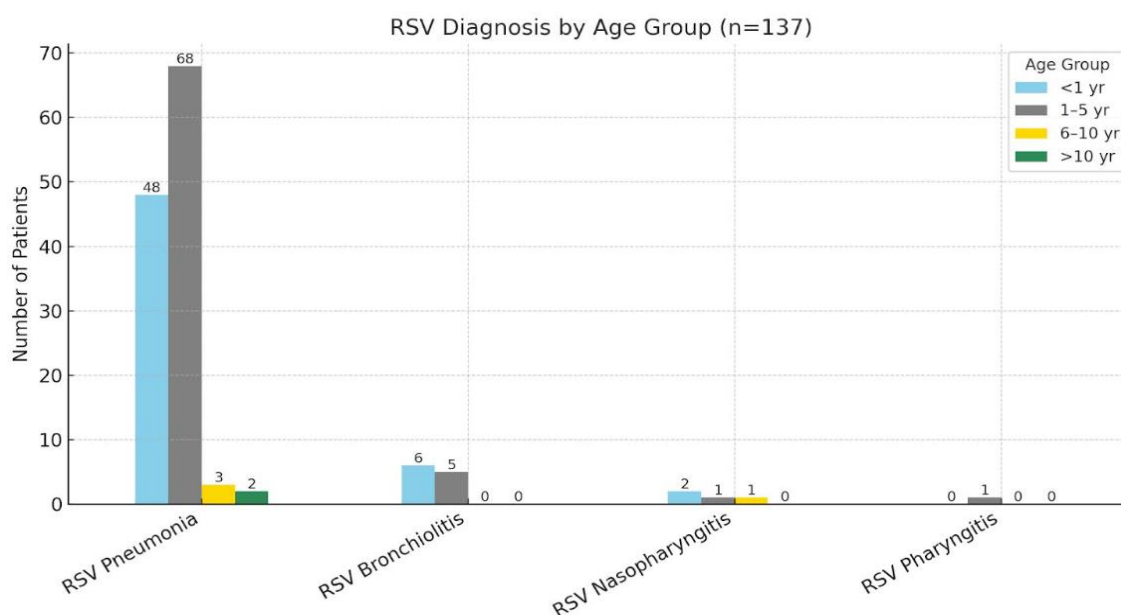


Figure 3 Distribution of RSV-related clinical diagnoses among 137 pediatric patients

Table 2. Annual distribution of RSV diagnoses in children

Year (A.D.)	RSV pneumonia	RSV bronchiolitis	RSV nasopharyngitis	RSV pharyngitis	Total cases
2018	39	4	0	0	43
2019	10	2	0	0	12
2020	13	1	0	0	14
2022	25	1	1	1	28
2023	34	3	3	0	40
Total	121	11	4	1	137

**Figure 4** Age-specific distribution of RSV-related diagnoses (n=137).

During 1-year follow-up, 117 patients (85.4%) completed assessment. The prevalence of airway hyperresponsiveness (AHR) is shown in Figure 5. AHR was similar between period (34.5% pre-COVID-19 vs. 33.9% post-COVID-19). However, the age distribution shifted, with a higher median age in the post-COVID-19 period (3.40 years, IQR 2.07-4.26) compared with the pre-COVID-19 period (0.85 years, IQR 0.61-1.86) (Figure 6). Analysis of comorbidities (Figure 7) demonstrated a shift in epidemiology: prior to COVID-19, AHR was more common among children with underlying conditions, whereas in the post-COVID-19 period it occurred more frequently in previously healthy children.

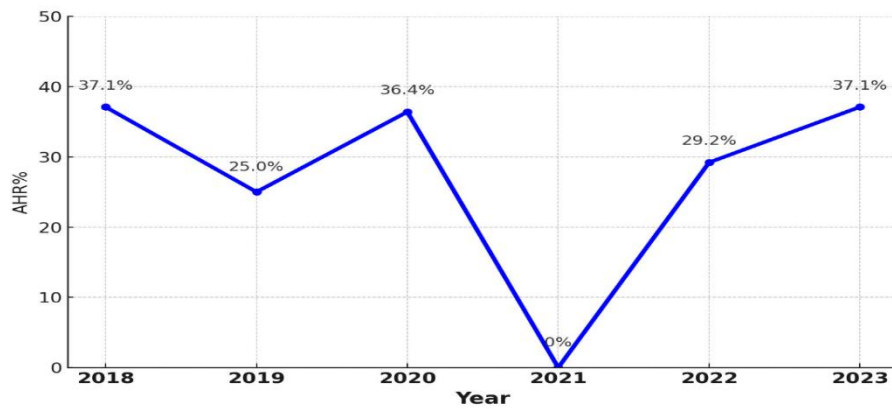


Figure 5 Annual proportion of post-RSV airway hyperresponsiveness, 2018-2023.

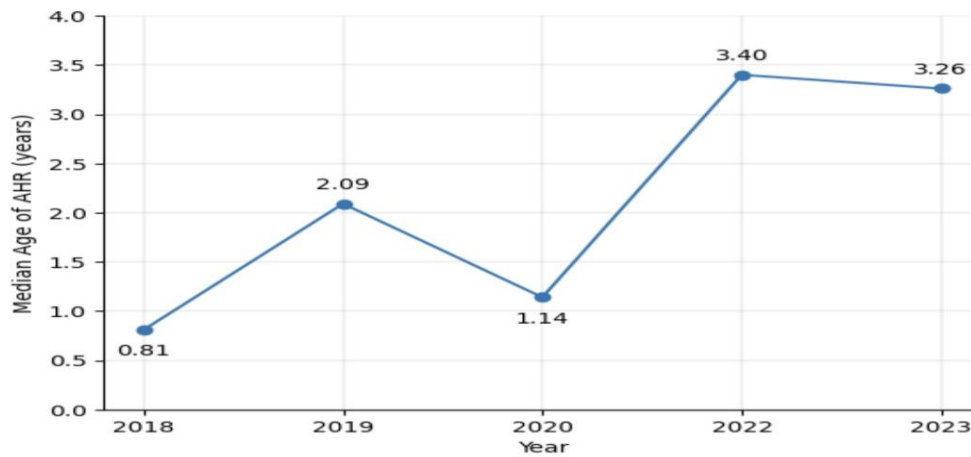


Figure 6 Median age of children who developed AHR, stratified by year, 2018-2023.

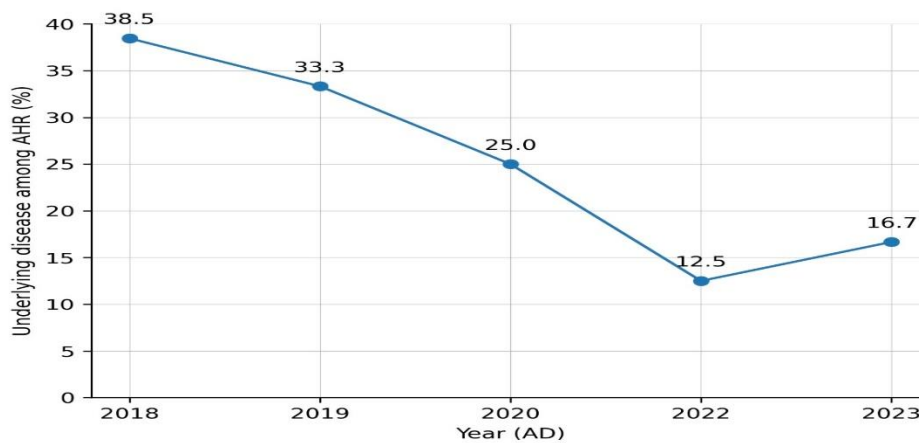


Figure 7 Proportion of children with underlying medical conditions among those who developed AHR, stratified by year, 2018-2023. (n = 10)

Among children with AHR, underlying conditions during the pre-COVID-19 era included prematurity (n=3), asthma (n=2), and congenital heart disease (n=1), whereas those during the post-COVID-19 era included prematurity (n=1) and asthma (n=2). As this was a retrospective study, some follow-up information was unavailable, potentially resulting in incomplete data on underlying conditions.

Discussion

This study demonstrated a marked shift in the epidemiology of pediatric RSV infection in Bangkok following the COVID-19 pandemic. RSV activity was profoundly suppressed during periods of stringent public health interventions, with complete absence of detected cases in 2021, followed by a pronounced and atypical resurgence in 2022-2023. This pattern paralleled observations from Australia and South Africa^{17,18}, underscoring a global disruption and subsequent re-emergence of RSV circulation.

The temporal changes in RSV incidence correspond closely with the implementation of non-pharmaceutical interventions (NPIs), including universal masking, physical distancing, school closures, and enhanced hygiene practices. This epidemiologic pattern aligned with global observations and highlighted the close interplay between public health measures and the transmission dynamics of pediatric respiratory pathogens.^{8,14,19-23} The absence of reported RSV cases in 2021 underscored the effectiveness of pandemic-related public health interventions in suppressing viral transmission. Following the gradual relaxation of NPIs, RSV activity rebounded significantly in 2022 and 2023, consistent with observations from Australia, South Africa, and multiple regions across Europe.^{4,8,14,23-27}

The resurgence of RSV likely reflected the phenomenon of "immunity debt" whereby reduced viral exposure during the pandemic led to increased susceptibility in young children.⁸ In our cohort, the post-pandemic period showed a shift in age distribution, with the median age increasing to 18 months, aligning with international reports, in which median ages ranged from 6 to 19.6 months.^{8,14,22,23,27-30} This shift was plausibly due to delayed primary infection resulting from reduced early-life exposure.

Despite these epidemiologic changes, overall disease severity—assessed by length of hospital stay, treatment cost, oxygen requirement, and need for advanced respiratory support (HFNC or endotracheal intubation)—did not differ significantly between pre- and post-pandemic periods. These findings were consistent with prior studies showing no overall increase in RSV severity after the pandemic.^{22,23,25,31-35}

However, the absolute number of severe RSV pneumonia cases increased, which might reflect a larger susceptible population rather than increased viral virulence.

A notable finding was the reduction in antibiotic use during the post-pandemic period. This trend was consistent with that reported in Jordan.³⁶ Several factors might explain this decline among children with RSV infection. First, improved diagnostic capacity, particularly the widespread use of multiplex PCR, enhanced the ability to distinguish viral from bacterial infections, reducing empirical antibiotic use. Second, antimicrobial stewardship efforts were strengthened during the pandemic and appeared to have been sustained. Third, NPIs likely reduced bacterial co-infections, including those caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*.

Finally, the expansion of telemedicine and structured triage systems might have promoted adherence to evidence-based prescribing practices. Nevertheless, in severe RSV pneumonia cases requiring oxygen therapy, clinicians might still initiate empirical antibiotics due to concern for bacterial co-infection, especially in the presence of non-specific radiographic findings or elevated inflammatory markers.

The prevalence of airway hyperresponsiveness (AHR) remained similar before and after the pandemic, indicating no significant impact of COVID-19 on the overall risk of post RSV AHR. Post-pandemic AHR tended to occur in older children and was more common among those without pre-existing comorbidities. This may reflect delayed antigen exposure, altered immune maturation, or changes in RSV transmission dynamics. Although the overall burden of AHR did not increase, its changing demographic patterns had important clinical implications. Pediatricians might increasingly encounter AHR in older, previously healthy children, highlighting the need for continued surveillance and long-term follow-up.

Overall, these findings emphasized the importance of sustained RSV surveillance and adaptive preparedness strategies. The post-pandemic resurgence of RSV in Bangkok highlighted the vulnerability of pediatric populations during periods of rapid change in public health measures and underscored the need for flexible approaches to mitigate future outbreaks.

Conclusion

Respiratory Syncytial Virus (RSV) remained an important cause of pneumonia and respiratory morbidity in young children. In Bangkok, the epidemiology of pediatric RSV pneumonia changed substantially following the COVID-19 pandemic, with a marked decline in cases during periods of stringent

public health interventions followed by an atypical resurgence after these measures were relaxed. Children with RSV pneumonia in the post-pandemic period were older at presentation than those in pre-pandemic period. Despite this epidemiologic shift, key clinical outcomes including length of hospital stay, treatment costs, and the need for supplemental oxygen or advanced respiratory support remained largely unchanged.

These findings highlighted the importance of sustained surveillance of RSV pneumonia to detect changes in disease activity and seasonality and to support timely healthcare preparedness. Prevention strategies, particularly immunoprophylaxis with monoclonal antibodies for infants and young children at increased risk of severe RSV disease, remained important. Continued implementation of effective RSV prevention measures might help reduce the burden of RSV pneumonia in children.

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Limitations

This study had several limitations. First, its retrospective, single-center design relied primarily on medical records and, where applicable, parental telephone interviews. Consequently, some clinical information, underlying conditions, and follow-up data might have been incomplete or subject to recall bias. Second, RSV testing was performed according to clinical practice and physician judgment rather than a standardized population-based testing protocol. Children with more severe respiratory symptoms or lower respiratory tract involvement might therefore have been more likely to undergo laboratory testing, resulting in potential selection bias and an overrepresentation of clinically significant RSV disease, including bronchiolitis and pneumonia.

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