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Effects of COVID-19 pandemic on epidemiological features of viral respiratory tract infections in children: a single-centre study

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Abstract

The epidemiology of respiratory infections may vary depending on factors such as climate changes, geographical features, and urbanization. Pandemics also change the epidemiological characteristics of not only the relevant infectious agent itself but also other infectious agents. This study aims to assess the impact of the COVID-19 pandemic on the epidemiology of viral respiratory infections in children. We retrospectively reviewed the medical records of children aged ≤18 years with laboratory-confirmed viral respiratory infections other than COVID-19 from January 2018 to March 2023. Data on demographic characteristics, month and year of admission, and microbiological results were collected. During the study period, 1,829 respiratory samples were sent for polymerase chain reaction testing. Rhinovirus was identified in 24% of the patients, mixed infections in 21%, influenza virus in 20%, and respiratory syncytial virus in 12.5%. A 38.6% decrease in viral respiratory infections was observed in 2020, followed by a 188% increase in 2021. The respiratory syncytial virus was significantly more common in the post-pandemic period (13.8%) compared to the pre-pandemic period (8.1%), but no seasonal shift in respiratory syncytial virus infection was observed. There was also a yearly increase in influenza infections in the post-pandemic period compared to the pre-pandemic period. After the COVID-19 pandemic, the frequency of parainfluenza virus infections increased during the summer months, and this finding provides a new contribution to the existing literature.

Introduction

The epidemiology of respiratory infections may vary depending on conditions such as climate changes, geographical features, and urbanization [1]. After the COVID-19 pandemic, significant changes have been observed in the epidemiology of both viral and bacterial respiratory infections [2, 3]. Prior to the pandemic, coronaviruses and other respiratory viruses exhibited predictable yearly epidemics in children, and each had individual epidemiological features [4–7]. However, the usual predictable epidemics of respiratory viruses were disrupted by the non-pharmaceutical interventions (NPI) such as masking and social distancing implemented due to the COVID-19 pandemic [8, 9]. During the early stages of the pandemic, strict measures led to a significant global decrease in all infectious agents [10, 11]. Afterwards, following the relaxation in the restrictions, there were reports of resurgence in viral respiratory infections, delays in peaks, and unexpected changes in seasonal epidemic patterns [12, 13]. Therefore, follow-up epidemiological studies are crucial for identifying epidemiological changes and developing strategies for the prevention and treatment of these infections.

The aim of this study is to evaluate the impact of the COVID-19 pandemic on the frequency and epidemiological characteristics of viral respiratory tract infections (RTIs) in children by comparing pre- and post-pandemic data.

Materials and methods

Study design and inclusion criteria

We retrospectively reviewed the medical records of children aged ≤18 years who were admitted to the Department of Pediatrics at Gazi University Faculty of Medicine with laboratory-confirmed viral RTIs other than COVID-19, from January 2018 to March 2023. Our institution is located in Ankara, Turkey, a Mediterranean country in the Northern Hemisphere. The following data were extracted from the patients' medical records and laboratory database: age, sex, month and year of

admission, final diagnosis which was recorded by paediatricians using the International Classification of Disease 10th edition, and results of multiplex polymerase chain reaction (PCR) and rapid antigen tests. No clinical data were collected.

The patients were divided into five groups according to age: under 1 year of age, 1–5 years of age, 5–10 years of age, 10–15 years of age, and more than 15 years of age.

Since the main purpose of the study was to evaluate the effects of COVID-19 on the epidemiology of viral respiratory infections, bacterial infections were not included in the study. The first COVID-19 case was announced in Turkey on 11 March 2020. Therefore, January 2018 to March 2020 was categorized as the pre-COVID period, and March 2020 to March 2023 as the post-COVID period. The data from these periods were then compared.

Some of the measures implemented in the country were as follows:

- Social planning: Most of the activities that require public gatherings were restricted. Rules were applied in areas such as markets where people congregate out of necessity.
- Education: On 17 March 2020 face-to-face education in schools was suspended till the end of the term and planned to be completed entirely online. Face-to-face education, which started gradually in September 2020 was suspended from 17 November 2020 until March 2021 again. All levels resumed full-time education with intermittent control on 6 September 2021.
- Vaccination: As of 14 January 2021, vaccination with inactive vaccine started. After May 2021 vaccination was initiated also with mRNA vaccine. Children who were 12 years or older were optionally vaccinated.

The controlled normalization processes were applied intermittently from May 2020 till the end of the year. By July 2021, many of the restrictions that have existed for 15 months were eliminated gradually [14].

Specimen collection and molecular detection of respiratory pathogens

Nasopharyngeal swab, nasal swab, or bronchoalveolar lavage samples were collected using a standard method into a tube containing transport medium. The samples were collected according to the Centers for Disease Control and Prevention (CDC) recommendations [15]. The rapid antigen test was the first diagnostic test performed in patients with clinically and epidemiologically suspected influenza. Rapid influenza diagnosis was conducted using the DiagnoFast Influenza A + B Ag Rapid Test (Labsystem, Turkey) kit. When the patient was diagnosed with influenza using the rapid diagnostic test, multiplex PCR was not performed. Patients whose rapid influenza diagnostic test was negative or not performed were tested using multiplex PCR.

Multiplex PCR was performed with the isolated genetic materials on the Qiagen Rotor-Gene Q device using the Fast Track Diagnostics Respiratory Pathogens 21 (FTD, Luxembourg) test kit. This test detects a total of 21 respiratory tract pathogens, including parainfluenza (PIV) 1, PIV 2, PIV 3, PIV 4, influenza A, influenza B, influenza A (H1N1), coronavirus (CoV) NL63, CoV OC43, CoV HKU1, CoV 229E, human metapneumo virus (HMPV) A/B, human rhinovirus (HRV), human bocavirus (HBoV), respiratory syncytial virus (RSV) A/B, adenovirus (ADV), enterovirus, human parechovirus, and mycoplasma pneumoniae.

Statistical analysis

Categorical variables were expressed as numbers (%). Continuous variables were expressed as medians (interquartile range) or mean ± standard deviation due to whether normally distributed or not.

Medians for continuous variables were compared using the Kruskal–Wallis test for more than two independent variables which were not normally distributed, and proportions for categorical variables (detection rates of virus, sex, final diagnosis) were compared using the chi-square test. Normally distributed continuous variables were compared by Student t test or one-way Analysis of Variance (ANOVA). All of the tests were two-tailed, and a value of $p < 0.05$ represented statistical significance. Statistical analyses were conducted in SPSS version 23.0 software (IBM, New York, USA).

Ethical approval

Ethical approval was obtained from the Ethics Committee of Gazi University of Medicine and Pharmacy (No.2024.01.892).

Results

Primary results

During the study period, a total of 1,829 respiratory samples were sent for PCR testing. Of these samples, 22.3% were obtained in the pre-pandemic period, and 77.7% were obtained in the post-pandemic period. After the emergence of the COVID-19 pandemic in Turkey in March 2020, the total number of COVID-19 PCR-positive cases was 1,002 during our post-pandemic study period. The study group consisted of 123 patients in 2018, 233 in 2019, 143 in 2020, 555 in 2021, 459 in 2022, and 316 in 2023. A 38.6% decrease was observed in 2020, and a 188% increase was observed in 2021 (Table 1).

Of the total samples, 43.6% were collected from girls, while 56.4% were collected from boys. There was no significant difference in terms of gender in the distribution of patients across the years (p = 0.36). The mean age of the patients was 4.90 ± 4.54 years. The age distribution of the patients was as follows: 323 (17.7%) were < 1 year of age, 833 (45.5%) were between 1 and 5 years of age, 408 (22.3%) were between 5 and 10 years of age, 160 (8.7%) were between 10 and 15 years of age, and 105 (5.7%) were > 15 years of age. When all years were evaluated, it was observed that viral RTIs were most common in children between the ages of 1 and 5 years ($p = 0.001$) (Table 1).

During the study period, HRV was detected in 24% of samples, mixed viral infections in 21%, influenza virus in 20%, RSV in 12.5%, ADV in 7%, PIV and CoV in 5%, HBoV in 3%, and HMPV in 2% of the samples (Figure 1).

It was found that the mean age of RSV-infected patients was 3.5 ± 4.03 years, HRV-infected patients was 6.1 ± 5 years, influenza-infected patients was 4.4 ± 0.5 years, patients with mixed infections was 3.9 ± 3.8 years, ADV-infected patients was 4.1 ± 4.1 years, PIV-infected patients was 3.1 ± 2.6 years, CoV-infected patients was 5.7 ± 5.0 years, HBoV-infected patients was 3.4 ± 3.0 years, and HMPV-infected patients was 4.9 ± 3.9 years. When mean ages were compared, it was observed that patients with RSV infection were significantly younger than those with HRV ($p = 0.000$) and influenza virus infection ($p = 0.000$). Patients with CoV infection were significantly older than patients infected with other respiratory viruses except for HRV ($p = 0.000$).

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Table 1. The distribution and properties of patients with respiratory tract infections by year

	2018	2019	2020	2021	2022	2023	Total	*p*
RSV	6 (4.9%)	13 (5.6%)	21 (14.7%)	98 (17.7%)	54 (11.8%)	37 (11.7%)	229	**0.001**
HRV	32 (26.0%)	**67 (28.8%)**	**54 (37.8%)**	138 (24.9%)	96 (20.9%)	65 (20.6%)	452	
PIV	5 (4.1%)	14 (6.0%)	1 (0.7%)	41 (7.4%)	18 (3.9%)	5 (1.6%)	84	
ADV	7 (5.7%)	17 (7.3%)	17 (11.9)	18 (3.2%)	30 (6.5%)	37 (11.7%)	126	
Mixed	**53 (43.1%)**	30 (12.9%)	15 (10.5%)	**150 (27.0%)**	91 (19.8%)	56 (17.7%)	395	
Influenza	3 (2.4%)	62 (26.6%)	15 (10.5%)	32 (5.8%)	**147 (32.0%)**	**93 (29.4%)**	352	
HMPV	4 (3.3%)	3 (1.3%)	4 (2.8%)	12 (2.2%)	9 (2.0%)	12 (3.8%)	44	
HCoV	11 (8.9%)	21 (9.0%)	10 (7.0%)	34 (6.1%)	9 (2.0%)	7 (2.2%)	92	
BocaV	2 (1.6%)	6 (2.6%)	6 (4.2%)	32 (5.8%)	5 (1.1%)	4 (1.3%)	55	
Total	123	233	143	555	459	316	1829	

RSV, respiratory syncytial virus; HRV, human rhinovirus; PIV, parainfluenza virus;. ADV, adenovirus; HMPV, human metapneumo virus; HCoV, human corona virus; BocaV, human boca virus.

Table 2. The distribution of respiratory viruses by year

	2018	2019	2020	2021	2022	2023	Total	p
Age (mean ± SD)	4.76 ± 4.79	5.15 ± 5.03	5.29 ± 4.99	4.68 ± 4.23	4.83 ± 4.37	5.07 ± 4.60	4.90 ± 4.54	0.56
Age group								
0–1 year	35 (28.5%)	47 (20.2%)	18 (12.6%)	68 (12.3%)	93 (20.3%)	62 (19.6%)	323 (17.7%)	**0.001**
1–5 years	**39 (31.7%)**	**104 (44.6%)**	**68 (47.6%)**	**294 (53.0%)**	**200 (43.6%)**	**128 (40.5%)**	**833 (45.5%)**	
5–10 years	29 (23.6%)	40 (17.2%)	31 (21.7%)	134 (24.1%)	99 (21.6%)	75 (23.7%)	408 (22.3%)	
10–15 years	15 (12.2%)	22 (9.4%)	11 (7.7%)	32 (5.8%)	45 (9.8%)	35 (11.1%)	160 (8.7%)	
> 15 years	5 (28.5%)	20 (8.6%)	15 (10.5%)	27 (4.8%)	22 (4.8%)	16 (5.1%)	105 (5.7%)	
Gender (n. %)								
Male	64 (52.0%)	138 (59.2%)	70 (49.0%)	314 (56.6%)	262 (57.1%)	184 (58.2%)	797 (43.6%)	0.36
Female	59 (48.0%)	95 (40.8%)	73 (51.0%)	241 (43.4%)	197 (42.9%)	132 (41.8%)	1.032 (56.4%)	
Season								
Spring	28 (22.8%)	58 (24.9%)	35 (24.5%)	26 (4.7%)	0 (0.0%)	49 (15.5%)	196 (10.7%)	**0.001**
Summer	25 (20.3%)	18 (7.7%)	**55 (38.5%)**	99 (17.8%)	41 (8.9%)	0	238 (13.0%)	
Autumn	**36 (29.3%)**	55 (23.6%)	8 (5.6%)	**248 (44.7%)**	166 (36.2%)	0	513 (28%)	
Winter	34 (27.6%)	**102 (43.8%)**	45 (31.5%)	182 (32.8%)	**252 (54.9%)**	**267 (84.5%)**	**882 (48.2%)**	
Total	123	233	143	555	459	316	1829	

Comparison of pre- and post-pandemic periods and annual and seasonal pattern of the viruses respiratory syncytial virus

RSV was significantly more commonly observed in the post-pandemic period (13.8%) compared to the pre-pandemic period (8.1%) ($p = 0.002$). In 2020, RSV was the second most prevalent agent, with a detection rate of 14.7%, following HRV. In the winter of 2019, RSV was detected in 15.5% of respiratory samples, but it became the most common respiratory viral agent in the spring of 2020, with a prevalence of 30.6%. (Annual and seasonal distribution are shown in Table 2, Figure 1 and Supplementary Table and Supplementary Figure.)

Influenza virus

No significant difference was observed between pre- and post-pandemic periods regarding the frequency of the influenza virus. In 2019, the influenza virus was the second most common agent (26.6%) after mixed viral infections (28.8%). In 2022 and 2023, the most prevalent virus was the influenza virus, with detection rates of 32.0% and 29.4% respectively. The influenza virus was the most common viral respiratory agent in the winter seasons of 2019–2020 (49.6%) and 2022–2023 (37.0%). (Annual and seasonal distribution are shown in Table 2, Figure 1 and Supplementary Table and Supplementary Figure.)

When comparing the mean ages of patients between the pre- and post-pandemic periods, it was found that the mean age of patients with influenza virus in the pre-pandemic period was 4.95 ± 3.98, whereas in the post-pandemic period it was 6.12 ± 4.48 ($p = 0.028$).

Parainfluenza virus

There was no significant difference observed between pre- and post-pandemic periods or in annual comparisons regarding the frequency of PIV. When seasonal distribution is evaluated, PIV was

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Table 3. Distribution of mixed infections by season, year and age

	Mixed viral infection	*p*
Season		**0.009**
Spring	29 (14.8%)	
Summer	36 (15.1%)	
Autumn	135 (26.3%)	
Winter	195 (22.1%)	
Year		**0.000**
2018	**53 (43.1%)**	
2019	30 (12.9%)	
2020	15 (10.5%)	
2021	**150 (27.0%)**	
2022	91 (19.8%)	
2023	56 (17.7%)	
Age group		**0.000**
0–1 year	72 (22.3%)	
1–5 years	219 (26.3%)	
5–10 years	74 (18.1%)	
10–15 years	12 (7.5%)	
>15 years	18 (17.1%)	

the second most common virus in three consecutive summers (22.2% in 2019, 23.2% in 2021, and 22% in 2022), except for the 2020 summer season. (Annual and seasonal distribution are shown in Table 2, Figure 1 and Supplementary Table and Supplementary Figure.)

Human rhinovirus

There was no significant difference observed between pre- and post-pandemic periods regarding the frequency of HRV. When evaluating the annual distribution, it was either the most common or the second most common virus in each year of the study period. (Annual and seasonal distribution are shown in Table 2, Figure 1 and Supplementary Table and Supplementary Figure.)

Mixed infection

The frequency of mixed viral infection did not show a significant difference between the pre-pandemic and post-pandemic periods ($p = 0.774$). It was the second most common infection overall in our study group (21%) and the leading cause of RTIs in 2018 (43.1%) and 2021 (27%). Mixed infections were the lowest in 2020 (10.5%). (Annual and seasonal distribution are shown in Table 2, Figure 1 and Supplementary Table and Supplementary Figure.) Of mixed viral infections, 76.3% consisted of two, 20.6% consisted of three, and 3.1% consisted of four viruses. The highest tendency to cause mixed infection was observed in RSV (51.5%), HRV (48.4%), and HBoV (47.4%). The frequency of mixed infections was more common in children between 1 and 5 years of age (26.3%) and in autumn (26.3%) (Table 3).

Discussion

This retrospective study represents one of the largest paediatric epidemiological data about the viral dynamics before and after the

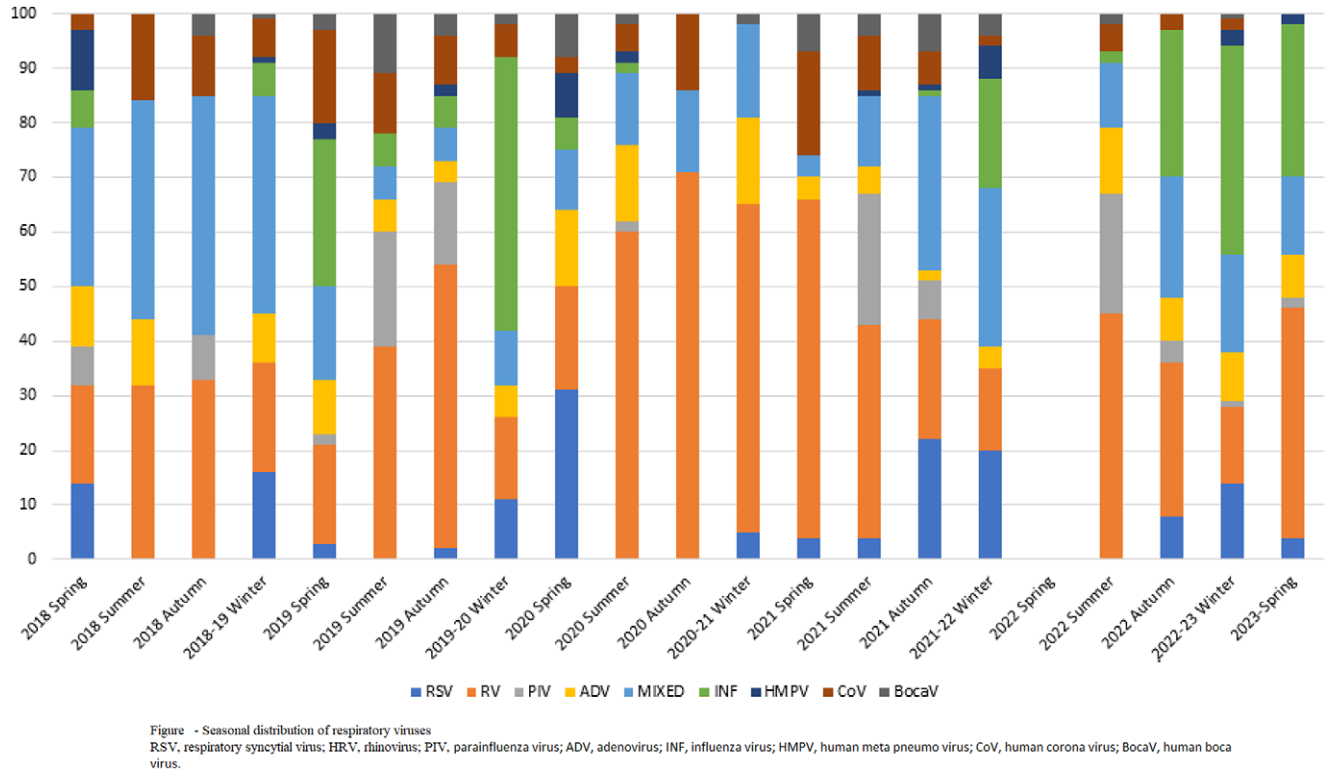

Figure - Seasonal distribution of respiratory viruses
RSV, respiratory syncytial virus; HRV, rhinovirus; PIV, parainfluenza virus; ADV, adenovirus; INF, influenza virus; HMPV, human meta pneumo virus; CoV, human corona virus; BocaV, human boca virus.

Figure 1. Seasonal distribution of respiratory viruses.

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COVID-19 pandemic in Turkey. We found that the implementation of NPIs such as masking, social distancing, and school closures during the COVID-19 pandemic led to a 38.6% decrease in the frequency of viral RTIs in 2020 compared to 2019. However, in the subsequent years following the relaxation of COVID-19 measures, viral RTIs increased to 288% in the 2021–2022 season and 220% in the 2022–2023 season compared to the 2019–2020 season.

According to various reports, during the height of the COVID-19 pandemic, infection control measures decreased the circulation of respiratory viruses during the fall and winter months of 2020 [16, 17]. Subsequently, in October 2023, the European CDC (ECDC). published a statement declaring that a high burden of respiratory viruses was observed in the 2022–2023 season [18]. Consistent with the literature, our findings indicate that as the impact of the pandemic has diminished and social living conditions have returned to normal, respiratory viruses have returned to their well-known epidemiological patterns.

In this study, we demonstrated that the frequency of RSV infections increased in the post-pandemic period compared to the pre-pandemic period. This increase may be explained by the long-term lack of immune stimulation by viruses, which can increase the number of immune-vulnerable individuals, especially children [19]. While this relationship can be observed with all viruses, it is noteworthy that this study specifically documents it with RSV.

Similar to the current literature [20, 21], RSV activity during the first winter season of the pandemic was markedly below the expected seasonal levels. However, the seasonal shift [13] and the earlier increase in RSV activity reported in other studies [22] were not observed in our study.

This study revealed that the influenza virus was the most commonly detected virus in 2022 and 2023, especially in the winter season. This finding indicates that influenza virus activity exceeded pre-pandemic levels during these years. Reduced activity of influenza viruses was reported worldwide as early as a couple of weeks after NPI implementation, remaining significantly below the values recorded in the years preceding the pandemic up to the entire 2020–2021 season [23]. By the 2022–2023 influenza season, influenza virus activity had returned to nearly pre-pandemic levels in European Union/European Economic Area (EU/EEA) countries [18].

According to this study, mixed viral infections are the second most common viral RTIs in children. The most common viruses in mixed infections were RSV, HRV, and HBoV. In a recent paediatric study, it was found that the most common viruses in mixed infections were HRV, PIV, and RSV [24]. Various studies have revealed the prevalence of HBoV in mixed infections. A report by Wang et al. [25] stated that the mixed infection rate of HBoV with other viruses was 25%. Moreno et al. [26] reported a rate of 54.5%, and Lekane-Douki et al. [27] showed a rate of 84.4%. Future studies are warranted to further investigate the role of HBoV infection in mixed infections.

Notably, PIV emerged as the second most common cause of viral RTIs for three consecutive summers after the COVID-19 pandemic in our study. According to Olsen et al. [28], PIV infections increased after January 2021 but were not prevalent in the summer season. Similarly, in another study, an increase in PIV infections was observed during the autumn of 2021 [29]. Additionally, Li et al. [30] reported a peak in the detection rate of PIV in December 2020 and January 2021 after the pandemic. Although the increase in summer periods is an important and new finding to the current literature, its course should be monitored in future studies.

HRV was either the most common or the second most common virus in all seasons, and its yearly distribution appeared to be the least affected by the pandemic. Additionally, there were no significant differences observed in the annual or seasonal epidemiological features of AV, HMPV, and HBoV infections.

While various studies have reported higher numbers of patients under 1 year of age [31, 32], our findings indicate that, during the study period, the number of patients with viral RTIs was higher in the 1–5 age group compared to other age groups. The higher proportion of patients in the 1–5 age group in our study may be attributed to the fact that, although schools were frequently interrupted or closed during the pandemic, kindergartens and preschools often continued face-to-face education in Turkey. Additionally, this age group is less likely to adhere to personal infection precautions.

This study has the following limitations. Firstly, this is a single-centre, retrospective study, thus, cannot allow generalization of the findings. Additionally, the variability in the number of respiratory multiplex PCR tests due to test availability during the study period may limit the generalizability of the study results.

Conclusion

After the COVID-19 pandemic, significant changes have been observed in the epidemiology of viral RTIs. In our study, we observed a decrease in viral RTIs during the initial phases of the pandemic, followed by an increase in subsequent seasons. Although our study did not show seasonal variation in RSV infection reported in other regions, there was a noticeable increase in RSV infections following the COVID-19 pandemic. HRV was the virus least affected by the pandemic during the study period and maintained its normal annual pattern. Mixed viral infections were common throughout the study period, with RSV, HRV, and HBoV being the most frequently co-infecting agents. An important and novel finding of our study is the increase in PIV infections during summer seasons. Future epidemiological studies are needed to support these findings.

Supplementary material. The supplementary material for this article can be found at http://doi.org/10.1017/S0950268824001158.

Data availability statement. The data that support the findings of this study are available from the Gazi University Faculty of Medicine. Restrictions apply to the availability of these data.

Author contribution. Writing–review & editing: T.B.D., M.O., M.P., F.C.K., A.T.. Conceptualization: G.B., H.T.. Formal analysis: T.B.D., M.P., A.T., N.A.U., N.K., E.G., F.D.. Methodology: T.B.D, M.O., A.T.. Supervision: T.B.D., M.O., M.P., F.C.K., A.T.. Validation: T.B.D., M.O., M.P., F.C.K., A.T. Writing – original draft: T.B.D.. Investigation: T.B.D., M.P., A.T., M.O., F.C.K., N.A.U., N.K., E.G., F.D, G.B.

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