



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Letter to the Editor

The impact of COVID-19 on the molecular epidemiology of seasonal viral respiratory infections, Cyprus


Dear Editor,

As a global health problem, the COVID-19 pandemic continues to surge with more than 428 million cases and over 5.9 million deaths reported as of February 2022.¹ The global response aimed at fighting the pandemic, including temporary lockdowns, mask wearing, social distancing, enhanced personal hygiene and reduced travel has had a significant impact on the prevention of new cases and has slowed down local transmission within communities. Importantly, the infection prevention strategies implemented to slow down the spread of COVID-19 has aligned with the strategies used for other common seasonal respiratory viral infections which share the same transmission route.²

We read with interest the systematic review by Fricke et al. which showed that the impact of non-pharmaceutical interventions aimed at COVID-19 pandemic have led to a lower number of influenza cases in the 2019/2020 season compared to former seasons.³ There are several other reports which indicate that the COVID-19 pandemic has affected the incidence of influenza and of infections with other human respiratory viruses such as respiratory syncytial virus (RSV) and rhinovirus.^{4–6} Although there is strong evidence to indicate that the COVID-19 pandemic and the implemented control measures have impacted the rates of other respiratory illnesses that are spread via respiratory droplets and aerosols, data on viral seasonal trends particularly on other often neglected alpha- and betacoronaviruses such as HKU1, NL63, 229E and OC43 are lacking from multiple countries.

In the light of this information, we performed real-time reverse transcription polymerase chain reaction (RT-PCR) on nasopharyngeal samples collected from patients who were admitted to Near East University Hospital in Nicosia, Cyprus with respiratory disease symptoms (fever, cough, rhinitis, sore throat or myalgia) between January 2016 and December 2020. For each patient sample, viral respiratory RT-PCR panel (FTD Respiratory pathogens 21, Fast Tract Diagnostics, Luxembourg) was used on the Rotor-Gene Q (Qiagen, Germany) instrument which detects influenza A virus, influenza A (H1N1) virus, influenza B virus, rhinovirus, human coronaviruses (hCoV) NL63, 229E, OC43 and HKU1 and human RSV A/B. Nucleic acid extraction was performed using GeneAll Ribospin VRD nucleic acid isolation kit following manufacturer's instructions. The number of positive tests in five consecutive seasons, from 2015 to 2016 through 2019–2020, for influenza A/B viruses, RSV, hCoVs and rhinovirus was retrospectively determined in order to demonstrate any fluctuations in the seasonal trends of respiratory viruses following the emergence of SARS-CoV-2. SPSS Version 23.0 (IBM, Armonk, NY) was used for the statistical analysis of the dataset. Chi-

square test was used for the comparison of viral incidences in different groups within the dataset.

The total number of RT-PCR tests performed for the detection of viral respiratory pathogens was 187, 150, 138, 160, and 133 during the periods of 2015–2016, 2016–2017, 2017–2018, 2018–2019 and 2019–2020, respectively. The number of positive cases was 260 (33.9%) for influenza A/B viruses, 143 (18.6%) for RSV, 104 (13.5%) for rhinovirus, and 87 (11.3%) for hCoVs between 2016 and 2020. When average test positivity was compared in the pre- (2015–2019) and post-pandemic (2019–2020) period, a statistically significant reduction was observed in the percent positivity of influenza A/B viruses ($p < 0.001$) as well as hCoVs ($p < 0.001$) in the post-pandemic period (Table 1). Rhinovirus positivity was found to increase in the post-pandemic period ($p < 0.001$), while no major fluctuations were detected in the average test positivity for RSV ($p = 0.068$).

Overall, a decline in influenza A/B infections were observed in the 2019–2020 influenza season compared to all the previous seasons from an average of 35.5% to 19.5%, except during the 2016–2017 season in which a similar rate of positive cases was reported for influenza A/B in Cyprus (Fig. 1). No changes in the influenza peak period were observed after the emergence of SARS-CoV-2 in 2019–2020 with influenza A/B cases peaking in January (epidemiological week 4). The number of positive cases for hCoV (HKU1, NL63, 229E and OC43) and RSV infections declined in 2019–2020 compared to 2018–2019. Overall, a 2-fold decrease was observed in hCoV positivity from an average of 12.3% in all preceding seasons to 6.0% in 2019–2020. Interestingly, a higher number of rhinovirus infections was observed in the 2019–2020 season compared to previous seasons from an average of 12.7% test positivity to 19.5% with a peak in January. However, the number of cases dropped after the implementation of COVID-19 restrictions in March 2020.

The distribution of viral respiratory infections according to patient age and gender between 2016 and 2020 is shown in Suppl. Table 2. While gender statistically had no impact on the rate of infections ($p = 0.963$), rhinovirus, RSV and hCoV infections were more commonly observed in the 0–12 group compared to the ≥ 19 age group, and were particularly low in the 13–18 age group ($p < 0.001$). Co-infections with respiratory viruses were observed in 92 (15.5%) of the positive samples ($n = 594$) (Suppl. Table 3).

Several surveillance teams across the world have reported a changing epidemiology of viral respiratory diseases following the COVID-19 pandemic. In accordance with these data, the prevalence of viral respiratory pathogens in Cyprus has shown a variable trend in the 2019–2020 epidemiological season compared to previous seasons with an overall reduction in reported cases of influenza viruses and endemic (non-SARS-CoV-2) hCoVs. The imposition of strict lock-down measures in Cyprus in the early stages of the pandemic as well as the implementation of face mask use and social distancing in public areas aimed at the containment of COVID-19

Table 1
Test positivity rates in the pre- and post-pandemic period.

| | 2015–2016% | 2016–2017% | 2017–2018% | 2018–2019% | 2019–2020% | Mean 2016–2019 (%) | % Decline in 2019–2020 | p value |
|---------------|------------|------------|------------|------------|------------|--------------------|-------------------------|---------|
| Influenza A/B | 58.3 | 24.7 | 29.7 | 29.4 | 19.5 | 35.5 | 16.0 | <0.001 |
| hCoVs | 13.9 | 12.7 | 8.7 | 13.8 | 6.0 | 12.3 | 6.3 | <0.001 |
| | | | | | | | % Increase in 2019–2020 | |
| Rhinovirus | 17.0 | 9.3 | 19.6 | 15.0 | 19.5 | 12.7 | 6.8 | <0.001 |
| RSV | 10.7 | 19.3 | 22.5 | 23.1 | 19.5 | 18.9 | 0.6 | 0.068 |

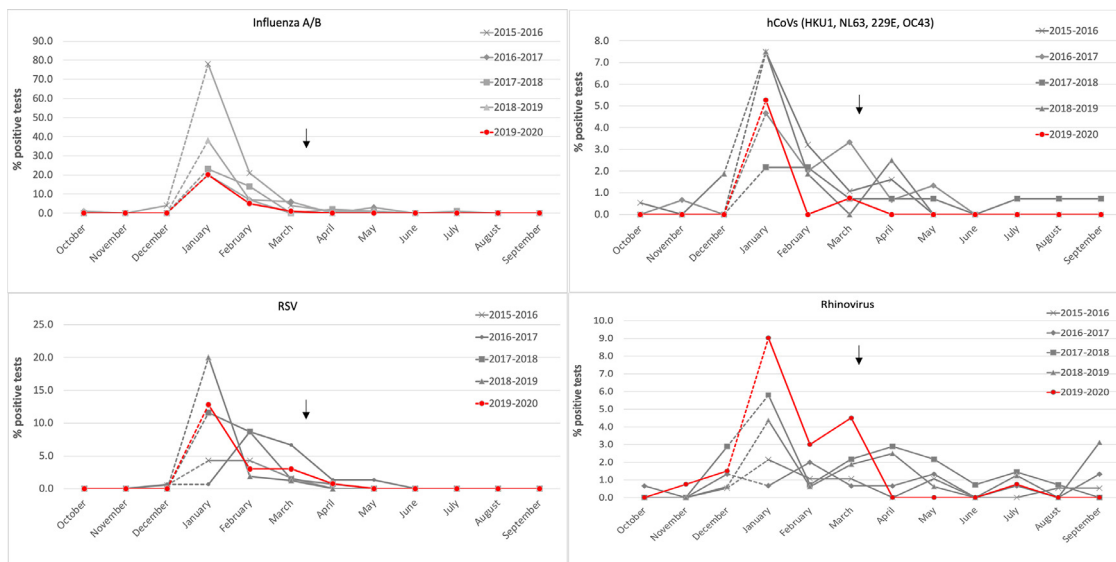


Fig. 1. Trends in positivity rates of viral respiratory infections detected over five consecutive seasons, 2016–2020 (arrows indicate the implementation of COVID-19 lock-down measures).

is likely to have influenced the decline in the rate of infections of non-SARS-CoV-2 respiratory pathogens.⁷ The use of stringent non-pharmaceutical interventions have been effective for the prevention of influenza and other viral respiratory infections in multiple countries together with a marked decline in the number of positive cases after the emergence of SARS-CoV-2.^{8,9}

The reason for the lower number of cases could be either insufficient testing or reporting, yet it can also be attributable to the effectiveness of policies and community mitigation measures such as hygiene measures and social distancing that could have reduced the transmission of SARS-CoV-2 as well as reducing the incidence of influenza and other respiratory pathogens. During the 2019–2020 period, rhinoviruses have become predominant and appeared to be relatively unaffected by the COVID-19 restrictions. Similar to reports from several countries which have demonstrated large spikes of rhinovirus cases when compared to previous years,¹⁰ our data revealed an increase in rhinovirus infections in Cyprus in the post-pandemic period.

This study has the limitation of being retrospective and single-centered, nevertheless, our findings highlight the impact of the COVID-19 pandemic on the circulation of seasonal respiratory viruses and demonstrate a consequent benefit of COVID-19 restrictions, despite their general unpopularity.

Declaration of Competing Interest

All authors declare no competing interests regarding the present study.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics approval

This study was approved by the Institutional Review Board at Near East University (YDU/2021/90–1333) including a waiver of patient consent.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions

AB and BB designed the study and performed the experiments. AB coordinated sampling. BB performed the data analysis. AB and BB drafted the manuscript. All authors have read and approved the manuscript.

Acknowledgments

The authors would like to thank the members of the Near East University Hospital Medical Genetics Laboratory for their help with the collection of the samples used in this study.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jinf.2022.04.008.

References

1. World Health Organization. COVID-19 Weekly Epidemiological Update on COVID-19 - 22 February; 2022. Available Online: <https://www.who.int/>

- [publications/m/item/weekly-epidemiological-update-on-covid-19–22-february-2022access](#). Accessed 25 February 2022.
- Di Wu, Jianyun Lu, Yanhui Liu, Zhoubin Zhang, Lei Luo. Positive effects of COVID-19 control measures on influenza prevention. *Int J Infect Dis* 2020;**95**:345–6. doi:[10.1016/j.ijid.2020.04.009](#).
 - Lara Marleen Fricke, Stephan Glöckner, Maren Dreier, Berit Lange. Impact of non-pharmaceutical interventions targeted at COVID-19 pandemic on influenza burden – a systematic review. *J Infect* 2021;**82**(1):1–35. doi:[10.1016/j.jinf.2020.11.039](#).
 - Sullivan Sheena G, Sandra Carlson, Cheng Allen C, Chilver Monique BN, Dwyer Dominic E, Melissa Irwin, et al. Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020. *Eurosurveillance* 2020;**25**(47). doi:[10.2807/1560-7917.ES.2020.25.47.2001847](#).
 - Takahiro Itaya, Yuki Furuse, Kazuaki Jindai. Does COVID-19 infection impact on the trend of seasonal influenza infection? 11 countries and regions, from 2014 to 2020. *Int J Infect Dis* 2020;**97**:78–80. doi:[10.1016/j.ijid.2020.05.088](#).
 - European Centre for Disease Prevention and Control. COVID-19 situation update for the EU/EEA and the UK, as of 9 December 2020. Available at: <https://www.ecdc.europa.eu/en/cases-2019-ncov-eueea>. Accessed 15 January 2021
 - Nazife Sultanoglu, Buket Baddal, Kaya Suer, Tamer Sanlidag. Current situation of covid-19 in northern cyprus. *East Mediterr Heal J* 2020;**26**(6):641–5. doi:[10.26719/emhj.20.070](#).
 - Sue Huang Q, Tim Wood, Lauren Jelley, Tineke Jennings, Sarah Jefferies, Karen Daniells, et al. Impact of the COVID-19 nonpharmaceutical interventions on influenza and other respiratory viral infections in New Zealand. *Nat Commun* 2021;**12**(1001). doi:[10.1038/s41467-021-21157-9](#).
 - Oster Yonatan Michael-Gayego, Ayelet Rivkin, Mila Levinson, Leonid Wolf, Dana G. Nir-Paz Ran. Decreased prevalence rate of respiratory pathogens in hospitalized patients during the COVID-19 pandemic: possible role for public health containment measures? *Clin Microbiol Infect* 2021;**27**(5):811–12. doi:[10.1016/j.cmi.2020.12.007](#).
 - Nicola Jones. How COVID-19 is changing the cold and flu season. *Nature* 2020;**588**:388–90. doi:[10.1038/d41586-020-03519-3](#).

Buket Baddal*

Department of Medical Microbiology and Clinical Microbiology,
Faculty of Medicine, Near East University, Nicosia, Cyprus
Microbial Pathogenesis Research Group, DESAM Institute, Near East
University, Nicosia, Cyprus

Aysegul Bostanci

Department of Medical Microbiology and Clinical Microbiology,
Faculty of Medicine, Near East University, Nicosia, Cyprus
Medical Genetics Laboratory, Near East University Hospital, Nicosia,
Cyprus

*Corresponding author at: Department of Medical Microbiology
and Clinical Microbiology, Faculty of Medicine, Near East
University, Nicosia, Cyprus.
E-mail address: buket.baddal@neu.edu.tr (B. Baddal)