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RESEARCH

Changes in seasonal respiratory viral infections among pediatric population around the COVID-19 pandemic; 2019–2023

Mashael Alzaydi[1] · Aeshah Alosaimi[2] · Atheer A. Alghamdi[1] · Israa Y. Bamogaddam[1] · Maryam A. Altassan[1] · Afnan Almazrua[2] · Sahar Althawadi[3] · Salem M. Alghamdi[1,2]

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Abstract

Purpose This study aims to describe the prevalence and the fluctuations of respiratory viral infections among the pediatric population in a tertiary care center during 2019–2023, parallel with the COVID-19 pandemic, and the specific preventative measures applied in the region during this time.

Methods In this observational study, we extracted all respiratory virus PCR tests collected from pediatric patients (< 15 years old) between January 2019 and March 2023. Data on the positivity rate and prevalence of 18 respiratory viruses were presented over the study period.

Results The lowest rate for the studied respiratory viruses was observed in 2020/2021 (during the COVID-19 pandemic), followed by a gradual increase in positive cases in the 2021/2022 season. Timing (seasonality) was altered during 2022/2023 with an early circulation of respiratory viruses in May-June followed by an early start of the usual respiratory viruses' season in September, leading to prolonged respiratory virus activity. Most respiratory viruses were circulating at unprecedented levels during the 2022/2023 season, with rhinovirus/enterovirus being the most commonly detected virus in all seasons. Other viruses that had atypical activity after the COVID-19 pandemic were influenza A(H3) virus, adenovirus, and parainfluenza 3 virus.

Conclusion Our study demonstrates the extended influence of the COVID-19 pandemic and its associated community restriction measures on the timing and distribution of other respiratory viruses. Continuous monitoring of changes in the circulation of respiratory viruses is crucial for the success of related public health measures such as vaccination distributions and epidemic preparedness.

Keywords COVID-19 · Respiratory viral infections · Pediatrics · Respiratory virus · RSV · Flu · Influenza

Introduction

In Saudi Arabia, the majority of acute respiratory tract infections in pediatrics are due to respiratory syncytial virus (RSV), mostly affecting children under 2 years of age. The first cases are usually detected in October, reaching a peak in January, and declining through May [1]. However, there is a lack of local data regarding the impact of the COVID-19 pandemic on respiratory viral infections in the country. A study conducted at Stamford Hospital in Connecticut compared the incidence of respiratory viral infections between the historical years 2016–2019 and the year 2020, which coincides with a high level of COVID-19 infections specifically from April to July. The study results showed a decrease in the percentage of influenza viruses from 10 to 1% during the COVID-19 pandemic [2].

✉ Aeshah Alosaimi
aalosaimi1@kfshrc.edu.sa

[1] Department of Pediatrics, King Faisal Specialist Hospital and Research Center, Riyadh, Kingdom of Saudi Arabia

[2] Infection Control and Hospital Epidemiology Department, King Faisal Specialist Hospital and Research Centre, P.O. Box 3354, Riyadh 11211, Kingdom of Saudi Arabia

[3] Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Center, Riyadh, Kingdom of Saudi Arabia

There have been many speculations about the effectiveness of different protective measures in limiting the spread of COVID-19 and other respiratory viral infections. Based on the literature, the incidence of influenza viruses in the northern hemisphere decreased to a new historically low level during the COVID-19 pandemic. A similar result was observed in three countries in the southern hemisphere (Australia, Chile, and South Africa) [3]. However, the previous studies have some limitations. The diagnostic detection methods used were direct fluorescent antibody (DFA), which is less sensitive to newly discovered viruses such as human metapneumovirus, human bocavirus, and human polyomavirus. This could be improved by using polymerase chain reaction (PCR) [1]. Also, the data were collected from 2013 to 2014 on adult patients, which may not have a similar reflection on the current epidemiology of respiratory viral infection in the pediatric population [1, 4, 5].

This study aims to identify the rate of respiratory viral infections before, during, and after the COVID-19 pandemic. Specifically, we aim to describe the distribution of circulating respiratory viruses and to identify the seasonality peak of each respiratory virus.

Materials and methods

This observational study was conducted at King Faisal Specialist Hospital and Research Center (KFSHRC) in Riyadh, Kingdom of Saudi Arabia. The study included pediatric patients (< 15 years old) who underwent respiratory virus testing between January 2019 and March 2023. Respiratory virus testing was performed based on physician order according to symptoms. All nasopharyngeal swabs were subjected to direct detection according to the testing method used in different time frames. These tests include:

Multiplex PCR respiratory

QIAstat-Dx Respiratory Panel from Qiagen was used in 2019 and then was upgraded to QIAstat-Dx Respiratory SARS-CoV-2 Panel in 2020 (**Rapid Multiplex PCR Respiratory**). It is a cartridge-based multiplex real-time PCR Syndromic approach to accurately detect and identify the pathogens most commonly associated with respiratory infections within 70 min. Testing was done according to manufacturer recommendations.

MERS and respiratory panel

The BioFire® Respiratory 2.1 panel (RP2.1) was used in 2019 and then was upgraded by adding SARS-2 virus in 2020. It is a syndromic approach to accurately detect and identify the pathogens most commonly associated with respiratory infections in 45 min utilizing film array technology on the BioFire® FilmArray® Torch Systems.

Pneumonia panel

The BioFire *Pneumonia Panel* utilizes syndromic *testing* for Pneumonia identifying 33 clinically relevant targets to diagnose patients in about an hour. It utilizes BioFire® FilmArray® Torch Systems.

Rapid flu, RSV, SARS-2

Used with GeneXpert following manufacturer recommendations.

More details on the targets of each method and the year it was used during the study period are displayed in Supplementary Fig. 1. Only the results of the respiratory viruses were analyzed, excluding bacterial and atypical targets. The test was considered positive if any of the included 18 viruses came back positive. Positive results for the same virus within 30 days were considered one infection episode and counted once in the analysis.

Data on the total number of respiratory virus tests performed monthly from January 2019 to March 2023 were extracted to serve as the denominator for calculating the positivity rate. The number and percentage of positive results for the 18 respiratory viruses were also reported. Data is presented graphically using R software version 4.3.0.

Results

A total of 12,974 respiratory PCRs viruses were identified over 2019–2023. Amongst those, 480 tests were positive for the same virus within 30 days, so they were considered the same infection and excluded from the analysis. Around 55% (6897 tests) of the remaining sample showed positive results for respiratory viruses, as illustrated in Fig. 1.

Seasonality of respiratory viral infection

Figure 2 illustrates the overall seasonal pattern of respiratory viral infections among pediatric patients between 2019 and 2023. Before the COVID-19 pandemic, the usual respiratory viral infection season occurred in Saudi Arabia during the winter months (October to March) with a peak in December. This applies to the 2019–2020 season, which displayed an increase in respiratory virus cases starting in October, peaking at 268 cases in December 2019, and then declining in March 2020. At the beginning of the COVID-19 pandemic, there was a notable decrease in cases of respiratory viruses due to the precautionary measures implemented. As a result,

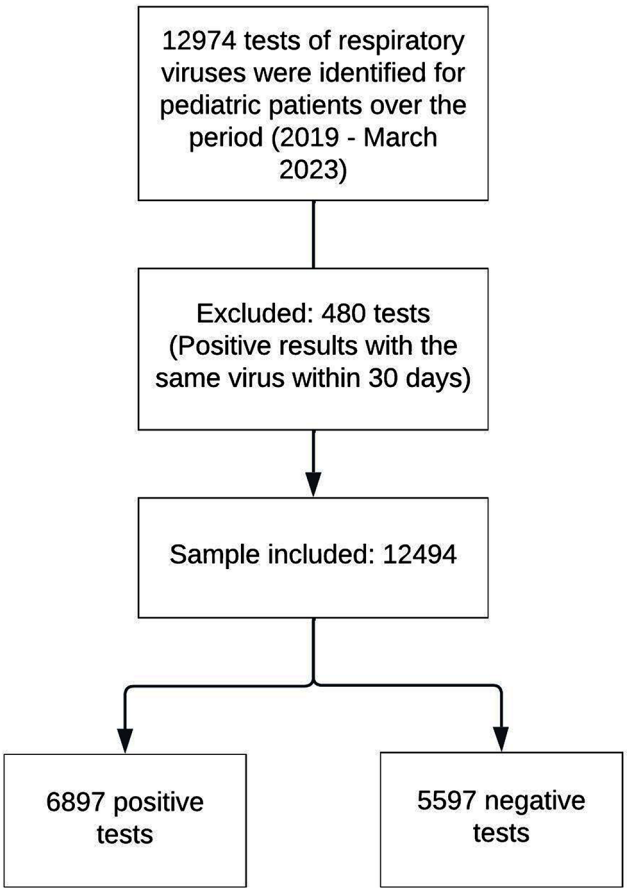

Fig. 1 Flowchart of total sample included in the study

the number of respiratory cases during 2020/2021 ranged between six and 86 cases/month, increasing gradually in the following year (2021/2022). The seasonality of the respiratory viral infection remained consistent in 2020/2021 and 2021/2022, maintaining its peak during December/January. However, in 2022/2023, there were marked changes in the circulation of respiratory viruses. There was an early activity during May and June, with around 226 and 344 cases/month, respectively. This activity decreased during July and August but resumed with an early start of respiratory viral infection in September, reaching an early peak during November, with a total of 455 cases. The circulation of respiratory viruses remained at high levels until the end date of the data collection period in March 2023, making this season the longest season of all years.

Positivity rate and prevalence of respiratory viruses

During 2019/2020, which was just before the COVID-19 pandemic, the total number of tests conducted ranged between 148 and 390 tests per month with an increase during the respiratory viral infection season (October – March). The peak in testing occurred in December with a positivity rate of around 70% (Fig. 3). Detection of respiratory viruses increased in the 2019/2020 winter season with predominant activity of rhinovirus/enterovirus followed by RSV and influenza A(H3) virus. At their peak, the number of cases for each virus was as follows: rhinovirus/enterovirus 110

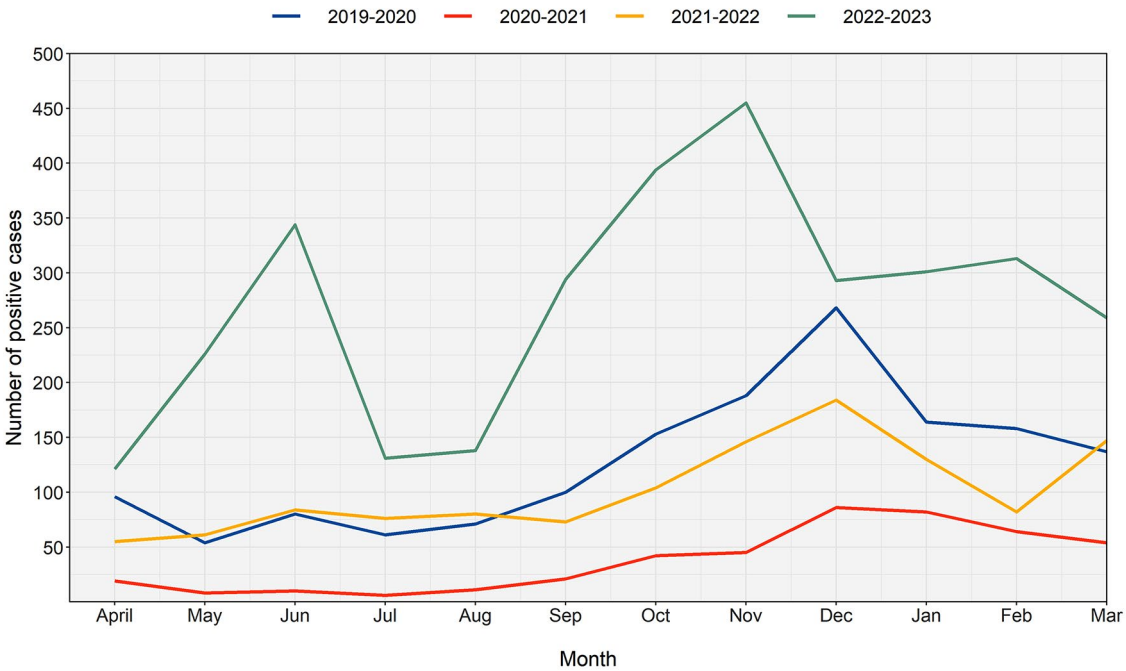

Fig. 2 Seasonal respiratory viral infection (PCR positive with at least one virus) during 2019–2023 in pediatric population in a tertiary care hospital, Saudi Arabia

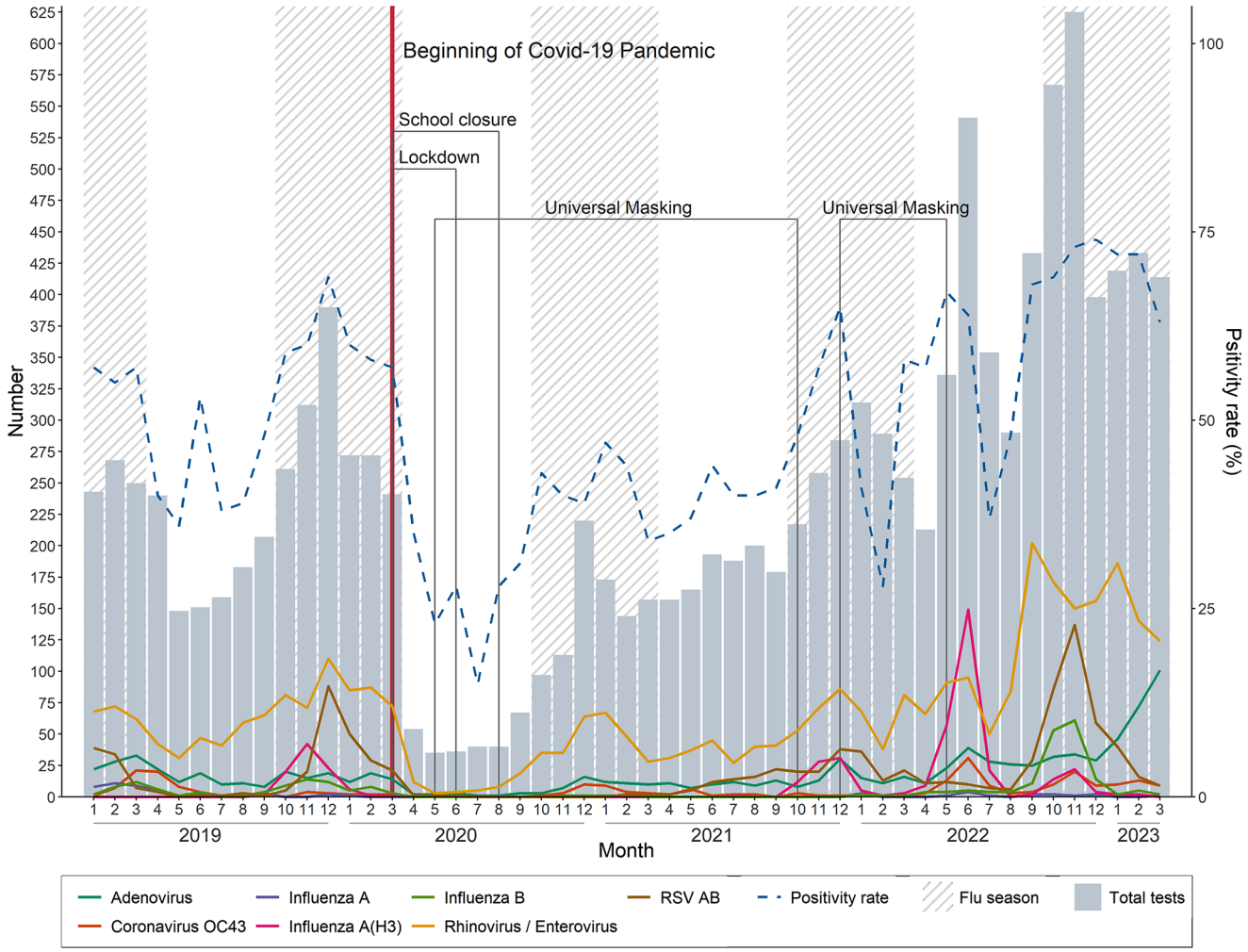

Fig. 3 The bars show the total number of respiratory virus tests done each month since 2019 till March 2023. The solid lines represent the number of positive results of common viruses and the dashed line represent positivity rate over the same depicted period

(33%), RSV 88 (26%), and influenza A(H3) virus 42 (19%) (Fig. 3).

During the COVID-19 pandemic and specifically in the 2020/2021 season, the total number of tests done had a notable decrease ranging between 35 and 220 tests/month (Fig. 3). This decrease in testing was associated with a decrease in the number of positive respiratory viruses and also with a decrease in the positivity rate ranging from 15 to 47%. However, it is worth mentioning that rhinovirus/enterovirus resumed its activity during the 2020/2021 winter season and reached its peak in January 2021 with a total of 67 (66%) cases (Fig. 3).

During the 2021/2022 season, the number of tests continued to recover following their nadir during the COVID-19 pandemic. All respiratory viruses continued to show low levels of detection during 2021/2022 despite reasonable test numbers being performed. An exception was the rhinovirus/enterovirus, which exhibited a similar level of activity compared to the pre-pandemic seasons with 86 cases (37%) being reported during December 2021. RSV did not show its typical activity during 2021/2022. The mid-season peak for RSV occurred in December 2021, with a total of 38 cases (16%). However, RSV activity was scattered throughout the year, contrary to the previous seasons where RSV activity was restricted to winter months. Parainfluenza 3 virus showed unusual off-season activities, mainly between March and September 2021 as seen in Fig. 4.

During the 2022/2023 winter season, the number of tests done was almost double the baseline of pre-pandemic seasons and 2021/2022 seasons (Fig. 3). Unusual increase in respiratory viruses' detection with peaks during the months of May and June was seen in 2022. The early peak was mainly led by influenza A(H3) virus, which reported 149 (36%) cases during June 2022. The number of rhinovirus/enterovirus cases doubled during the 2022/2023 season compared to all previous seasons. It peaked early in September 2022 with 202 (57%) cases followed by another peak in January 2023 with 186 (51%) cases. The number of rhinovirus/

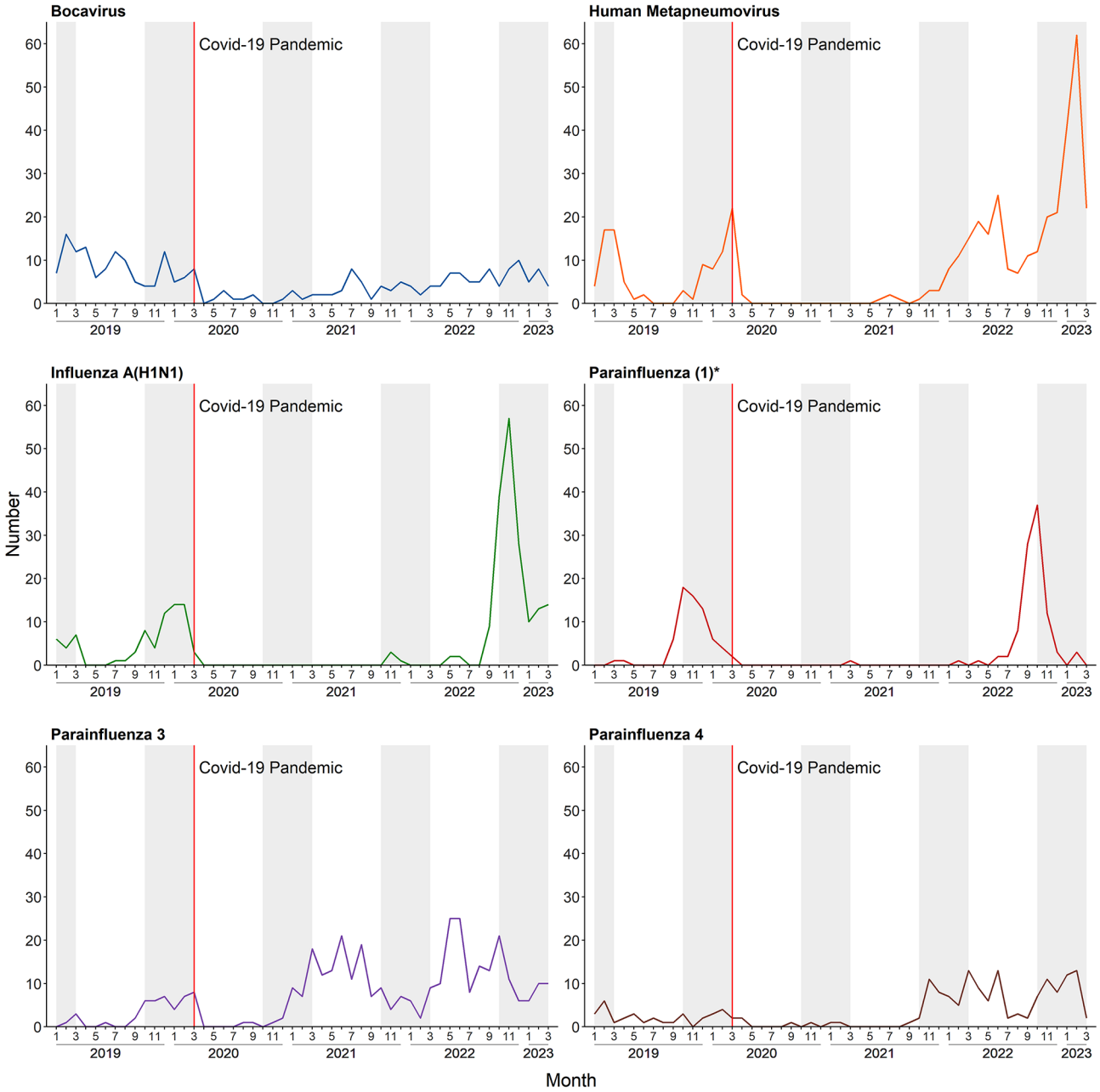

Fig. 4 Number of positive results of less common respiratory viruses (2019–2023) in pediatric population. The grey columns refer to typical flu season months. *Parainfluenza (1) refers to parainfluenza not subtyped or parainfluenza subtype 1

enterovirus cases remained at high levels until March 2023. Unprecedented activity of influenza B virus was observed in the 2022/2023 winter season, reaching a peak in November 2022 with 61 (11%) cases (Fig. 3). Parainfluenza 1 virus, influenza A(H1N1), and human metapneumovirus AB viruses were also circulating at levels not typically observed in previous seasons (Fig. 4). The positivity rate remained at high levels throughout the 2022/2023 season, reaching its maximum around 74% in December 2022 (Fig. 3). Interestingly, at the end of the season, adenoviral infection showed a notable increase reaching a total of 101 (33%) cases. The number of other respiratory viruses detected between 2019 and March 2023 is presented in Fig. 5.

Discussion

The present study showed fluctuation in the rate of seasonal respiratory viral infection in the pediatric population in Saudi Arabia throughout the study period (2019–2023),

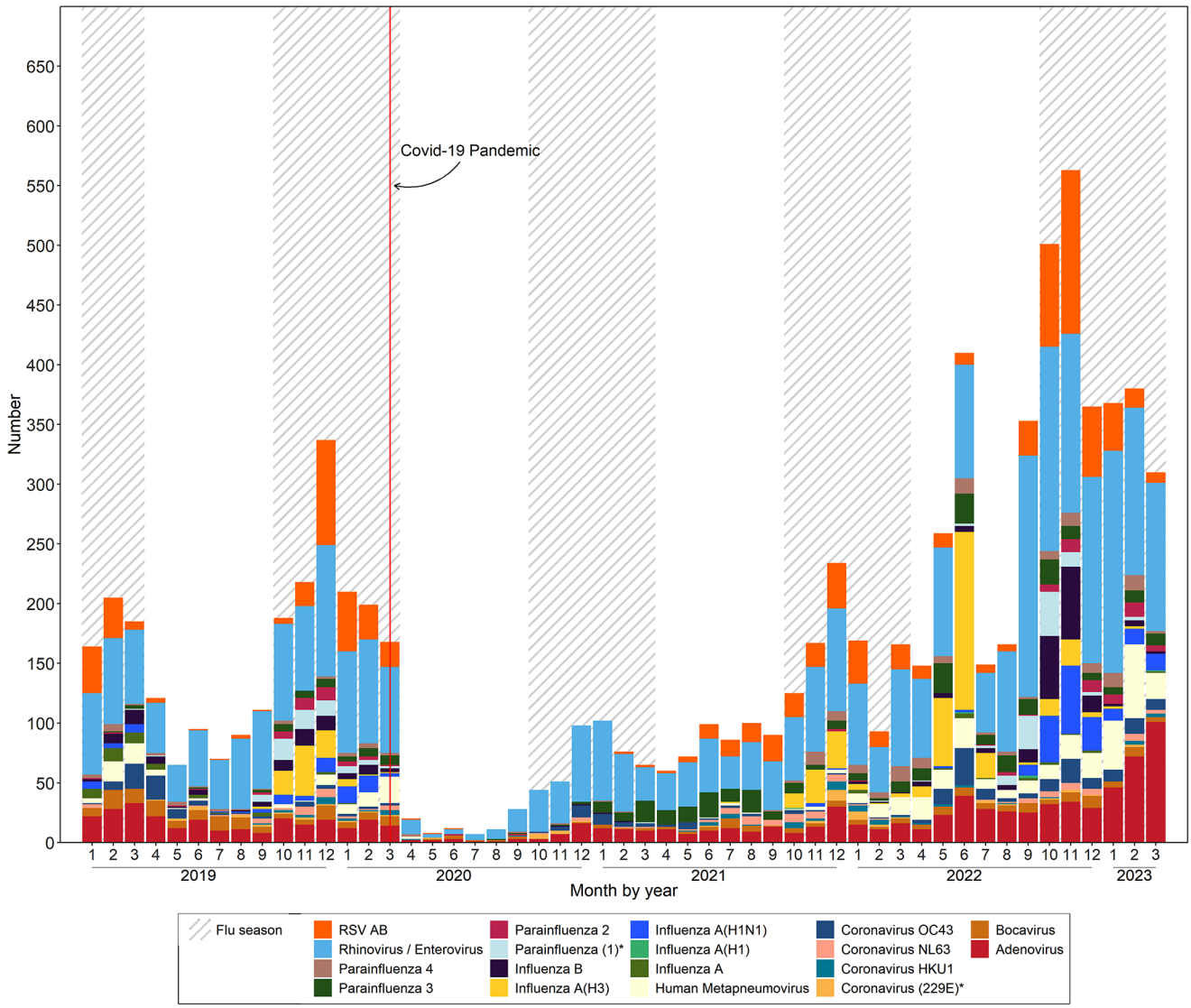

Fig. 5 Cumulative number of all positive respiratory viruses in pediatric patients during 2019- March 2023. *Parainfluenza (1) refers to parainfluenza not subtyped or parainfluenza subtype 1. *Coronavirus (229E) refers to coronavirus not subtyped or coronavirus subtype 229E

with the lowest in the season (2020–2021) and the highest in the season 2022–2023 with atypical activity of influenza A(H3), adenovirus, RSV, and parainfluenza 3 following the COVID-19 pandemic.

The data presented here is consistent with reports from the United States [6], other Northern Hemisphere countries [7, 8], and Asian countries [9, 10], which showed a sharp decline in the influenza viruses within a few weeks of the implementation of community restriction measures due to the COVID-19 pandemic, including social distancing, the closure of schools, and the obligation of wearing a face mask. The same might explain the decline observed in the present study (2020/2021 season), as after discovering the first confirmed cases, the Saudi government was very proactive in controlling the spread of the disease by implementing a range of measures, including international and internal travel restrictions, suspension of prayers at mosques, closure of schools, universities, and shopping malls, suspension of employee's attendance at government and private workplaces, implementation of curfew hours, and increase COVID-19 testing [11, 12].

Precautionary measures implemented during earlier epidemics, such as the 2003 SARS epidemic in Hong Kong, were also associated with low activity of respiratory viruses [13]. Cauchemez et al. (2008) reported that the closure of schools might play an important role in slowing the spread of influenza [14]. The use of face masks by infected persons can dramatically decrease the transmission of viral respiratory infections and protect the healthy persons who wear them from acquiring an infection [15].

Generally, the respiratory viral infection season in Saudi Arabia occurs during the winter season between October and March, with a peak in December. However, the 2022/2023 season in our study, exhibited remarkable changes in the circulation of respiratory viruses. Early activity was observed in May and June, with a decrease in July and August, followed by a resumption of the respiratory viral infection season in September. Similar findings were reported in Australia, where a peak in weekly influenza cases was detected in June 2022 [16]. Public health measures introduced during the COVID-19 pandemic had diminished the spread of influenza viruses but the prolonged lack of regular exposure to these viruses could impact the intensity and timing of the following influenza seasons, as suggested by epidemiological modeling [17]. An unprecedented increase in the number and duration of respiratory virus activity was observed in our study during the 2022/2023 season (455 cases in November 2022 compared to 268 in December 2019). A cross-sectional study conducted in Saudi Arabia showed a marked decline in influenza vaccination rates during the COVID-19 pandemic [18]. Decreased levels of immunity among the community, particularly among the pediatric population, could indicate a higher likelihood of widespread illness and a potentially more severe outbreak once influenza viruses return. Fear of the interaction between influenza and the COVID-19 vaccine and the excessive administration of multiple doses of the COVID-19 vaccine during the pandemic were reported as factors that contributed to the rejection of the flu vaccine [19]. Given these circumstances, it might be necessary to contemplate initiating vaccination campaigns earlier, specifically as soon as the vaccine becomes accessible, which can be as early as July or August. This would provide sufficient time to vaccinate the population and prevent individuals from remaining unvaccinated for influenza.

Our study showed that rhinovirus/enterovirus were the predominant isolated viruses overall seasons. The respiratory PCR assays used in our study cannot differentiate between rhinovirus and enterovirus which limits our understanding of prevalence changes in each virus. Such discrimination might be of great value for clinicians due to their heterogeneous clinical manifestation [20]. Rhinovirus mainly presents with respiratory symptoms, however; enterovirus and enterovirus-related viruses can cause a broad range of illnesses; some could be serious and possibly fatal, especially in children [20, 21]. Future research might use more sensitive methods that provide deferential detection of rhinovirus and enterovirus to monitor the impact of epidemics and other infectious disease changes on their existence.

Other increase in incidence during the years following the beginning of the COVID-19 pandemic was reported in influenza A(H3), RSV, adenovirus, human metapneumovirus, and parainfluenza 3 viruses which is in concordance with previous reports [22, 23]. In the United States, Chow et al. (2023) observed that the prevalence of respiratory viruses varied throughout the phases of the COVID-19 pandemic, with alternations in the detection of influenza virus, RSV, rhinovirus, and respiratory enterovirus infections [13]. Continuous monitoring of changes in respiratory viruses activity following the COVID-19 pandemic is crucial for better prediction and preparedness of potential epidemics.

Our study poses some limitations. First, the study population was limited to patients attending a tertiary care hospital, and hence, the results may not be generalized to the entire community. Second, during the COVID-19 pandemic, most patients with respiratory symptoms were prioritized for testing for COVID-19, leading to a reduction in testing for influenza viruses and other respiratory viruses, which might have an impact on the data. However, this practice did not last long as molecular multiplexes PCR assays that detect COVID-19 and other respiratory viruses simultaneously were made available early during the pandemic season.

In conclusion, this observational study reported an unprecedented difference in the seasonality and positivity rate of influenza and other important respiratory viral infections, most likely due to the use of mitigation measures. These data can be of use to enhance future influenza epidemics preparedness, as some of these mitigation measures could be implemented to reduce transmission, particularly in populations at high risk for developing severe disease or complications. However, the influenza vaccine for everyone aged ≥ 6 months remains the most effective method to prevent influenza and is particularly important in the upcoming season when COVID-19 and the influenza virus might co-circulate.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10096-024-04860-5.

Author contributions M.A., A.A., A.A. A., I.Y. B., M.A. A., A.A., S.A., and S.M. A. contributed to the study conception and design. Material preparation, data collection and analysis were performed by M.A., A.A., A.A. A., I.Y. B. and M.A. A.. The first draft of the manuscript was written by M.A. A.A., A.A. A., I.Y. B., M.A. A., A.A., S.A., and S.M. A. commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability Data are available from the corresponding author upon reasonable request, after required approvals from the Ethics Committee at King Faisal Specialist Hospital and Research Center are obtained.

Declarations

Ethical approval Ethical approval was obtained from the local Ethics Committee of KFSHRC in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The need for informed consent was waived in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

Competing interests The authors declare no competing interests.

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