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Pediatric respiratory admissions and related viral infections during the COVID-19 pandemic

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Abstract

Introduction: The COVID-19 pandemic has affected the incidence of respiratory viral infections. Our aim was to assess changes in pediatric admissions due to respiratory diseases and associated respiratory viral infections.

Methods: An observational study including all respiratory admissions to the pediatric departments from January 2015 to August 2021. We compared respiratory admission percentage, respiratory viral panel results and clinical characteristics of these admissions between two study periods, January 2015 to February 2020 (pre-COVID-19 era) and March 2020 to August 2021 (COVID-19 era).

Results: A total of 8774 respiratory admissions were included, 7157 pre-COVID-19 era and 1617 COVID-19 era. Relative to all pediatric admissions, there was a 17% decrease in respiratory admission percentage during the COVID-19 era ($p < 0.001$) and a 31% and 22% decreased in the admission percentages due to bronchiolitis ($p < 0.001$) and pneumonia ($p < 0.001$), respectively. However, admission percentages for asthma, wheezing illness, complicated pneumonia, and stridor remained the same. There was a significant decrease in the detection of a respiratory viral pathogen associated with these respiratory admissions ($p < 0.001$). This was related to a significant decrease in the detection of respiratory syncytial virus (RSV) (37% vs. 27%, $p < 0.001$) and influenza (5% vs. 0.3%, $p < 0.001$), but not other respiratory viruses. An alteration in the circulation pattern of most respiratory viruses, was observed.

Conclusions: During the COVID-19 pandemic, a decrease in the prevalence of RSV and influenza was associated with a significant decrease in admissions for bronchiolitis and pediatric pneumonia. This may allow us to estimate the significance of preventive measures for RSV and influenza on pediatric respiratory admissions.

KEYWORDS

asthma, influenza, pneumonia, RSV, wheezing

Abbreviations: HMPV, human metapneumovirus; LOS, length of stay; PCR, polymerase chain reaction; PICU, pediatric intensive care unit; RSV, respiratory syncytial virus; URTI, upper respiratory tract infection.

1 | INTRODUCTION

In 2020, the novel virus SARS-CoV-2 began to rapidly spread, resulting in a worldwide pandemic. Public health measures were imposed to prevent the viral spread. In Israel, these measures included social distancing, suspension of workplaces and schools, duty of mask protection, gathering restrictions, and travel limitations.

Although these precautions aimed to decrease the spread of SARS-CoV-2, data from several studies show that several respiratory viruses were also affected.

Multiple studies reported a global decline in the prevalence of respiratory syncytial virus (RSV) and influenza infections during the early months of the pandemic (March 2020 to early 2021).[1–3] Later, in the spring of 2021, RSV re-emerged, with an out of season rise in prevalence. Influenza virus did not reappear during winter and spring of 2021[4–6] despite the rise in RSV detection. The prevalence of rhinovirus was reported to increase during the pandemic[7,8] and a study from Australia described a significant decline in the detection of parainfluenza and human metapneumovirus (HMPV), but not adenovirus.[9]

These changes in the respiratory viruses' circulation patterns, were associated with a reduction in the admission rates for pediatric respiratory but also nonrespiratory diseases. There was a global decline in admissions for bronchiolitis during the pandemic,[10] and the usual winter bronchiolitis infection peak was not evident in 2020.[11] Studies also show a decrease in admission for croup, upper respiratory tract infections (URTIs), pneumonia,[12] exacerbations in asthma patients,[13] and wheezing.[14] Furthermore, a decrease in respiratory infections requiring admission to the pediatric intensive care unit (PICU) was also described.[15]

The aim of this study was to perform a comprehensive assessment of pediatric respiratory admissions to the Hadassah Hebrew University Medical center, Jerusalem, Israel, and associated respiratory viral infections during the pandemic.

2 | METHODS

2.1 | Study design

After institutional review board approval (HMO-0003-21), we conducted an observational study evaluating pediatric respiratory admissions in the two campuses of Hadassah-Hebrew University Medical Center, informed consent was waived due to the retrospective nature of the study. Included were all admissions in children up to 18 years of age hospitalized between January 2015 to August 2021, with a respiratory illness as the cause for their admission. Differences in respiratory admissions and respiratory viral panel polymerase chain reaction (PCR) results between the pre-COVID-19 era (January 2015 to February 2020) and the COVID-19 era (March 2020 to August 2021) were evaluated.

A respiratory illness was defined according to the following primary diagnosis as specified in the discharge summary: URTI, laryngotracheobronchitis, stridor, wheezing, bronchiolitis, pneumonia, pneumonia with pleural effusion (complicated pneumonia), and asthma with asthma exacerbation. No children were excluded from the study.

Admissions due to acute gastroenteritis and foreign body aspirations were also evaluated to assess also changes in nonrespiratory communicable diseases and noncommunicable respiratory diseases, respectively.

2.2 | Data extraction

Data were collected using an institutional patient records data retrieval engine (Hayadata, https://www.hadassah-clinicaltrials.org.il/en/hayadata-hadassah-data-research-unit/).

For all included cases, the following data were retrieved from electronic medical records: demographic data, hospital length of stay (LOS), admission to the PICU, diagnosis at admission and respiratory viral panel PCR results. The respiratory viral panel included the detection of adenovirus, influenza A, influenza B, parainfluenza 1,2,3, HMPV, and RSV.

2.3 | Evaluated outcomes

The main outcome measures evaluated in the study were the admission percentages for respiratory illnesses and associated PCR respiratory viral panel results. Percentages were calculated per overall admission numbers to control for a decreased seek for medical care, observed during the COVID-19 pandemic. Specific respiratory admission percentages and associated PCR respiratory viral panel results were additionally related to the total number of respiratory admissions, to assess for a change in the pattern of respiratory morbidity. Additional minor outcomes included hospital LOS, age at admission, admission to the PICU.

2.4 | Statistical analysis

Data were summarized by standard descriptive statistics. Values are presented as medians with interquartile range for continuous variables, and percentages for nominal variables. Differences in outcomes between pre-COVID-19 and COVID-19 eras were evaluated using the Mann–Whitney *U* test for continuous variables and Wald chi-square or Fisher exact tests for categorical variables, as appropriate. We graphically examined changes in weekly respiratory admissions from January 2015 to August 2021, controlled for the number of total admissions. Changes in the weekly patterns of respiratory viral PCR results during the COVID-19 era, were graphically evaluated using unobserved-components time series models, assessing differences between forecasted predictions and actual patterns. The statistical analysis was performed using STATA 15.1 (StataCorp LLC), $p < 0.05$ were considered significant.

3 | RESULTS

3.1 | Study population

During the study period (January 2015 to August 2021), there were a total of 43,467 pediatric admissions (respiratory and nonrespiratory). Of these admissions, 8774 respiratory admissions were included in the study, 7157 admitted during the pre-COVID-19 era and 1617 admitted during the COVID-19 era. During the COVID-19 pandemic, there was a 6.7% annual decrease in all pediatric admissions ($p < 0.001$) and an 20% annual decrease in respiratory pediatric admissions ($p < 0.001$) when compared to the pre-COVID-19 era (Figure 1). The clinical characteristics of these respiratory admissions are presented in Table 1. When evaluating only the first year of the COVID-19 era (March 2020 to February 2021) this marked decrease in admissions was even more pronounced with a 48% reduction in respiratory admissions when compared to the average number of pre-COVID-19 respiratory admissions (Table S1).

3.2 | Changes in the percentages and pattern of specific respiratory admissions

When evaluating changes in the admission of specific respiratory etiologies as a percentage of (all pediatric admissions), the COVID-19 pandemic era was associated with a reduction in admissions for bronchiolitis (6.8% vs. 4.72%, $p < 0.001$) and pneumonia (6.3% vs. 4.9%, $p < 0.001$), but not other respiratory etiologies (Table 2 and Figure 2). Asthma (3.9% vs. 3.8%), wheezing illness (2.4% vs. 2.6%), complicated pneumonia (2.0% vs. 2.0%), and stridor (1.7% vs. 1.8%). This decrease in the percentage of admissions for bronchiolitis and pneumonia was associated with a change in the distribution of respiratory admissions. Thus, during the COVID-19 era, several etiologies showed an increase in their admission percentage relative to all respiratory admissions but not relative to all pediatric admissions (Table 2). Of note, an increase in the relative admissions for asthma (from 18.7% pre-COVID-19 era to 22.0% COVID-19 era, $p = 0.002$) and a wheezing illness (from 11.4% pre-COVID-19 era to 15.02% COVID-19 era, $p < 0.001$), of all respiratory admissions.

When evaluating age stratified distribution of specific respiratory admissions (Tables S3 and S4) we demonstrate that the reduction in admissions for pneumonia were more prominently observed in school age children. With a decrease in admissions for pneumonia from 41.7% pre-COVID-19 to 29.5% during the COVID-19 era ($p = 0.019$), of all respiratory admissions (Table S3). During the COVID-19 era, there was also a change in the annual weekly pattern of respiratory admissions. The typical respiratory morbidity seasonal peak usually present in Weeks 45 to 5 (fall-winter) before the COVID-19 era, was missing in fall-winter 2020–2021 and a delayed peak during the spring of 2021 (Weeks 15–30) appeared (Figure 1). This change in the annual weekly pattern of respiratory admissions was associated with a significant change in the annual weekly pattern of admissions for bronchiolitis and pneumonia, but only minor differences in the annual weekly pattern of admissions for other respiratory diseases (Figure 2).

Despite this alteration in the annual weekly pattern of respiratory admissions during the COVID-19 era, there were no major differences in most clinical characteristics of specific respiratory admissions. Detailed clinical characteristics of specific respiratory admissions are provided in Table S2.

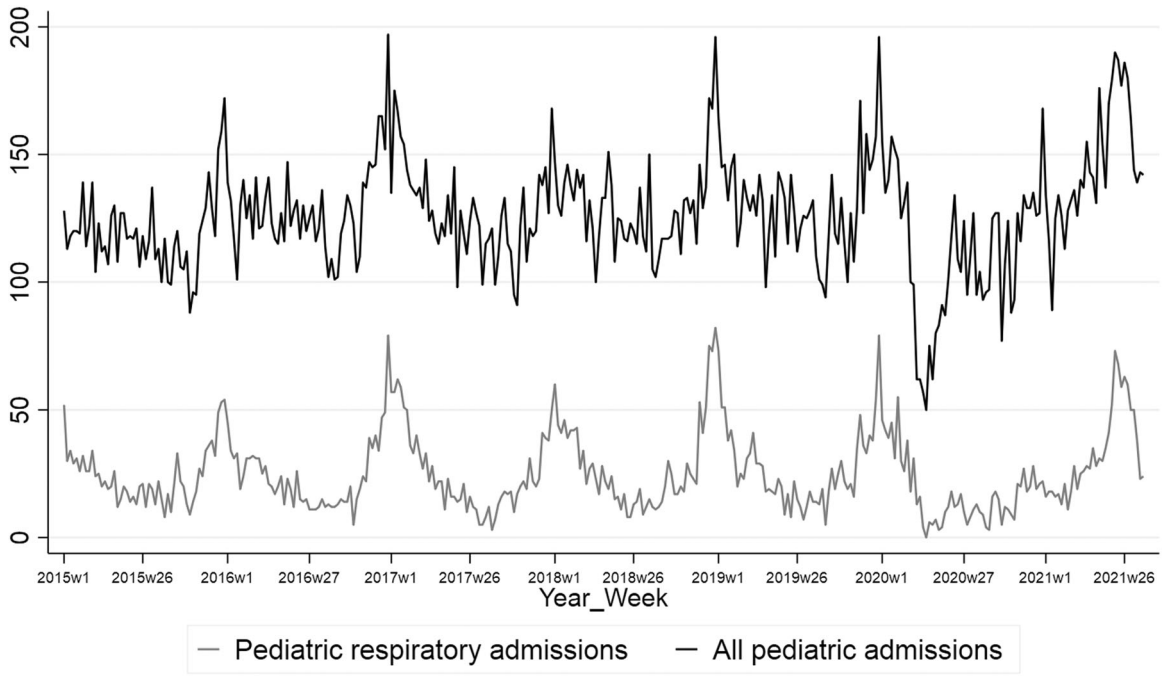

FIGURE 1 Weekly pediatric admissions and weekly pediatric respiratory admissions during the study period (January 2015 to August 2021).

TABLE 1 Characteristics of admissions before and during the COVID-19 pandemic.

	pre-COVID	COVID	*p* Value
All pediatric admissions	*n* = 34,204	*n* = 9263	
Average number of pediatric admissions[a], per year	6620.1	6175.3	<0.001
Average number of emergency departments visits[b], per year	33,788.9	30,749.5	<0.001
Pediatric respiratory admissions	**7157 (20.9)**	**1617 (17.4)**	<0.001
Average number of respiratory admissions, per year	1385.23	1108.8	<0.001
Age, months, median [IQR]	14.4 [6–40.8]	15.6 [7.2–39.6]	0.004
Sex, M (%)	4121 (57.6)	959 (59.3)	0.20
Duration of stay, days, median [IQR]	3 [2–4]	3 [2–4]	0.31
ICU admissions (%)	560 (7.8)	141 (8.7)	0.23

[a]Admissions refers to all admissions (respiratory and nonrespiratory) in the pediatric departments.

[b]ER visits refers to all visits (respiratory and nonrespiratory) in the pediatric emergency departments. pre-COVID is January 2015–February 2020, COVID is March 2020–August 2021.

TABLE 2 Distribution of specific respiratory diseases and PCR respiratory viral panel results relative to the number of all pediatric admissions and the number of respiratory pediatric admissions.

	pre-COVID	COVID		pre-COVID	COVID	
	All pediatric admissions			Pediatric respiratory admissions		
	n = 34,204	*n* = 9263	*p* Value	*n* = 7157	n = 1617	*p* Value
Bronchiolitis	2327 (6.8)	438 (4.7)	<0.001	2327 (32.5)	438 (27.1)	<0.001
Pneumonia	2143 (6.3)	452 (4.9)	<0.001	2143 (29.9)	452 (28.0)	0.11
Asthma	1335 (3.9)	356 (3.8)	0.79	1335 (18.6)	356 (22.0)	0.002
Stridor	590 (1.7)	166 (1.8)	0.66	590 (8.2)	166 (10.2)	0.009
Wheezing	815 (2.4)	243 (2.6)	0.18	815 (11.4)	243 (15.0)	<0.001
Foreign body aspiration	232 (0.7)	72 (0.7)	0.31	232 (3.2)	72 (4.4)	0.020
URTI	443 (1.3)	98 (1.1)	0.070	443 (6.2)	98 (6.0)	0.840
Gastroenteritis infection	386 (1.1)	98 (1.1)	0.560	–	–	
Evaluated by a viral respiratory PCR panel	**6052 (17.7)**	**1270 (13.7)**	<0.001	**3591 (50.2)**	**753 (46.6)**	0.125
Viral etiology detected	2863 (47.3)	458 (36.1)	<0.001	1989 (55.4)	344 (45.7)	0.006
RSV	1463 (24.2)	219 (17.2)	<0.001	1332 (37.1)	201 (26.6)	<0.001
Influenza	318 (5.2)	4 (0.3)	<0.001	179 (5.0)	2 (0.2)	<0.001
HMPV	283 (4.7)	74 (5.8)	0.030	226 (6.3)	56 (7.4)	0.280
Adenovirus	572 (9.4)	119 (9.4)	0.700	294 (8.2)	57 (7.6)	0.602
Parainfluenza	188 (3.1)	72 (5.7)	0.001	65 (1.8)	11 (1.5)	0.330

Note: Data presented as *n* (%). Pre-COVID-19 is January 2015–February 2020, COVID-19 is March 2020– August 2021.

Abbreviations: HMPV, human metapneumovirus; PCR, polymerase chain reaction; RSV, respiratory syncytial virus; URTI, upper respiratory tract infection.

3.3 | Respiratory viral PCR panel results and associated respiratory morbidity

During the study period, a respiratory viral PCR panel was performed in 49.5% (4344) of the evaluated respiratory admissions (50.2% of pre-COVID-19 and 46.6% of COVID-19 respiratory admissions; $p = 0.125$). The detection of a viral respiratory pathogen decreased from 55% of evaluated respiratory admissions during the pre-COVID-19 era to 45% of evaluated respiratory admissions during the COVID-19 era ($p = 0.006$). This decrease in the detection of a viral respiratory pathogen was due to a 30% decrease in hospitalizations associated with RSV ($p < 0.001$) and a 95% decrease in

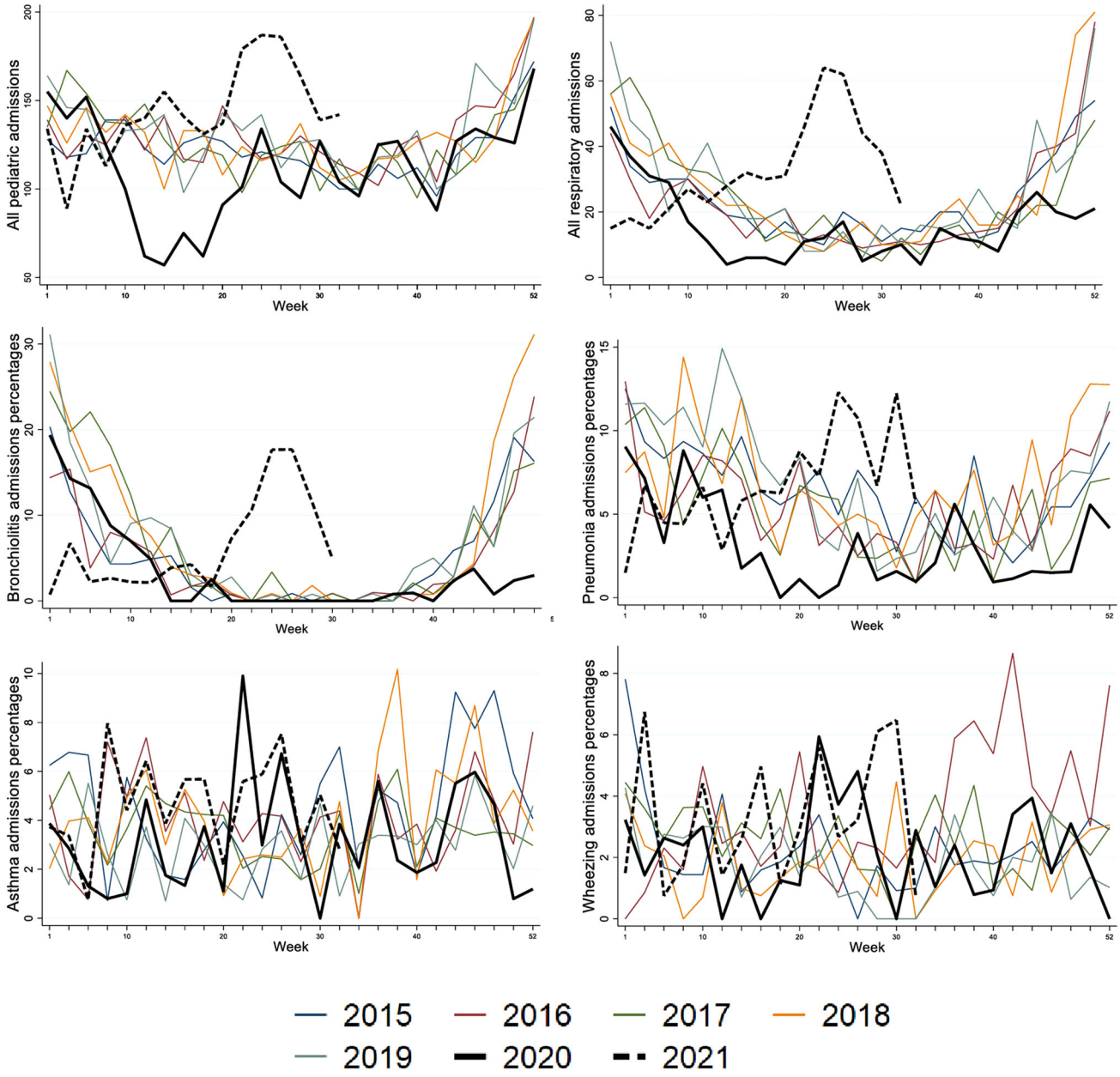

FIGURE 2 Weekly admission rate for specific pediatric respiratory diseases (bronchiolitis, pneumonia, asthma, and wheezing illness) per total number of pediatric admissions, according to calendar year.

hospitalizations associated with influenza viruses ($p < 0.001$). The detection of other respiratory viruses (HMPV, parainfluenza viruses, and adenovirus) associated with both respiratory admissions and all pediatric admissions did not significantly decrease during the COVID-19 era (Table 2). Moreover, the detection of HMPV and parainfluenza possibly even increased during the COVID-19 era (Table 2), especially in children younger than 6 years of age (Table S4). The decrease in the detection of RSV and influenza was associated with a 31% decrease in admission for bronchiolitis and a 22% decrease in admissions for pneumonia.

Specifically, we observed a significant decrease in bronchiolitis cases attributed to RSV (from 60.65% in pre- COVID-19 era to 51.6% during the COVID-19 era, $p = 0.002$) and influenza (from 3.8% to 0%, $p < 0.001$) and a significant decrease in influenza-related admissions for pneumonia (from 6.99% pre-COVID-19 era to 0 cases during the COVID-19 era, $p < 0.001$). The rate of detection of respiratory viruses associated with other specific respiratory etiologies did not significantly change during the COVID-19 era (Table 3).

An alteration in the circulation pattern of respiratory viruses during the COVID-19 era was observed, with marked differences between the different respiratory viruses. During the COVID-19 era, influenza viruses completely disappeared. The peak in RSV infection was delayed from the 1st week of 2021 to the 25th week; HMPV had an attenuated peak in 2020 and peaked normally in 2021;

TABLE 3 PCR respiratory viral panel results detected in specific respiratory diseases compared between pre-COVID-19 and COVID-19 eras.

n (%)	Bronchiolitis			Pneumonia			Asthma			Stridor			Wheezing			URTI		
	pre-COVID n = 1949	COVID n = 337	p Value	pre-COVID n = 1030	COVID n = 209	p Value	pre-COVID n = 472	COVID n = 126	p Value	pre-COVID n = 186	COVID n = 56	p Value	pre-COVID n = 404	COVID n = 126	p Value	pre-COVID n = 190	COVID n = 41	p Value
Viral infections	1480 (76.0)	219 (65.8)	<0.001	423 (41.1)	82 (41)	0.98	144 (30.5)	28 (24.1)	0.17	41 (22.0)	11 (23.4)	0.84	130 (32.2)	33 (26.2)	0.20	58 (30.5)	0.29	0.03
RSV	1182 (60.6)	177 (51.6)	0.002	215 (20.8)	43 (19.5)	0.65	74 (15.7)	9 (7.03)	0.012	13 (7.0)	3 (5.4)	0.66	85 (21.0)	22 (17.5)	0.38	28 (14.7)	2 (4.9)	0.08
Influenza	74 (3.8)	0 (0)	<0.001	72 (7.0)	0 (0)	<0.001	26 (5.5)	0 (0)	0.007	9 (4.8)	0 (0)	0.09	18 (4.5)	0 (0)	0.02	10 (5.3)	0 (0)	0.13
HMPV	176 (9.0)	31 (9.2)	0.92	72 (7.0)	27 (12.9)	0.004	14 (4.43)	5 (6.49)	0.48	4 (2.1)	0 (0)	0.27	19 (4.7)	3 (2.4)	0.25	5 (2.6)	0 (0)	0.29
Adenovirus	169 (8.7)	30 (8.9)	0.21	95 (9.2)	17 (8.1)	0.61	37 (7.8)	7 (5.6)	0.38	12 (6.5)	2 (3.7)	0.44	32 (7.9)	7 (5.6)	0.37	16 (8.4)	4 (9.8)	0.78
Parainfluenza	16 (0.8)	1 (0.3)	0.30	31 (3.0)	4 (1.9)	0.38	6 (1.3)	3 (2.4)	0.36	11 (5.9)	7 (13.2)	0.07	9 (2.2)	3 (2.4)	0.91	5 (2.6)	0 (0)	0.29

Note: Pre-COVID-19 is January 2015–February 2020, COVID-19 is March 2020–August 2021.

Abbreviations: HMPV, human metapneumovirus; PCR, polymerase chain reaction; RSV, respiratory syncytial virus; URTI, upper respiratory tract infection.

parainfluenza viruses did not peak during 2020 with uncharacteristic relative peak in the 1st week of 2021; adenovirus circulation pattern was only minimally affected (Figure 3).

4 | DISCUSSION

In this observational study, we present comprehensive data regarding respiratory admissions and the associated respiratory viral infections in pediatric patients during the COVID-19 pandemic. Our study shows a significant decrease, during the pandemic, in the admissions for and annual pattern of bronchiolitis and pneumonia relative to all pediatric admissions, and a change distribution of respiratory admissions. This change was associated with a decrease in the prevalence of RSV and influenza, and varying changes in the annual circulation pattern of most viral respiratory infections. To our knowledge, this is the first study to evaluate the association between respiratory viruses and respiratory morbidity during the COVID-19 era.

Our results of an overall decrease in pediatric admissions, and a decrease in pediatric respiratory admission and the change in the annual pattern of admissions are consistent with numerous previous worldwide reports.[12,16,17]

These reports show a decrease in admissions for croup, viral wheeze, URTI, pneumonia, bronchiolitis, asthma, stridor, wheezing,[10–14,16–18] and as well as a decrease in emergency department visits for respiratory diseases during the COVID-19 pandemic.[19,20]

We similarly show a decrease in all pediatric respiratory admissions, as well as decrease in all pediatric admissions. However, when evaluating the decrease in respiratory admissions relative to all pediatric admissions, we demonstrate a decrease in admissions for bronchiolitis and pneumonia and not for other pediatric respiratory diseases. Previous studies describing the decrease in pediatric respiratory admissions,[10–14,16,17] did not evaluate the change in admissions relative to the overall decreased seek for medical attention (and overall reduction in all pediatric admissions) observed during the COVID-19 pandemic.[21,22] Our consideration for the change in respiratory admission relative to the overall reduction in seek for medical care allows a better estimation of the effect of social distancing on communicable pediatric respiratory diseases.

We show a specific effect on admissions for bronchiolitis in young children and pneumonia in school age children, but not other communicable respiratory diseases, causing a change in the relative distribution of respiratory admissions. We also show no reduction in the admission percentages of a nonrespiratory communicable disease, gastroenteritis, suggesting that the change in social behavior during the COVID-19 pandemic had a particular effect on specific respiratory infections.

Numerous reports have described a worldwide disappearance of RSV and influenza infections in the winter season of 2020–2021[3,23–29] and a late emergence of RSV in the spring of 2021.[4,30–32] Similarly, our study found a significant reduction in the detection of RSV and influenza during the COVID-19 era. We also observed that this reduction in RSV

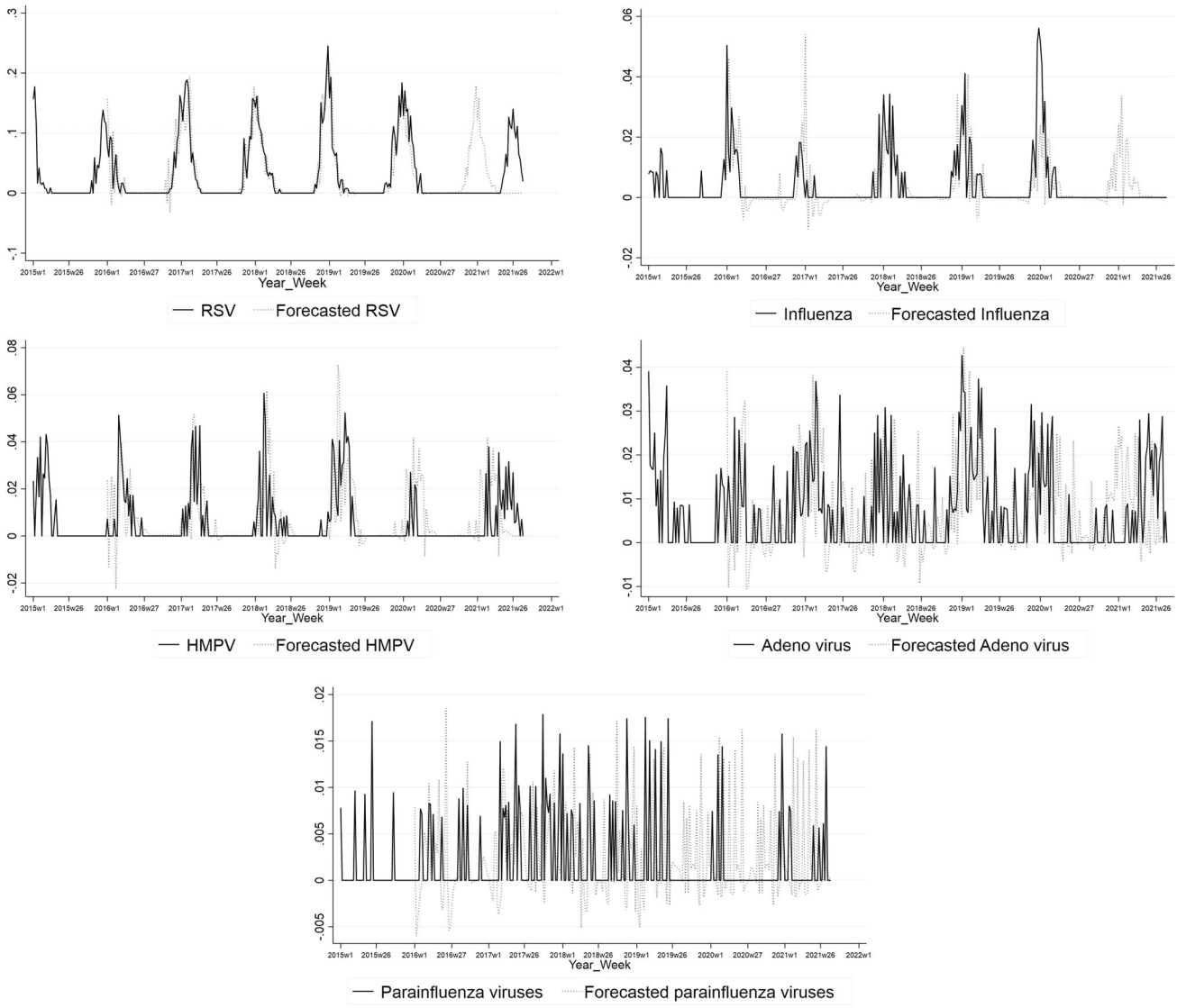

FIGURE 3 Respiratory viruses (RSV, influenza viruses, HMPV, adenovirus, and parainfluenza viruses) observed weekly prevalence and forecasted weekly prevalence, during the study period (January 2015–August 2021). Forecasts were computed using unobserved-components time series models (UCM procedure in STATA 15.1).

and influenza specifically influenced the observed decline in the relative admission percentages for bronchiolitis and pneumonia with no significant effect on other respiratory diseases such as asthma, croup, and acute wheezing illnesses.

Our results further show that respiratory viruses other than RSV and influenza, were not as affected by the COVID-19 pandemic. We show that the detection of adenovirus did not decrease during the pandemic, neither in association to all pediatric admissions nor specifically in relation to pediatric respiratory admissions, and that the detection of HMPV and parainfluenza infections increased relatively.

Reports regarding respiratory viruses other than RSV and influenza during the COVID-19 pandemic are scarce and show inconsistent results. A study from Israel describes that during the pandemic, adenovirus, rhinovirus, and parainfluenza infection activities did not change.[33] Another study from Finland shows that rhinovirus remained prevalent in near normal rates during the pandemic.[7] Moreover, regional studies from Korea and Austria show a reduction in HMPV during the pandemic.[24,34] However, a study from Australia showed a significant decline in parainfluenza and HMPV detection, but adenovirus remained prevalent and showed similar patterns to previous years.[9]

Thus, the COVID-19 pandemic and social distancing did not similarly affect all respiratory viruses. The persistence of adenovirus, HMPV, parainfluenza viruses and possibly also rhinovirus, in our study, may explain the observation of the unchanged occurrence of respiratory admissions for asthma, wheezing, and croup, which are known to be associated with these infections.[18,35–37]

Importantly, even though we did not observe a reduction in the overall detection of some respiratory viruses, we did notice a change

in their annual circulatory pattern, suggesting that the social distancing did influence the spread of these viruses.

Regardless, this unique situation encountered during the COVID-19 pandemic allowed us to assess the impact of measures to reduce the transmission of respiratory viruses, especially RSV and influenza, on child health at our center. These findings may be applicable globally. Novel vaccination strategies for RSV[38] may significantly influence pediatric respiratory admissions. The experience gained during the COVID-19 pandemic and the results of this and prior studies, may allow national healthcare systems to estimate the consequence of these strategies and better assess a cost–benefit effect. Specifically, we show that a 30% decrease in the prevalence of RSV and a 95% decrease in the prevalence of influenza viruses were associated with a 31% decrease in admission for bronchiolitis and a 22% decrease in admissions for pediatric pneumonia.

The major strength of this study lies in the inclusion of multiple admissions over a large period of time, and the available PCR results for multiple respiratory viruses, allowing comprehensive evaluation of the association between respiratory disease viral infection and the COVID-19 pandemic.

The main limitation of the study lies in its observational nature. Furthermore, rhinovirus which is the viral infection most frequently associated with asthma exacerbations and wheezing illnesses,[18,35,36] was not assessed in our study. However, a prior study in Israel showed that the prevalence of rhinovirus did not significantly decrease during the COVID-19 era,[33] suggesting its persistent impact on pediatric respiratory disease in our cohort.

5 | CONCLUSION

The unique social circumstances encountered during the COVID-19 pandemic triggered a significant change in the prevalence of RSV and influenza and affected the annual circulatory pattern of most respiratory viruses, significantly affecting pediatric respiratory admissions worldwide for both toddlers as well as school age children. This experience, may allow us to estimate the significance of preventive measures and vaccination programs for viral respiratory infections on global child health from infancy to late teenage years.

AUTHOR CONTRIBUTIONS

Dana Peer Moscovich: Writing—original draft; conceptualization; methodology; investigation. **Diana Averbuch**: Writing—review and editing; supervision; conceptualization. **Eitan Kerem**: Writing—review and editing; supervision. **Malena Cohen-Cymberknoh**: Writing—review and editing; supervision. **Yackov Berkun**: Writing—review and editing; supervision. **Rebecca Brooks**: Writing—review and editing; supervision. **Shimon Reiff**: Writing—review and editing; supervision. **Maskit Bar Meir**: Writing—review and editing; supervision. **Dana Wolf**: Writing—review and editing; supervision; conceptualization. **Oded Breuer**: Conceptualization; investigation; writing—original draft; writing—review and editing; visualization; methodology; validation; supervision; formal analysis.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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