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SARS-CoV-2 coinfection with additional respiratory virus does not predict severe disease: a retrospective cohort study

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Background: The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) claimed over 4 million lives by July 2021 and continues to pose a serious public health threat.

Objectives: Our retrospective study utilized respiratory pathogen panel (RPP) results in patients with SARS-CoV-2 to determine if coinfection (i.e. SARS-CoV-2 positivity with an additional respiratory virus) was associated with more severe presentation and outcomes.

Methods: All patients with negative influenza/respiratory syncytial virus testing who underwent RPP testing within 7 days of a positive SARS-CoV-2 test at a large, academic medical centre in New York were examined. Patients positive for SARS-CoV-2 with a negative RPP were compared with patients positive for SARS-CoV-2 and positive for a virus by RPP in terms of biomarkers, oxygen requirements and severe COVID-19 outcome, as defined by mechanical ventilation or death within 30 days.

Results: Of the 306 SARS-CoV-2-positive patients with RPP testing, 14 (4.6%) were positive for a non-influenza virus (coinfected). Compared with the coinfected group, patients positive for SARS-CoV-2 with a negative RPP had higher inflammatory markers and were significantly more likely to be admitted ($P = 0.01$). Severe COVID-19 outcome occurred in 111 (36.3%) patients in the SARS-CoV-2-only group and 3 (21.4%) patients in the coinfected group ($P = 0.24$).

Conclusions: Patients infected with SARS-CoV-2 along with a non-influenza respiratory virus had less severe disease on presentation and were more likely to be admitted—but did not have more severe outcomes—than those infected with SARS-CoV-2 alone.

Introduction

The novel coronavirus disease 2019 (COVID-19) pandemic has claimed over 4 million lives worldwide as of July 2021 and continues to pose a serious public health threat.[1] Many patients with COVID-19 are also coinfected with additional viruses; however, it remains unclear if coinfection leads to worse clinical outcomes.[2–4] Early in the pandemic, respiratory pathogen panel (RPP) testing was widely used to diagnose severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, the virus that causes COVID-19). Many centres are moving to combined testing for influenza, respiratory syncytial virus (RSV) and SARS-CoV-2 while restricting testing for other non-influenza, non-SARS infections. Therefore, it is critical to ascertain whether non-influenza RPP results may inform clinical decisions and prognosis for patients with SARS-CoV-2.[5,6] To date, there is no literature examining whether SARS-CoV-2 coinfection with a non-influenza respiratory virus leads to different clinical outcomes. To address this gap, we evaluated patients with SARS-CoV-2 infection alone and compared them with patients coinfected with SARS-CoV-2 and an additional non-influenza respiratory viral infection in terms of clinical presentation and severe outcomes in a New York City hospital system during the initial COVID-19 surge in early 2020.

Recent reports suggest coinfection with SARS-CoV-2 and an additional non-influenza virus is possible; however, the effect of this coinfection on clinical outcomes is unclear.[2–4,7–12] Some

authors suggest that viral coinfection generally leads to worse clinical outcomes.[13,14] Patients with respiratory coinfections have been observed to have more complications, severe disease and a higher rate of ICU admissions.[15–20] Contrary to this, other work suggests coinfections do not cause worse disease.[21–28] These varying findings may represent instances of viral interference, when one virus limits the replication of another virus through resource competition or an immunologic pathway.[14]

Given its cost and limited clinical actionability, RPP is not often routinely performed when patients present to the hospital. However, during the initial SARS-CoV-2 surge in New York City, RPP was utilized to a greater degree and was often done simultaneously with SARS-CoV-2 testing, although neither of these tests was permitted until patients had negative influenza and RSV testing, in order to conserve COVID-19 testing resources.[29] The increase in RPP testing, along with the early surge coinciding with the end of the respiratory viral season, provided a unique opportunity to examine SARS-CoV-2-coinfected patients.[30] As more basic syndromic tests include SARS-CoV-2 testing,[5,6] further moving us away from broad-based panels such as RPP, it becomes even more important to understand the significance of coinfection.

Our study utilized the RPP results for patients positive for SARS-CoV-2 to determine if coinfection (i.e. testing positive for SARS-CoV-2 plus a non-influenza respiratory virus) was associated with a more severe presentation or severe outcome, defined as the need for mechanical ventilation or death within 30 days of diagnosis.

Patients and methods

Ethics

This research was conducted in accordance with the Declaration of Helsinki and national and institutional standards. This study was approved by the Albert Einstein Medical School Institutional Review Board (approval number 2020-12023). The Institutional Review Board approved the waiver of informed consent, therefore no informed consent was obtained.

Study design and population

We conducted a retrospective cohort study of all adult (≥18 years old) SARS-CoV-2-positive patients who were also tested for other respiratory viruses via RPP at Montefiore Medical Center (MMC). MMC is a large, multihospital academic medical centre in the Bronx, New York City, with >1400 inpatient beds. During the pandemic, MMC created additional ICU and non-ICU beds as mandated by New York State.[31] SARS-CoV-2 and RPP specimens were obtained in the emergency department or inpatient setting between 11 March and 11 April 2020. We report the results of a severity and outcomes analysis (outcomes cohort) comparing those coinfected versus not, as well as the results of a viral profile analysis (virus cohort) comparing viruses identified in coinfected patients versus those with a non-SARS virus alone during the same time frame. Patients were considered to have entered the cohort at the time of their presentation to the hospital if they had a positive SARS-CoV-2 test within 3 days of presentation.

Testing algorithm

In early March 2020, aligned with regulatory recommendations to seek alternative explanations for respiratory symptoms and due to limited SARS-CoV-2 testing capacity, any patient presenting at MMC with acute respiratory symptoms without an alternative explanation underwent combined influenza and RSV testing.[32,33] If influenza/RSV testing was positive, no additional testing was performed on the patient. Per our institutional recommendation, a negative influenza/RSV test was followed by RPP and simultaneous SARS-CoV-2 testing, usually performed on the same sample. All testing for respiratory illnesses was performed at the providers' discretion.

RPP and SARS-CoV-2 diagnostic testing

RPP testing was performed on-site in our clinical laboratory using the GenMark ePlex RPP assay (Carlsbad, CA) on nasopharyngeal specimens. The GenMark assay detects multiple viruses such as influenza A (H1 and H3), influenza B, RSV A and B, human metapneumovirus (hMPV), enterovirus/rhinovirus, seasonal coronaviruses (229E, HKU1, NL63, OC43), adenovirus and parainfluenza 1–4. SARS-CoV-2 was detected using RT-PCR testing performed on nasopharyngeal specimens using various platforms, as outlined in Figure 1.

Severity and outcomes cohort

All adult (≥18 years old) patients presenting to the emergency department positive for SARS-CoV-2 who had RPP testing between 11 March 2020 and 11 April 2020 were included in the outcomes cohort. The outcomes cohort was divided into two groups: (i) the SARS-CoV-2-only cohort, which included SARS-CoV-2-positive patients with a negative RPP; and (ii) the SARS-CoV-2-coinfected cohort, which included SARS-CoV-2-positive patients who tested positive for at least one viral target on the RPP. SARS-CoV-2 testing and RPP testing occurred within 7 days of each other to represent potential concurrent infection.

Data collection

Demographic data, comorbidities, clinical data and laboratory values including virology results of SARS-CoV-2 testing and RPP testing were extracted from MMC's electronic medical record (Epic, Verona, Wisconsin). Demographic characteristics included age, sex, BMI and race/ethnicity. Comorbidities captured were a history of diabetes or of hypertension.

The primary outcome for the study, which we have called *severe COVID-19* outcome, was defined as any use of mechanical ventilation or death in the 30 days following presentation to the hospital. Admission to the hospital was monitored and, for those patients who were admitted, length of stay was calculated. For those patients discharged before 30 days, any subsequent documentation within 30 days in the electronic medical record system within MMC or other health systems was considered. Laboratory values including white blood cell count, creatinine, ferritin, fibrinogen, D-dimer and C-reactive protein (CRP) were chosen to evaluate disease severity.[34] Oxygen supplementation on presentation was defined as any supplemental oxygen, by any delivery method, documented in the initial 24 h of presentation to the hospital. Because there were no effective therapeutics at the time,[35] data on specific treatments were not assessed.

The SARS-CoV-2-only cohort was compared with the SARS-CoV-2-coinfected cohort in terms of severe disease on presentation—based on biomarkers and oxygen supplementation on presentation—and severe outcome, as defined above.

Viral profile analysis

A second retrospective cohort analysis was performed to determine whether patients with SARS-CoV-2 were infected with different respiratory viruses than patients without SARS-CoV-2. This analysis compared viruses identified by RPP testing in adults who presented to the emergency department or inpatient service at MMC during the same time period (11 March to 11 April 2020) among those who were SARS-CoV-2-positive versus -negative. All viruses identified by RPP in the SARS-CoV-2-coinfected cohort of patients, as outlined in the above methods, comprised the SARS-CoV-2-coinfected group. All viruses identified by RPP during the same

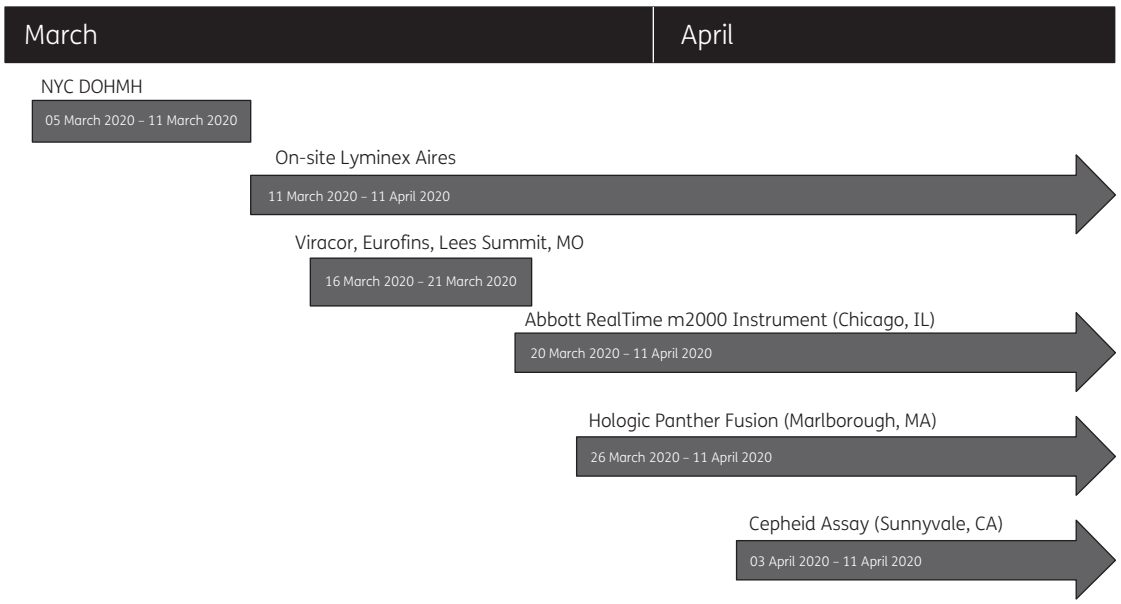

Figure 1. SARS-CoV-2 testing platforms by date of use. Abbreviations: NYC DOHMH, New York City Department of Health and Mental Hygiene; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. Listed testing continued beyond 11 April 2020 (not shown).

timeframe in patients who were SARS-CoV-2-negative within 7 days of RPP testing comprised the SARS-CoV-2-negative group.

Statistical analysis

For the severity and outcomes analysis, the SARS-CoV-2-only group and the SARS-CoV-2-coinfected group were compared in terms of categorical and continuous variables using chi-squared or Student's *t*-test analysis, or the non-parametric alternatives. Means and standard deviations or medians and IQR were reported for continuous variables based on normality. Logistic regression was used to identify any association between RPP positivity and severe outcome. Severe COVID-19 outcome was modelled using RPP coinfection, and the analysis was adjusted using the following variables (chosen *a priori*): age, gender, and hypertension.

The RPP virus analysis compared those viruses in the SARS-CoV-2-coinfected group and those viruses identified by RPP in the SARS-CoV-2-negative group using Chi-squared testing or Fisher's test as appropriate.

Statistical analyses were performed using Stata version 16.1 (StataCorp LLC, College Station, Texas). Statistical significance was determined at a *P* value of <0.05.

Results

Of the 6380 patients with positive SARS-CoV-2 testing from 11 March to 11 April 2020, 306 (5.0%) presented to the emergency department, had negative influenza and RSV test results and had RPP testing performed. Patients positive for SARS-CoV-2 with RPP testing had a median age of 56 years (IQR 43–69), were more likely to be male (52.3%) and Hispanic (38.6%) and had a median BMI of 29.8 (IQR 26.2–33.9) (Table 1). Most patients (60.1%) had a history of hypertension and over one-third (36.0%) had a history of diabetes. Overall, 146 (47.7%) patients received oxygen supplementation within 24 h of presentation and 111 (36.3%) patients met our criteria for severe COVID-19 outcome.

Of the 306 SARS-CoV-2-positive patients with RPP testing, 292 (95.4%) patients had a negative RPP and 14 (4.6%) had a positive RPP. When comparing these two groups, SARS-CoV-2-only patients were older (median age 56 versus 43 years, $P = 0.07$) and more likely to have a history of hypertension (61.0% versus 42.9%, $P = 0.18$) or diabetes (36.6% versus 21.4%, $P = 0.25$) (Table 1). The SARS-CoV-2-only patients had higher inflammatory laboratory markers (including CRP, ferritin, and fibrinogen) than the SARS-CoV-2-coinfected group, though no differences were significant. The SARS-CoV-2-coinfected group was less likely to be admitted to the hospital (42.9% versus 73.6%, $P = 0.01$). The SARS-CoV-2-coinfected group also had shorter length of stay overall (6.9 days versus 16.2 days, $P = 0.80$).

Of those in the SARS-CoV-2-only group, 142/292 (48.6%) patients required oxygen within 24 h of presentation compared with only 4/14 (28.6%) in the SARS-CoV-2-coinfected group ($P = 0.14$) (Figure 2). Severe COVID-19 outcome occurred in 108 (37.0%) patients in the SARS-CoV-2-only group and 3 (21.4%) of the SARS-CoV-2-positive cohort ($P = 0.24$) (Figure 2). In modelling, coinfection was not associated with worse outcomes in either unadjusted analysis (OR 0.46, 95% CI 0.13–1.7, $P = 0.25$) or after adjustment for age, gender, and hypertension (OR 0.62, 95% CI 0.15–2.5, $P = 0.50$).

For the viral profile analysis, 15 viruses in total were identified by RPP from the 14 SARS-CoV-2-positive patients (Table 2). This represented a positive result in 4.9% of all patients tested with RPP (15 of 306 total RPPs sent). In contrast, among the SARS-CoV-2-negative group during the same time period, 88 viruses were identified from 85 patients out of 446 total swabs performed (85/446 RPPs positive, 19.1%); three patients had two viruses identified on each RPP. The most commonly identified viruses on the RPP in SARS-CoV-2-coinfected patients were human coronavirus (identified seven times, 46.6% of viruses) and human rhinovirus/enterovirus (identified four times, 26.7%). Other viruses that were identified concurrent with SARS-CoV-2 included parainfluenza 3 (identified twice, 13.3%), adenovirus (identified once, 6.7%) and

Table 1. Baseline characteristics of patients in the SARS-CoV-2-only group as compared with those in the SARS-CoV-2-coinfected group

Characteristic	Total patients ($n = 306$)	SARS-CoV-2-only patients ($n = 292$)	SARS-CoV-2-coinfected patients ($n = 14$)	*P* value
Age, years, median (IQR)	56 (43–69)	56 (43–69)	43 (30–70)	0.07
Male sex, *n* (%)	160 (52.3)	153 (52.4)	7 (50.0)	0.86
Race/ethnicity, *n* (%)				0.81
Hispanic	118 (38.6)	111 (38.0)	7 (50.0)	
Black	112 (36.6)	108 (37.0)	4 (28.6)	
White	18 (5.9)	17 (5.8)	1 (7.1)	
Other	58 (19.0)	56 (19.2)	2 (14.3)	
BMI, kg/m^2, median (IQR)[a]	29.8 (26.2–33.9)	29.8 (26.2–34.0)	29.5 (25.8–33.3)	0.62
Hypertension, *n* (%)	184 (60.1)	178 (61.0)	6 (42.9)	0.18
Diabetes, *n* (%)	110 (36.0)	107 (36.6)	3 (21.4)	0.25
Laboratory tests[b] (with normal range)				
WBC (4.8–10.8 k/μL)[a]	6.5 (5.0–8.7)	6.5 (5.0–8.8)	6.8 (5.4–8.1)	0.90
Creatinine (<1.50 mg/dL)	1.0 (0.8–1.4)	1.0 (0.8–1.4)	1.0 (0.8–1.3)	0.92
D-Dimer (0.00–0.50 μg/mL)[a]	2.6 (1.0–6.8)	2.6 (1.0–6.7)	2.3 (0.3–9.2)	0.70
CRP (<0.8 mg/dL)[a]	11.0 (4.9–22.1)	11.1 (4.9–22.4)	4.8 (3.1–12.7)	0.12
Ferritin (25–270 ng/mL)[a]	1032 (480–1762)	1032 (477–1788)	923 (512–1672)	0.70
Fibrinogen (187–502 mg/dL)[a]	601 (469–723)	614 (469–728)	470 (464–524)	0.21
Admitted to the hospital, *n* (%)	221 (72.2)	215 (73.6)	6 (42.9)	0.01
Length of stay of admitted patients, days, mean (SD)	13.5 (16.1)	13.6 (16.2)	9.8 (6.9)	0.80
Oxygen supplementation (within 24 h of presentation), *n* (%)	146 (47.7)	142 (48.6)	4 (28.6)	0.14
Severe outcome (mechanical ventilation or death within 30 days of SARS-CoV-2 positivity), *n* (%)	111 (36.3)	108 (37.0)	3 (21.4)	0.24

Abbreviations: WBC, white blood cell; CRP, C-reactive protein; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a]Number of observations available for analysis: BMI, 269; WBC, 276; creatinine, 275; D-dimer, 130; CRP, 168; ferritin, 114; fibrinogen, 89.
[b]All reported as median (IQR).

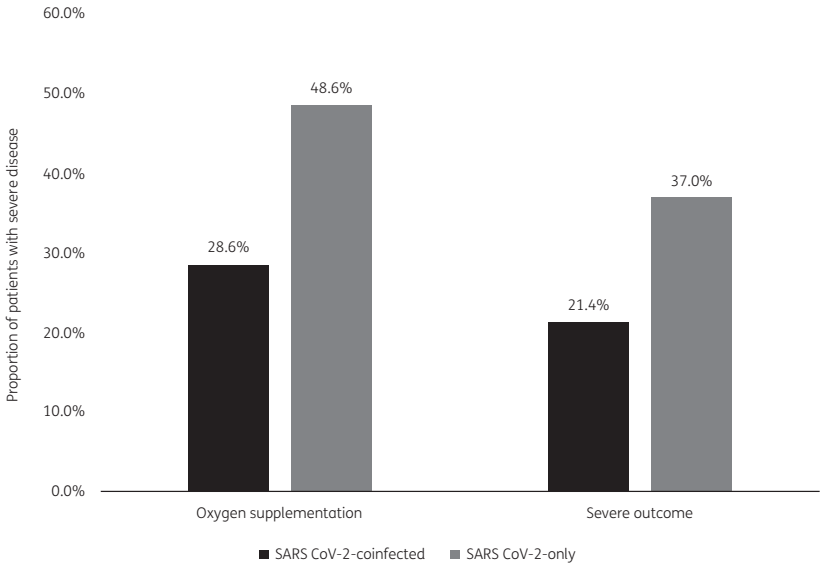

Figure 2. Oxygen supplementation on presentation and severe outcome in the SARS-CoV-2-coinfected group as compared with the SARS-CoV-2-only group (oxygen supplementation comparison $P = 0.14$; severe outcome comparison $P = 0.24$). There were a total of 292 patients in the SARS-CoV-2-only group and 14 patients in the SARS-CoV-2-coinfected group. Oxygen supplementation was defined as being within 24 h of presentation. Severe outcome was defined as mechanical ventilation or death within 30 days of presentation to hospital. Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 2. Comparison of viruses identified on respiratory pathogen panel in SARS-CoV-2-coinfected patients versus SARS-CoV-2-negative patients from 11 March 2020 to 11 April 2020

Virus	SARS-CoV-2-copositive group ($n = 15$)[a]	SARS-CoV-2-negative group ($n = 88$)[a]	*P* value[b]
Human coronavirus, *n* (%)	7 (46.6)	11 (12.5)	**0.001**
Human rhinovirus/enterovirus, *n* (%)	4 (26.7)	39 (44.3)	0.26
Parainfluenza virus 3, *n* (%)	2 (13.3)	2 (2.3)	0.10
Adenovirus, *n* (%)	1 (6.7)	2 (2.3)	0.38
Respiratory syncytial virus B, *n* (%)	1 (6.7)	7 (8.0)	>0.99
Respiratory syncytial virus A, *n* (%)	0	3 (3.4)	>0.99
Human metapneumovirus, *n* (%)	0	11 (12.5)	0.36
Influenza A, *n* (%)	0	8 (9.1)	0.60
Influenza B, *n* (%)	0	4 (4.5)	>0.99
Parainfluenza virus 1, *n* (%)	0	1 (1.1)	>0.99
Parainfluenza virus 2, *n* (%)	0	0	–
Parainfluenza virus 4, *n* (%)	0	0	–

Abbreviations: RPP, respiratory pathogen panel; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus syndrome coronavirus 2.
[a]*n* indicates the number of individual viruses identified on RPP testing. In the SARS-CoV-2-coinfected cohort of patients, 15 viruses were identified on 14 RPP patient samples (one patient had two viruses identified in a single sample). In the SARS-CoV-2-negative cohort of patients, 88 viruses were identified in 85 samples (three patients had two viruses identified on a single sample). Influenza was identified by RPP in 12 patients in the SARS-CoV-2-negative cohort despite being preceded by a negative specific influenza/RSV test.
[b]Comparison was performed using chi-squared or Fisher's exact testing used where appropriate. Statistically significant *P* values are shown in bold.

RSV B (identified once, 6.7%). The most commonly encountered virus on RPP among patients who were SARS-CoV-2-negative was human rhinovirus/enterovirus (identified 39 times, 44.3% of the identified viruses), followed by human coronavirus and human metapneumovirus (each identified 11 times, 12.5%) (Table 2). Notably, there was more human coronavirus seen in patients who were positive for SARS-CoV-2 than those who were negative ($P = 0.001$). No influenza was detected by RPP in those patients positive for SARS-CoV-2. Despite negative results of combined influenza and RSV testing, some patients negative for SARS-CoV-2 were diagnosed with influenza A (8 patients) or B (4 patients) on the RPP test.

Discussion

This retrospective study examined simultaneous RPP along with SARS-CoV-2 testing for all patients presenting at an academic medical centre with respiratory illness who had tested negative for influenza and RSV. We failed to find that coinfection with SARS-CoV-2 and another non-influenza respiratory virus was associated with more severe COVID-19 outcomes. On the contrary, we found that SARS-CoV-2 patients coinfected with another non-influenza respiratory virus had less elevation of inflammatory markers on presentation, were less likely to require oxygen supplementation on admission, were less likely to be admitted to the hospital, and had shorter lengths of stay when they were admitted. In addition, around 4.5% of patients who were positive for SARS-CoV-2 were also positive for a non-influenza virus on RPP. This exploratory analysis of SARS-CoV-2 patients coinfected with a non-influenza respiratory virus was the first study, to our knowledge, to examine clinical outcomes in this group. We found that coinfection was associated with a non-statistically-significant lower frequency of severe COVID-19 outcomes. Taken together, our findings suggest that viral interference may have played a role in mitigating the severity of SARS-CoV-2 infection.

Despite SARS-CoV-2 coinfection with an additional non-influenza virus, coinfected patients did not have higher inflammatory markers, more severe disease on presentation, or more severe COVID-19 outcomes as defined as mechanical ventilation or death within 30 days. We anticipated unfavourable outcomes based on previous research supporting worse outcomes in coinfected patients.[13–19] There are a few possible explanations for the lack of worse outcomes and the better clinical presentation of these coinfected patients. Although there is no statistically significant difference, the SARS-CoV-2-coinfected patients were younger and less likely to have hypertension or diabetes. They also had less elevation of inflammatory markers and were less likely to be admitted to the hospital. It is possible that because they were coinfected, the SARS-CoV-2-coinfected patients could have presented to the emergency department in a less-sick state than patients with SARS-CoV-2 only. However, the examination of viruses identified by RPP among SARS-CoV-2-positive and SARS-CoV-2-negative patients supports the explanation that SARS-CoV-2-coinfected patients were infected with similar non-influenza viruses as the underlying population and may have had similar exposures as the underlying population.[36] More human coronavirus was seen in the SARS-CoV-2-coinfected patients, but this was the only statistically significant difference. Another study from New York City showed a similar elevation in rates of human coronavirus positivity among patients testing positive for SARS-CoV-2.[10] SARS-CoV-2 is not detected by the assays that detect circulating human coronaviruses; therefore, assay overlap should not be the cause of more human coronavirus positivity being detected in those patients with SARS-CoV-2.[37]

Another possible explanation for the lack of worse outcomes in coinfected patients is that viral coinfection leads to viral interference, as was seen in some of the previous work in this area in animal models.[38–41] Viral interference is the process by which one virus limits the replication of another virus, often through resource competition or an immunologic pathway. This interference can suppress the pathogenicity of the second infection. Some early work on influenza coinfection with SARS-CoV-2 also demonstrated no difference in clinical outcomes.[14,42,43] In addition, Lee *et al.*[24] demonstrated no difference in clinical outcomes during the 2003 SARS outbreak in Hong Kong among those with and without nosocomially acquired human metapneumovirus. Based on mathematical modelling of respiratory viruses, it is possible that the competition in viral interference is a matter of speed: the fastest replicating virus outcompetes other viruses for replication materials.[44] Similar models have demonstrated that SARS-CoV-2 likely has a lower growth rate and therefore can be outcompeted by multiple other respiratory viruses, including influenza, rhinovirus and human metapneumovirus.[44] Viral interference may explain why patients testing positive for both SARS-CoV-2 and an additional respiratory virus appear to present with similar symptoms and outcomes.

We identified a difference between SARS-CoV-2-only patients and SARS-CoV-2-coinfected patients in the severity of presentation based on initial inflammatory laboratory values and the proportions of patients who were admitted to the hospital. CRP, ferritin, and fibrinogen were all higher in the SARS-CoV-2-only group. CRP is a marker of inflammation that is distinctly elevated in COVID-19 disease.[45–47] Evidence suggests that high CRP in COVID-19 disease may reflect the severity of the underlying disease and predict responsiveness to steroids.[48] It may even be the biomarker to demonstrate this response to corticosteroid treatment, one of the only therapeutics proven to decrease mortality in severe COVID-19 disease.[49,50]

Our data demonstrated that almost 5% of patients presenting with respiratory illness and positive for SARS-CoV-2 were also coinfected for an additional non-influenza respiratory virus. This estimate is aligned with those found in other healthcare systems during the beginning of the pandemic.[2,4] As our testing capability and technology shifts to combined testing for SARS-CoV-2, influenza and RSV, it is likely that RPP testing will again be limited to its pre-pandemic use in children and immunocompromised adults.[5,6] However, overlooking some coinfected patients misses the opportunity to identify a cohort who have less-severe disease on presentation and may have less-severe outcomes.

There are some limitations to this retrospective cohort study. Firstly, the small population of patients determined to be SARS-CoV-2 coinfected with an additional non-influenza virus. Secondly, we limited the analysis to patients who presented to the hospital, thereby limiting the utility of these findings in outpatients. Thirdly, we did not have information on exposures, symptoms or length of symptoms, or presenting complaint, all of which could be unmeasured confounders. All of the data came from one hospital system, which may have also biased the results. Given the small sample size, we could not adjust for treatment decisions. However, the treatment options were almost universally ineffective early in the pandemic, when this study was conducted.[35] We could not evaluate ICU admission as a possible severe outcome, given the massive bed expansion in the hospital and the routine and emergency use of very high levels of care (i.e. mechanical ventilation and pressor support) in non-ICU settings in our medical centre. Influenza and RSV could not be evaluated in this study, because any patient determined to be positive for these viruses on specific testing was not tested for SARS-CoV-2 or tested with the RPP.

This study demonstrated that patients coinfected with SARS-CoV-2 and another non-influenza respiratory virus had less-severe disease on presentation, were less likely to be admitted to the hospital, and did not have more-severe COVID-19 outcomes than those infected with SARS-CoV-2 alone. Viral interference may be one mechanism explaining these results; further research is needed to clarify the mechanisms by which this might occur. New diagnostics combining testing for SARS-CoV-2, influenza and RSV will likely shift hospitals away from diagnosing the approximately 5% of patients coinfected with other respiratory viruses tested for by RPP. More research into coinfected patients is needed to understand if there is a protective effect of coinfection. However, in an era of pandemic surges and limited resources, health systems could consider using RPP to help risk-stratify patients or could consider pivoting away from broad testing for non-influenza/non-RSV respiratory viruses in patients with proven SARS-CoV-2 infection.

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Transparency declarations

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