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Changing Infection Dynamics with the Pandemic: Distribution of Viral Agents of Respiratory Tract Infections in the Last 5 Years

Pandemi ile Değişen Enfeksiyon Dinamikleri: Son 5 Yılda Solunum Yolu Enfeksiyonlarının Viral Ajanlarının Dağılımı

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Abstract

Introduction: The measures taken against Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) positively impacted the reduction of its transmission. In addition, these measures also significantly decreased the spread of infections caused by other respiratory viruses. In this study, we aimed to determine the frequency of respiratory virus infections, other than SARS-CoV-2, during the Coronavirus disease-2019 (COVID-19) pandemic and investigated their course during both the quarantine and normalization periods.
Materials and Methods: Swab samples sent to Necmettin Erbakan University Meram Faculty of Medicine Hospital Medical Microbiology Laboratory between May 2017 and May 2022 to determine the viral agents of respiratory tract infections by polymerase chain reaction (PCR) were retrospectively scanned.
Results: A total of 187,240 SARS-CoV-2 PCR tests were performed between April 1, 2020, and May 31, 2020, and 14,773 (9.82%) tests were reported as positive. Based on our observation, the viruses demonstrating a decrease during the pandemic period were influenza A and B, seasonal H1N1, human metapneumovirus, respiratory syncytial virus A and B, and human herpes virus 7. No changes were observed in the infection rates of parvovirus B19, adenovirus, and human rhinovirus.
Conclusion: In our study, we observed a serious decline in the cases caused by other respiratory viral agents and the detection rates of these agents during the pandemic period compared to the pre-pandemic period. This can be attributed to the extensive impact of the measures implemented during the COVID-19 pandemic to mitigate the spread of respiratory infections. Our results are a reflection of this situation. We believe that the data obtained from a large number of samples will serve as a guide for managing infections during the current pandemic and for future experiences.
Keywords: COVID-19, PCR, respiratory viruses, SARS-CoV-2

Öz

Giriş: Şiddetli akut solunum yolu sendromu-Koronavirüs-2'ye (SARS-CoV-2) karşı alınan önlemler, sadece SARS-CoV-2'nin yayılmasını azaltmada olumlu bir etki yaratmakla kalmamış, aynı zamanda diğer solunum yolu virüsleri tarafından kaynaklanan enfeksiyonların yayılmasını önemli ölçüde azaltmıştır. Bu çalışmada, Koronavirüs hastalığı-2019 (COVID-19) pandemisi sırasında SARS-CoV-2 dışındaki solunum yolu virüs enfeksiyonlarının sıklığı belirlenmiş ve bunların hem karantina dönemi hem de normalleşme dönemindeki seyri araştırılmıştır.
Gereç ve Yöntem: Mayıs 2017 ile Mayıs 2022 arasında Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Hastanesi Tıbbi Mikrobiyoloji Laboratuvarına gönderilen polimeraz zincir reaksiyonu (PCR) ile solunum yolu enfeksiyonlarının viral ajanlarını belirlemek amacıyla alınan sürüntü örnekleri retrospektif olarak tarandı.

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Bulgular: 01.04.2020 ile 31.05.2022 arasında 187.240 SARS-CoV-2 PCR testi gerçekleştirildi ve 14.773 (%9,82) test pozitif olarak raporlandı. Pandemi döneminde azalan virüsler: İnfluenza A/B, Mevsimsel H1N1, HMPV, RSV A/B ve HHV7. Parvovirus B19, adenovirus ve rhinovirusun enfeksiyon oranlarında bir değişiklik gözlenmedi.
Sonuç: Çalışmamızda, pandemi döneminde diğer solunum yolu viral ajanlar tarafından kaynaklanan olgularda ve bu ajanların tespit oranlarında pre-pandemik döneme kıyasla ciddi bir azalma olduğu görülmektedir. Bu durumun, COVID-19 pandemisi sırasında alınan önlemlerin solunum yolu enfeksiyonlarının yayılmasına geniş kapsamlı etkisinin bir yansıması olduğuna inanıyoruz. Aslında, sonuçlarımız bu durumun bir yansımasıdır. Bu, mevcut pandemi sürecinde enfeksiyon yönetimi için ve sonraki deneyimler için bir rehber olacak olan geniş bir örnekle elde ettiğimiz verilere dayanmaktadır.
Anahtar Kelimeler: COVID-19, PCR, solunum virüsleri, SARS CoV-2

Introduction

Human respiratory viral infections, ranging from the common cold to acute respiratory distress syndrome represent a significant global health problem and a public health issue. The most prevalent among these viruses include respiratory syncytial virus (RSV), adenovirus (ADV), influenza virus type A and B (INF A/B), parainfluenza virus type 1-3 (PIV 1-3), human rhinovirus A/B (HRV A/B), enterovirus (EV), human coronavirus (HCoV), human bocavirus (HBoV), and human metapneumovirus (HMPV) as new respiratory viruses. Viral respiratory infections encompass a spectrum of conditions, including the common cold, otitis media, flu-like illness, croup, bronchiolitis, and pneumonia. All of these diseases can be clinically attributed to any of these viruses and diagnosed based on symptoms alone[1]. Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) has caused a global pandemic, leading to significant morbidity and mortality, particularly affecting the older and vulnerable adult population. With the onset of the pandemic, policymakers globally implemented serious measures to reduce the transmission of SARS-CoV-2. These measures included various quarantine practices, such as local and international travel restrictions, curfews, school closures, hand washing, physical distance, and face mask usage[2-4].

These measures impacted the transmission of SARS-CoV-2 positively. In addition, they also reduced the spread of infections caused by other respiratory viruses significantly. The most noteworthy impact is the significant reduction in cases caused by other respiratory viruses in both the Southern and Northern Hemispheres since March 2020. In particular, surveillance data from several countries around the world have shown a significant decline in detecting influenza between 2020 and 2021. From 2020 to 2021, the United States reported lower rates of influenza-related hospitalizations compared to any season since routine data collection began in 2005. Similarly, Australia reported reduced influenza activity starting in April 2020[5].

In this study, we aimed to assess the frequency of respiratory tract virus infections, other than SARS-CoV-2, during the COVID-19 pandemic and examine their course during both quarantine and normalization periods.

Materials and Methods

Swab samples sent to Necmettin Erbakan University Meram Faculty of Medicine Hospital Medical Microbiology Laboratory between May 2017 and May 2022 to determine the viral agents of respiratory tract infections by polymerase chain reaction (PCR) were scanned retrospectively. After DNA/RNA isolation of patient samples, multiplex PCR was performed on the Rotor-Gene Q MDx 5plex HRM platform (Qiagen, Germany) with the 'Respiratory RT-qPCR MX-24 panel' (Bioeksen, Turkey). The presence of 17 different viruses including influenza A and B virus, human coronavirus NL63/229E/OC43/HKU1, RSV A/B, ADV, EV, rhinovirus, parainfluenza virus 1, 2, 3, 4, metapneumovirus, bocavirus, parechovirus were searched.

Statistical Analysis

The demographic data of patients and detected viral load and rates were analyzed using the Statistical Package for the Social Sciences (Inc.; Chicago, IL, USA) using the 21st package program, taking into account age, gender, and seasons. The period from May 1, 2017, to March 20, 2020, was defined as the pre-pandemic period. The period from March 20, 2020, to December 31, 2021, was defined as the pandemic period. The period from January 1, 2022, to May 31, 2022, was defined as the last period of the pandemic. Categorical data of two-way tables were evaluated by the chi-square test (statistical significance $p<0.05$).

Results

In this study, the PCR results of 150,302 samples sent to the Necmettin Erbakan University Meram Faculty of Medicine Hospital, Medical Microbiology Laboratory for respiratory virus analysis between May 2017 and May 2022 were scanned retrospectively. The PCR tests were performed and 14,773 (9.82%) samples were reported as positive.

During the pandemic period, the incidence of some respiratory tract viruses, other than SARS-CoV-2, was observed to be lower compared to the pre-and post-pandemic periods. Nevertheless, it has been noted that the incidence of certain viruses remains unchanged during the pandemic period (Table 1, Figure 1).

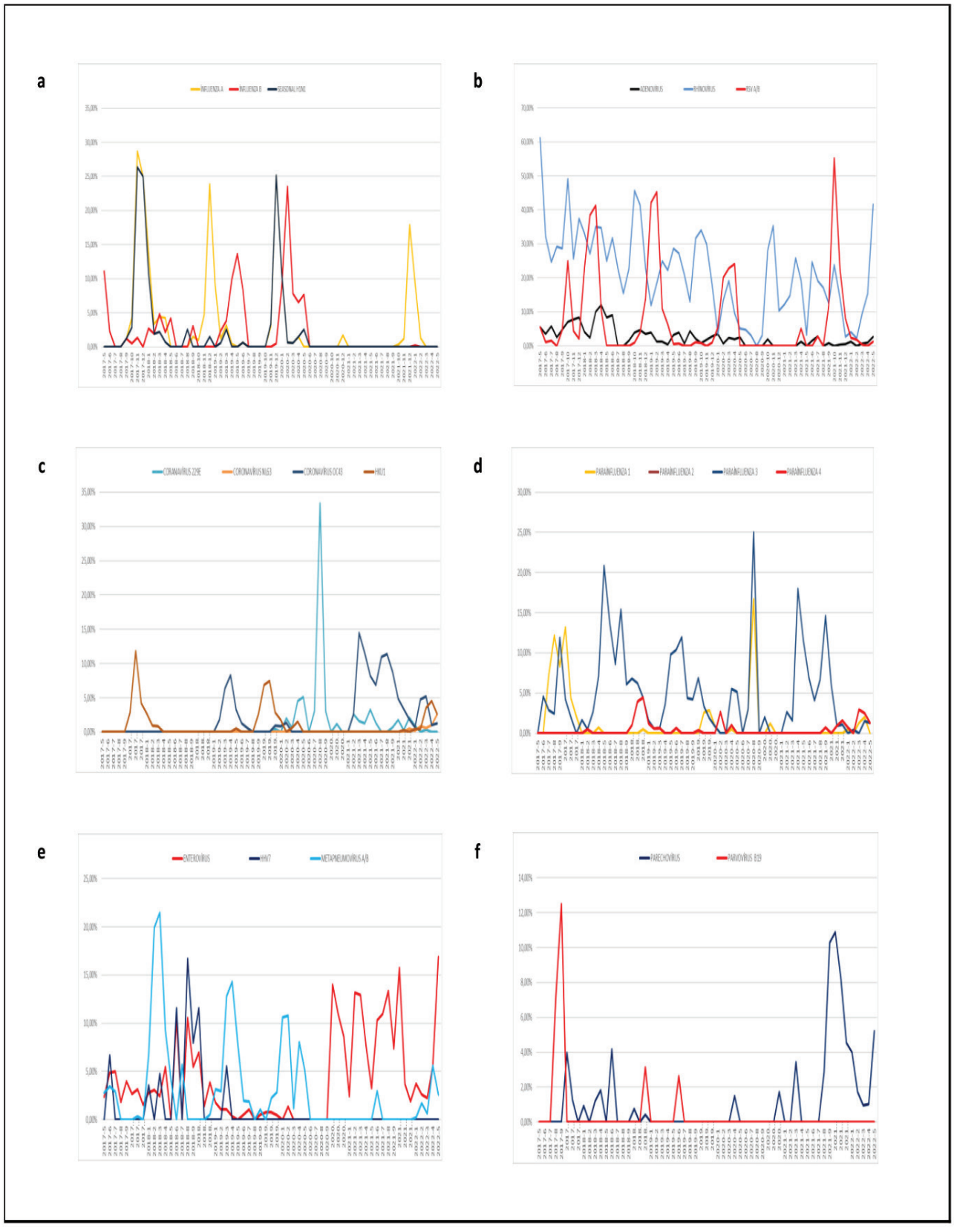

Figure 1. a-f) Incidence of respiratory viruses other than SARS-CoV-2 (May 2017-May 2022)
SARS-CoV-2: Severe acute respiratory syndrome-Coronavirus-2

Table 1. PCR test results for respiratory viruses other than SARS-CoV-2 (May 2017-May 2022)

Viruses	Positive, n (%)	Negative, n (%)	Total
Adenovirus	221 (2.5)	8450 (97.5)	8671
Bocavirus	413 (4.8)	8228 (95.2)	8641
RSV A/B	898 (8)	10346 (92)	11244
Parvovirus B19	5 (0.8)	590 (99.2)	595
Parainfluenza 1/2/3/4	628 (1.8)	34078 (98.2)	34706
Coronavirus 229E/NL63/OC43/HKU1	416 (1.7)	23665 (98.3)	24081
Enterovirus	319 (3.5)	8948 (96.5)	9267
Rhinovirus	1855 (21.4)	6819 (78.6)	8674
Parechovirus	154 (16.7)	9064 (83.3)	9218
HHV7	16 (2.7)	579 (97.3)	595
Metapneumovirus A/B	323 (2.9)	10641 (97.1)	10964
Influenza A/B/Seasonal H1N1	896 (3.9)	22750 (96.1)	23646

PCR: Polymerase chain reaction, SARS-CoV-2: Severe acute respiratory syndrome-Coronavirus-2, RSV: Respiratory syncytial virus

These observed declines indicate a reduction in positivity rates rather than a decrease in the total number of tests conducted for these viruses. Based on our observation, the viruses showing a decline during the pandemic period were INF A/B, seasonal H1N1, HMPV, RSV A/B, and HHV7. No change was observed in the infection rates of parvovirus B19, ADV, and HRV. HCoV 229E and PIV 1/3 peaked between July 2020 and September 2020 (Figure 2). It was found that the positivity rates of parechovirus from March 2020 to May 2022 and EV from September 2020 to May 2022 were higher compared to the pre-pandemic period (Table 2).

Discussion

In our study, we retrospectively evaluated a total of 150,302 tests for respiratory tract viruses, other than SARS-CoV-2, which were sent to Necmettin Erbakan University Meram Medical Faculty Hospital, Medical Microbiology Laboratory between May 2017 and May 2022. While conducting the evaluation, we defined three periods: from May 1, 2017, to March 20, 2020, as the pre-pandemic period; from March 20, 2020, to December 31, 2021, as the pandemic period; and from January 1, 2022, to May 31, 2022, as the last period of the pandemic. In this five-year evaluation, we analyzed monthly test numbers and positivity rates for each respiratory virus across all periods. When comparing the pre-pandemic and pandemic periods, we observed significant changes in the rates of respiratory viruses, other than SARS-CoV-2, during the COVID-19 pandemic. Laboratory tests, including coronaviruses other than SARS-CoV-2, showed that the usual seasonal increase in positivity rates for common respiratory viruses, especially influenza viruses, did not occur during the pandemic period[6]. A similar situation has been demonstrated in a series of studies conducted in Japan, Taiwan, Korea, and Thailand, indicating a significant decrease in influenza virus detection during the COVID-19 pandemic[7-11].

While the pandemic control measures persisted, studies in Australia and New Zealand have indicated the absence of a seasonal peak in the positivity rates of influenza and other respiratory viruses, but rather a significant decrease[12,13]. Compared to the pre-pandemic period, significant declines in INF A/B, seasonal H1N1, HCoV 229E, HCoV HKU1, and HMPV infections were observed during the pandemic period. HCoV 229E peaked between July 2020 and October 2020 in the early stages of the pandemic, INF A peaked between December 2021 and January 2022 and RSV A/B positivity rates peaked between October 2021 and December 2021. It was noted that the INF A and RSV A/B peaks are seasonal infections, occurring in autumn and winter. The decrease in nearly all seasonal respiratory virus infections during the COVID-19 pandemic is largely attributed to the implementation of multiple public health measures, including restriction of international travel, wearing face masks, hand washing, and curfews. While circulating seasonal coronaviruses were not detected during the pandemic period, it is observed that susceptibility to seasonal coronaviruses persists in the population that has recovered from SARS-CoV-2 infection. It is known that antibodies against seasonal HCoV do not protect against SARS-CoV-2 infection[14].

On comparing the pandemic period with the pre-pandemic period, we observed that the five-year course of rhinoviruses, enteroviruses, and adenoviruses remained unchanged despite public health measures implemented to control COVID-19. This can be partially attributed to variations in regional pandemic measures and the intermittent easing of pandemic measures. A study in New Zealand reported that, while there were significant declines in HRV infections with the introduction of the first

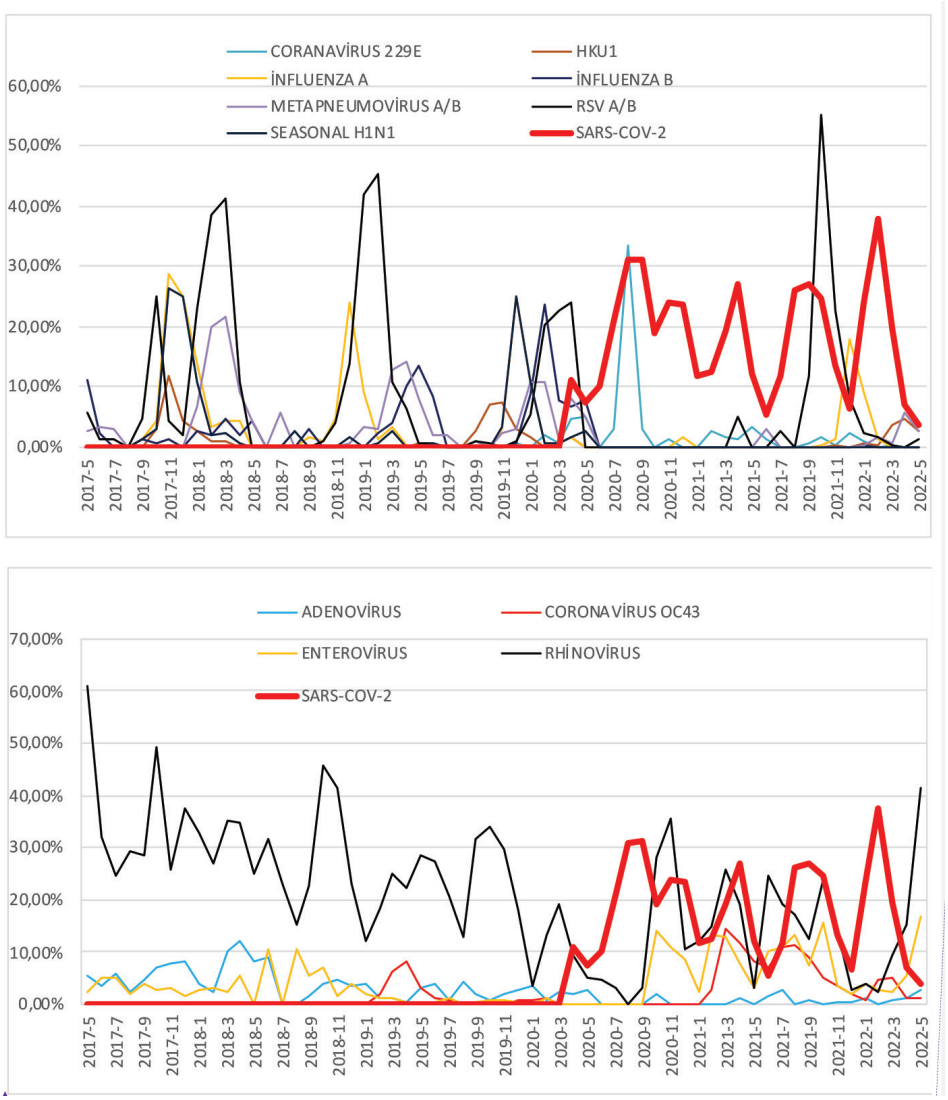

Figure 2. Incidence of respiratory viruses other than SARS-CoV-2 during the pandemic period
SARS-CoV-2: Severe acute respiratory syndrome-Coronavirus-2, RSV: Respiratory syncytial virus

quarantine measures, a significant increase was observed with the easing of restrictions[12]. In Australia and New South Wales, an upsurge in HRV detection was reported in June 2020 within the pediatric population. However, contrary to seasonal expectations, RSV infections showed a significant decline between April 2020 and June 2020[13]. Similarly, following the reopening of schools and childcare centers in Hong Kong, there were multiple outbreaks of acute upper respiratory tract infections, with HRV/EV infections reported as the causative agent[15].

HRV is a non-enveloped virus that is less susceptible to inactivation by handwashing[16,17]. EV can be transmitted fecally/orally. The differences in the transmission mechanism of EV/HRV compared to other seasonal respiratory viruses suggest the need for more stringent measures to reduce transmission of these viruses. The clinical symptom similarity of HRV and EV with those of SARS-CoV-2 is important for the differential diagnosis of COVID-19 cases. Upon analyzing the data obtained in our study, we observed a serious decline in cases and detection rates caused by respiratory viral agents, other than SARS-CoV-2, during the pandemic period. This can be attributed to the comprehensive impact of the measures implemented to prevent the spread of respiratory infections in the COVID-19 pandemic.

Despite the decreasing number of COVID-19 cases from time to time, it has been observed that some viral agents maintain their incidence and occur at similar rates to those in other periods. On the other hand, we can state that the transmission of viruses, such as INF A/B, seasonal H1N1, HCoV 229E, HCoV HKU1, and HMPV, has decreased relatively during the pandemic period. In the context of infectious disease epidemiology, it

Table 2. Pre-pandemic period, pandemic period, and the last period of the pandemic incidences of respiratory tract viruses other than SARS-CoV-2

Viruses	Pre-pandemic period				Pandemic period				Last period of the pandemic				
	Results				Results				Results				
	Negative		Positive		Negative		Positive		Negative		Positive		
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	p
Adenovirus	5250	96.3%	200	3.7%	582	99.5%	3	0.5%	2618	99.3%	18	0.7%	0.000
Bocavirus	5191	95.9%	221	4.1%	563	96.2%	22	3.8%	2474	93.6%	170	6.4%	0.000
Coranavirus 229E	1561	99.2%	13	0.8%	571	97.6%	14	2.4%	2622	99.2%	22	0.8%	0.002
Coranavirus NL63	1543	98.0%	31	2.0%	580	99.1%	5	0.9%	2631	99.5%	13	0.5%	0.000
Coranavirus OC43	2798	98.1%	54	1.9%	562	96.1%	23	3.9%	2541	96.1%	103	3.9%	0.000
Enterovirus	5924	98.0%	120	2.0%	544	93.0%	41	7.0%	2480	94.0%	158	6.0%	0.000
HHV7	579	97.3%	16	2.7%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0.000
HKU1	5299	97.9%	111	2.1%	584	99.8%	1	0.2%	2373	98.9%	26	1.1%	0.000
Influenza A	5112	93.8%	337	6.2%	584	99.8%	1	0.2%	2530	95.7%	114	4.3%	0.000
Influenza B	5237	96.1%	211	3.9%	582	99.5%	3	0.5%	2643	100.0%	1	0.0%	0.000
Metapneumovirus	0	0.0%	0	0.0%	0	0.0%	0	0.0%	2187	99.1%	20	0.9%	0.000
Metapneumovirus A	1543	98.1%	30	1.9%	584	99.8%	1	0.2%	431	99.8%	1	0.2%	0.000
Metapneumovirus B	5181	95.1%	269	4.9%	584	99.8%	1	0.2%	431	99.8%	1	0.2%	0.000
Parainfluenza 1	5373	98.6%	76	1.4%	581	99.3%	4	0.7%	2633	99.6%	10	0.4%	0.000
Parainfluenza 2	5420	99.5%	29	0.5%	585	100.0%	0	0.0%	2616	98.9%	28	1.1%	0.003
Parainfluenza 3	5214	95.7%	236	4.3%	557	95.4%	27	4.6%	2572	97.5%	67	2.5%	0.000
Parainfluenza 4	5336	97.9%	114	2.1%	581	99.3%	4	0.7%	2610	98.8%	33	1.2%	0.003
Parechovirus	5975	99.5%	29	0.5%	570	99.5%	3	0.5%	2519	95.4%	122	4.6%	0.000
Parvovirus B19	590	99.2%	5	0.8%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0.000
Rhinovirus	3995	73.3%	1454	26.7%	486	83.6%	95	16.4%	2338	88.4%	306	11.6%	0.000
RSV A/B	0	0.0%	0	0.0%	0	0.0%	0	0.0%	2052	93.0%	155	7.0%	0.000
RSVA	1510	95.9%	64	4.1%	568	99.6%	2	0.4%	424	97.0%	13	3.0%	0.000
RSVB	4800	88.1%	649	11.9%	568	99.6%	2	0.4%	424	97.0%	13	3.0%	0.000
SARS-CoV-2 N	0	0.0%	0	0.0%	0	0.0%	0	0.0%	2074	95.4%	100	4.6%	0.000
Seasonal H1N1	5221	95.8%	228	4.2%	584	99.8%	1	0.2%	257	100.0%	0	0.0%	0.000

SARS-CoV-2: Severe acute respiratory syndrome-Coronavirus-2, RSV: Respiratory syncytial virus

can be anticipated that the protective measures implemented to mitigate the impact of the pandemic, along with evolving individual-social behavior patterns, will directly impact the spread of respiratory-borne agents.

Study Limitations

This study has some limitations. The distribution of non-SARS-CoV-2 respiratory viruses among different age groups has not been provided. Owing to the absence of post-pandemic data, the distributions of non-SARS-CoV-2 respiratory viruses in children during the post-pandemic period could not be illustrated.

Conclusion

Our results reflect this situation, especially during the normalization process. The impacts of the relative relaxation in the measures taken against the spread of respiratory infections and the documentation of these effects during the pandemic period are important clues for the epidemics that may await us in the future. We believe the data we obtained from a large number of samples, will serve as a guide for managing infection in the current pandemic process and for future experiences.

Ethics

Ethics Committee Approval: The study was approved by the Necmettin Erbakan University of Non-Drug and Non-Medical Device Research Ethics Committee (meeting no: 155, date: 03.06.2022).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.F., Design: K.K., M.Ö., B.F., Data Collection or Processing: M.K., H.K., A.C., Z.T., Analysis or Interpretation: M.K., H.K., K.K., A.C., Z.T., M.Ö., B.F., Literature Search: M.K., Writing: M.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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