



Coinfection in SARS-CoV-2 infected patients: Where are influenza virus and rhinovirus/enterovirus?

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Infection with the new pandemic pathogen severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) can cause a wide range of disease varying from mild cold-like symptoms to complicated pneumonia, severe inflammatory response, and death.¹ Although available data have been limited, recent case reports of concurrent infections with influenza virus,² human metapneumovirus,³ and seasonal coronaviruses such as CoV-HKU-1⁴ in adults and children with SARS-CoV-2 infection have suggested that coinfection may influence morbidity and mortality. A recent study by Kim et al⁵ found that coinfections were frequent in their patient population in Northern California; more than 20% of 116 SARS-CoV-2 positive specimens also contained one or more additional respiratory pathogens, most often rhinovirus/enterovirus, respiratory syncytial virus, and non-SARS Coronaviridae. Conversely, 7.5% of their specimens positive for a non-SARS-CoV-2 respiratory pathogen were also positive for SARS-CoV-2.⁵ In addition, a study from Wuhan examining 8274 patients with 2745 confirmed SARS-CoV-2 cases revealed that 5.8% of SARS-CoV-2 infected and 18.4% of non-SARS-CoV-2-infected patients had coinfections.⁶

To determine whether coinfections with other respiratory pathogens represent a significant subset of SARS-CoV-2 infections in our patient population, we reviewed results from our laboratory, which performs diagnostic testing for eight inpatient and associated outpatient facilities in the greater New York City metropolitan area. During the period from 16 March 2020 through 20 April 2020, our laboratory tested 16 408 patients for SARS-CoV-2 by real-time reverse transcription polymerase chain reaction amplification (cobas 6800 System; Roche Diagnostics); of those, 2049 were also tested with the multiplex FilmArray Respiratory Panel (RPPCR2; BioMerieux) or Cepheid Xpert Xpress Flu/RSV (Flu/RSV). Our findings are notable for high rates of SARS-CoV-2 positivity (54.8%) during that time period, and very low rates of coinfection with other non-SARS-CoV-2 pathogens. Specific data for the detection of other respiratory

pathogens in our SARS-CoV-2 positive patients are presented in Table 1, and compared with findings for patients in whom SARS-CoV-2 was not detected.

Of the 8990 patients who tested positive for SARS-CoV-2, 1204 patient were also tested by RPPCR2 or Flu/RSV, and concurrent infection was found in only 36 patients (2.99%). In comparison, of the 7418 patients who tested negative for SARS-CoV-2, 845 were tested by RPPCR2 or Flu/RSV, and 111 patients (13.1%) were found positive for at least one non-SARS-CoV-2 respiratory viral pathogen. In contrast to patients who tested negative for SARS-CoV-2, in whom the most common respiratory virus coinfections were rhinovirus/enterovirus, influenza viruses, and coronavirus NL63, reflecting the non-SARS-CoV-2 respiratory viruses circulating in our community, non-SARS-CoV-2 Coronaviridae were the most common concurrent respiratory viruses found in specimens from SARS-CoV-2 positive patients.

The mean age of patients tested for SARS-CoV-2 was 55.4 years (60.2 and 49.6 years in the SARS-CoV-2 positive and negative subsets, respectively). The proportion of sexes was 50% female and 50% male overall (44% female and 56% male in the SARS-CoV-2 positive subset, 54% female and 46% male in the SARS-CoV-2 negative subset). Those patients detected SARS-CoV-2 positive with one or more additional respiratory pathogens had a mean age of 60.1 years, and were 56% female and 44% male. Patients detected SARS-CoV-2 negative with one or more additional respiratory pathogens had a mean age of 42.3 years, and were 45% female and 55% male.

Although coinfection with other respiratory viruses appears to be uncommon in patients with SARS-CoV-2 infection in our community, our data do not address whether patients who do develop coinfection experience more severe illness or an otherwise modified disease course. However, our results are in keeping with a recent paper from Spain showing that hospitalized SARS-CoV-2 patients with pneumonia were infrequently coinfecting with other respiratory viruses.⁷

Pathogen	SARS-CoV-2 status					
	Detected			Not detected		
	Tested	Detected	Percent	Tested	Detected	Percent
Influenza	1204	1	0.08	845	13	1.54
Influenza A	1204	1	0.08	845	10	1.18
Influenza B	1204	0	0.00	845	3	0.36
Respiratory syncytial virus	1270	4	0.31	845	13	1.54
Other Coronaviridae	1103	17	1.54	776	28	3.61
Coronavirus NL63	1103	7	0.63	776	16	2.06
Coronavirus HKU1	1103	5	0.45	776	8	1.03
Coronavirus 229E	1103	4	0.36	776	2	0.26
Coronavirus OC43	1103	1	0.09	776	2	0.26
Rhinovirus/Enterovirus	1103	8	0.73	776	46	5.93
Human metapneumovirus	1103	4	0.36	776	15	1.93
Adenovirus	1103	2	0.18	776	3	0.39
Parainfluenza virus	1103	0	0.00	776	4	0.52
Parainfluenza virus 1	1103	0	0.00	776	2	0.26
Parainfluenza virus 2	1103	0	0.00	776	0	0.00
Parainfluenza virus 3	1103	0	0.00	776	2	0.26
Parainfluenza virus 4	1103	0	0.00	776	0	0.00

TABLE 1 Proportions of patients positive for non-SARS-CoV-2 respiratory pathogens by SARS-CoV-2 result

The absence of other respiratory viruses, particularly rhinovirus/enterovirus and influenza virus among our SARS-CoV-2 patients tested for other respiratory pathogens, is particularly interesting in light of the studies suggesting that some viruses,^{8,9} particularly rhinovirus,¹⁰ are able to interfere with the ability of other viruses to establish infection.

Currently, we have little understanding of the viral kinetic parameters of SARS-CoV-2 infection, which makes it difficult to determine the dynamics of coinfection. In addition, the different mechanisms through which viruses elicit immune responses and interactions have been demonstrated to trigger competitive advantage between coinfecting viruses.¹⁰ We hypothesize that competitive advantage may play a role in the SARS-CoV-2 interaction with other respiratory viruses during coinfection, and that perhaps this is one reason why coinfection rate in SARS-CoV-2 patients is much lower. Conversely, disease progression and outcome in SARS-CoV-2 infection are also highly dependent on the host immune response, particularly in the elderly in whom immunosenescence may predispose to increased risk of coinfection.

Additional studies to establish whether simultaneous viral infection in SARS-CoV-2 patients could potentially drive viral interference or influence disease outcome are required.

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