Reduction and persistence of co-circulating respiratory viruses during the SARS-CoV-2 pandemic

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Title: Reduction and persistence of co-circulating respiratory viruses during the SARS-CoV-2 pandemic

Short Title: Respiratory viruses during COVID-19

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Highlights

- Rhinovirus/enterovirus continued to circulate during the SARS-CoV-2 pandemic.
- No influenza viruses were detected during the study period of 15 January – 15 April 2021.
- COVID-19 mitigation strategies worked to reduce overall respiratory virus circulation but had a larger impact on some viruses versus others.

Abstract

To evaluate co-circulation of respiratory viruses during the SARS-CoV-2 Alpha surge, we performed a molecular respiratory panel on 1,783 nasopharyngeal swabs collected between January 15 and April 15, 2021 from symptomatic outpatients that tested negative for SARS-CoV-2 in North Carolina. Of these, 373 (20.9%) were positive for at least one virus tested on the panel. Among positive tests, over 90% were positive for rhinovirus/enterovirus, either as a single infection or coinfection, illustrating persistent co-circulation of some respiratory viruses despite active infection control measures.

Background

During the COVID-19 pandemic, mitigation strategies have been instituted to decrease SARS-CoV-2 transmission. On an individual level, behaviors such as physical distancing, hand

washing, and masking were adopted while prohibitions on mass gatherings, closing of indoor dining, and shifting students to virtual classrooms were implemented.

A consequence of these measures was a profound decrease in influenza cases. According to the Centers for Disease Control and Prevention, nationwide only 0.2% of respiratory specimens tested positive for influenza virus between September 28, 2020 and May 22, 2021.[1] In contrast, during the previous three influenza seasons peak positivity rates were 26.2-30.3%.[2] This stark reduction in influenza circulation demonstrates the efficacy of mitigation measures to reduce transmission of influenza; however, it is unclear whether the efficacy of these control strategies generalizes to other respiratory viruses ordinarily considered endemic during the period the study was conducted. To determine if other respiratory viruses were also impacted by COVID-19 mitigation approaches, we performed a molecular respiratory pathogen panel on nasopharyngeal (NP) swabs collected from symptomatic patients presenting to a drive thru COVID-19 testing site between January 15 and April 15, 2021 who were negative for SARS-CoV-2.

Materials and Methods

Study site and participants

Symptomatic patients tested for SARS-CoV-2 at the University of North Carolina Hospitals Respiratory Diagnostic Center (RDC) drive thru testing site between January 15 and April 15, 2021 were included.[3] Symptomatic patients were diverted from outpatient clinics to the RDC for testing during the study period. Patients were considered symptomatic if they reported one of the following symptoms: subjective fever, chills, severe fatigue, muscle aches, runny nose, sore throat, loss of taste or smell, cough, shortness of breath, nausea or vomiting, headache, abdominal pain, or diarrhea (≥3 loose stools in 24 hours).

Respiratory panel testing

NP swabs were initially tested for SARS-CoV-2 RNA by either Abbott Alinity m or Abbott m2000 EUA tests. Specimens that were negative and had remnant sample available were tested by a molecular respiratory panel. The BioFire RP 2.0 (bioMerieux, Durham, NC) is an FDA cleared multiplex PCR panel that detects adenovirus, endemic coronaviruses (HKU1, NL63, 229E, OC43), metapneumovirus, rhinovirus/enterovirus, influenza A (A/H1, A/H3, A/H1-2009), influenza B, parainfluenza virus (PIV) 1, PIV2, PIV3, PIV4, respiratory syncytial virus, *Bordetella parapertussis, Bordetella pertussis, Chlamydia pneumoniae,* and *Mycoplasma pneumoniae*. The result of rhinovirus/enterovirus indicates the inability of the molecular panel to differentiate between these closely related viruses. Samples were stored in universal transport media at 4°C if tested within 3 days of collection or frozen at -80°C. Only one swab per patient was included in the study.

Hospital epidemiology data

Results of molecular respiratory testing during January 15 to April 15 in 2019, 2020, and 2021 were collated from outpatients, including emergency department patients, to compare positivity rates.

This study was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

Results

During the study period, 15,149 outpatients were tested for SARS-CoV-2 through the RDC; 5,068 patients were symptomatic, with the remainder being asymptomatic and tested for exposure, prior to travel, or other reasons. Of the symptomatic patients, 433 (8.5%) tested

positive for SARS-CoV-2. Remnant sample was available in the laboratory for 1,783 of the patients with undetectable SARS-CoV-2 RNA for additional testing by the molecular respiratory panel with 373 (20.9%) testing positive for at least one virus. Rhinovirus/enterovirus alone was detected in 329 (18.5%) samples. An additional nine specimens tested positive for rhinovirus/enterovirus and at least one other virus indicating a coinfection (RSV, n=4; adenovirus, n=4; or coronavirus NL63, n=1; Figure 1). Endemic coronaviruses (229E, NL63, OC43) represented 18 single infections and two coinfections (Figure 1). Other viruses detected included adenovirus, RSV, PIV2, PIV3, and metapneumovirus. Influenza viruses and the bacterial targets were not detected in any of the tested specimens.

Patients seen at outpatient facilities during the 2021 study period had 5,459 molecular respiratory tests performed with the largest number being positive for rhinovirus/enterovirus (n=80), followed by RSV (n=17) and adenovirus (n=15) (Figure 2). Influenza viruses were not detected in these patients. In previous years (2019 and 2020) for the period January 15 – April 15 percent positivity was higher across all virus types except rhinovirus/enterovirus and adenovirus. Notably, influenza B had a low level of circulation in 2019.[2] Outpatient respiratory viral testing volumes during the study months for 2019 and 2020 were 4,897 and 7,392, respectively.

Discussion

Although the decrease in transmission of influenza is multifactorial, the implementation of mitigation strategies to decrease SARS-CoV-2 transmission likely played a significant role. The continued detection of rhinovirus/enterovirus and not influenza during the SARS-CoV-2 Alpha surge suggests that the transmissibility of these respiratory viruses differs, as does their ability to be prevented. In comparing the positivity rate of specimens collected from outpatients tested over the same months for the prior three years, the proportion that were positive for

rhinovirus/enterovirus was slightly increased in 2021.This is in contrast to all the other tested viruses that either dropped significantly (influenza, RSV, and others) or stayed the same (adenovirus) (Figure 2). Our observed trend in rhinovirus/enterovirus detections is also mirrored in national syndromic trend data for the same time period.[4]

Our results suggest that while some respiratory viruses, such as influenza, are likely to be mitigated through implementing infection prevention measures such as changes in social behavior, other viruses such as rhinovirus/enterovirus may continue to propagate. Much of the emphasis on COVID-19 mitigation measures has been on preventing respiratory aerosols and droplets from spreading SARS-CoV-2 with relatively less attention paid to transmission that occurs via contaminated surfaces. Enveloped viruses such as influenza and SARS-CoV-2 are readily inactivated by routine disinfectants and hand washing, whereas non-enveloped viruses such as rhinovirus/enterovirus are more refractory to these measures.[5] Therefore, our data may represent the continued transmission of viruses by surfaces during times of enhanced respiratory hygiene (i.e., masking, distancing).

Throughout the COVID-19 pandemic the reduction of non-SARS-CoV-2 respiratory viruses has been demonstrated throughout the world.[6-10] Even though respiratory viruses continued to circulate, the implemented mitigation measures likely helped to limit the spread of the majority of respiratory viruses compared to previous seasons. This finding suggests that the use of non-pharmaceutical prevention measures to reduce the spread of respiratory viruses especially via surfaces should be considered for high-risk institutions such as hospitals and nursing homes during periods of peak community transmission. Overall, these results provide support for adoption of COVID-19 prevention strategies to limit transmission of other respiratory viral pathogens, especially those most vulnerable to adverse clinical outcomes of infection.

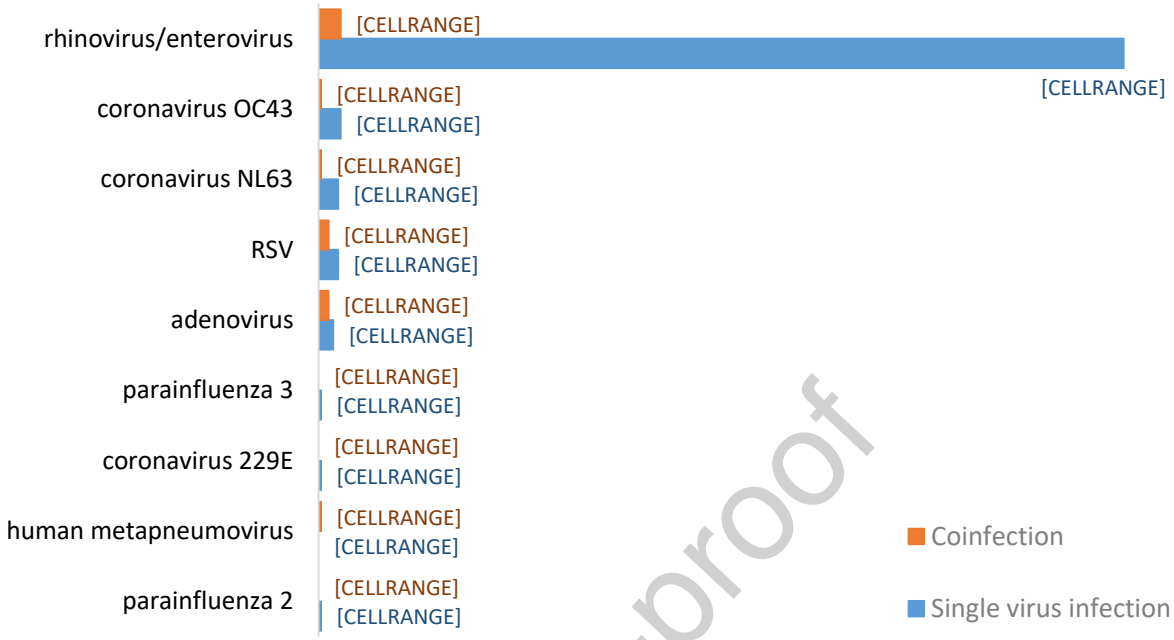

Figure 1

Results from the respiratory pathogen panel for symptomatic outpatients at a COVID-19 testing center who tested negative for SARS-CoV-2 RNA. Number displayed is percent positivity.

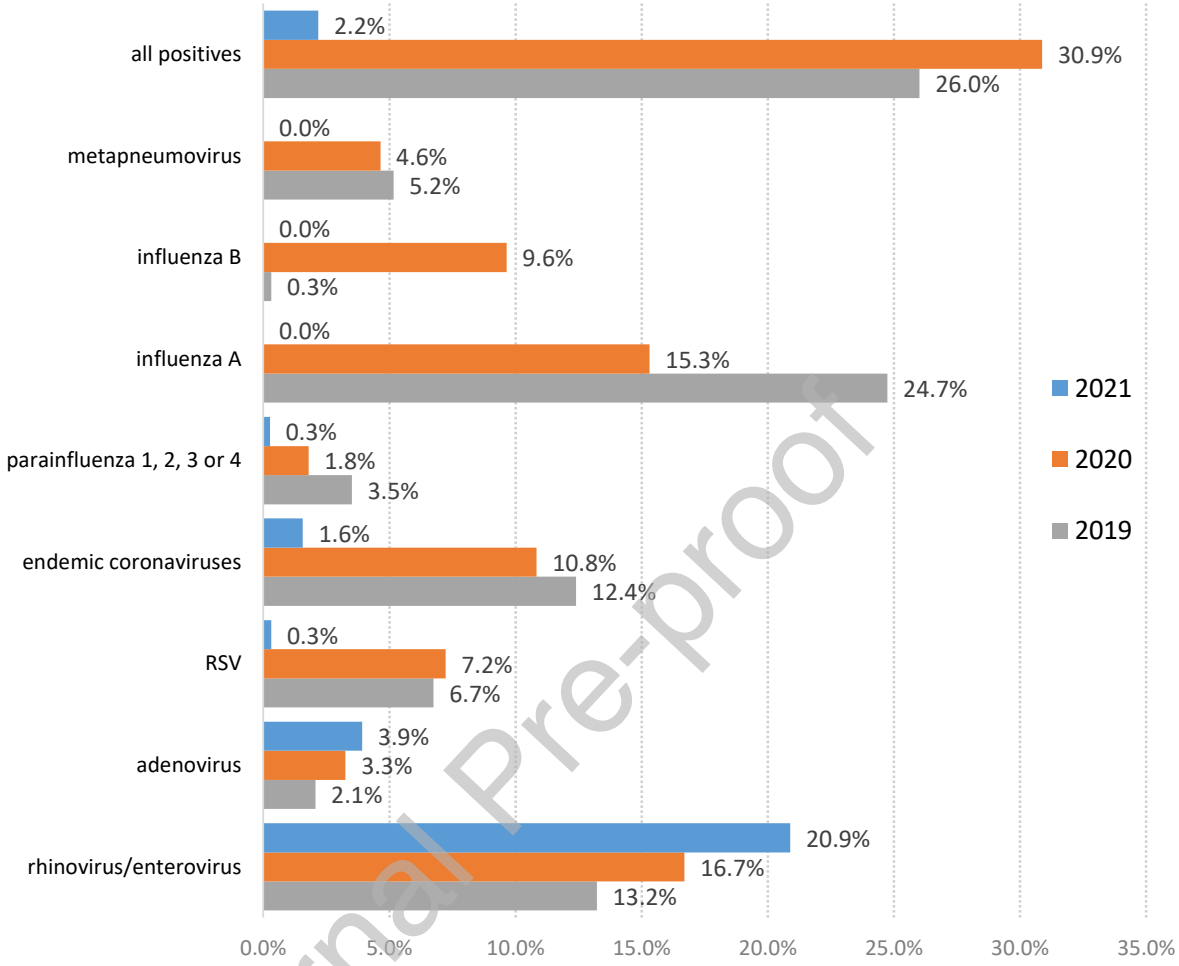

Figure 2

Positivity rates by virus for outpatients tested by a molecular respiratory panel during January 15 to April 15 in 2019, 2020 and 2021. Number displayed is percent positivity.

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