

LETTER TO THE EDITOR

Coinfection with SARS-CoV-2 and other respiratory pathogens in patients with COVID-19 in Guangzhou, China

To the Editor,

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; previously provisionally named 2019 novel coronavirus or 2019-nCoV) disease (COVID-19) in China at the end of 2019 has caused a global pandemic and remains as a major public

health issue.¹ As of 20 May 2020, data from the World Health Organization (WHO) have shown that more than 4735 622 confirmed cases have been identified in 216 countries/regions.² Previous studies have found that the immune system is damaged when the human body is infected with influenza virus, which may lead to

TABLE 1 Baseline characteristics of study population

Characteristic	Total (n = 32)	Coinfection (n = 14)	Noncoinfection (n = 18)	P*
Age, y	52 (41,65)	57 (47,69)	48 (38,59)	.367
Male sex no.(%)	20 (62.5%)	11 (78.6%)	9 (50.0%)	.098
ICU admission	13 (40%)	11 (78.6%)	2 (11.1%)	<.001
Symptom				
Fever	22 (68.8%)	10 (71.4%)	12 (66.7%)	1.000
cough	23 (71.9%)	9 (64.3%)	14 (77.8%)	.453
Expectoration	19 (59.4%)	8 (57.1%)	11 (61.1%)	1.000
Thoracalgia	1 (3.1%)	0	1 (5.6%)	
Rhinobyon/pharyngalgia	4 (12.5%)	1 (7.1%)	3 (16.7%)	
Headache	1 (3.1%)	0	1 (5.6%)	
Dyspnea	12 (37.5%)	8 (57.1%)	4 (22.2%)	.068
Breathlessness	9 (28.1%)	7 (50.0%)	2 (11.1%)	.022
Myalgia	7 (21.9%)	3 (21.4%)	4 (22.2%)	1.000
Fatigue	7 (21.9%)	3 (31.4%)	4 (22.2%)	1.000
Diarrhea	3 (9.4%)	2 (14.3%)	1 (5.6%)	
Conscious disturbance	3 (9.4%)	2 (14.3%)	1 (5.6%)	
Complication				
ARDS	10 (31.3%)	9 (64.3%)	1 (5.6%)	.001
Shock	5 (15.6%)	5 (35.7%)	0	.012
Acute renal injury	6 (18.8%)	5 (35.7%)	1 (5.6%)	.064
Radiographic findings				
GGO only	11 (34.4%)	3 (21.4%)	8 (44.4%)	.025
GGO + consolidation	17 (53%)	11 (78.6%)	6 (33.3%)	
Consolidation	4 (12.5%)	0	4 (22.2%)	
Respiratory support				
No need	7 (21.9%)	1 (7.1%)	6 (33.3%)	.003
Nasal catheter oxygen	12 (37.5%)	2 (14.3%)	10 (55.6%)	
Noninvasive ventilation	3 (9.4%)	3 (21.4%)	0	
Invasive ventilation	6 (18.8%)	4 (28.6%)	2 (11.1%)	
ECMO	4 (12.5%)	4 (28.6%)	0	

Abbreviations: ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation; GGO, ground-glass opacity; ICU, intensive care unit.
*Comparison of clinical characteristics between patients with COVID-19 with and without coinfection.

coinfection of bacteria and even secondary fungal coinfection, with high mortality.³⁻⁶ Cases of coinfection with SARS-CoV-2 and other respiratory pathogens have also been recently reported in China.^{7,8} We herein report 14 cases of COVID-19 coinfecting with other respiratory pathogens and compare the clinical characteristics and laboratory results of patients with COVID-19 with or without coinfection in Guangzhou, China.

In this study, we included 32 confirmed COVID-19 cases between 1 January and 1 March 2020. Demographic, clinical, and radiological features and laboratory data were collected. Pathogenic species in sputum specimens that were collected from 10 to 25 days of onset of symptoms and single sample from each patient, were identified by the reverse transcription polymerase chain reaction and culture. Among these cases, 14 patients were infected with other pathogens, including viral, bacterial, and fungal infections. Five cases were infected with the respiratory syncytial virus (RSV), human parainfluenza virus (HPIV), human metapneumovirus (hMPV), rhinovirus (rRhV), and enterovirus (EV) (Table S1), which are prevalent in children and infants; however, these viruses are also common in adults with immunodeficiency. Whether infections by these viruses were also due to the immunodeficient state of patients with COVID-19 was unclear. Moreover, we found two interesting cases of coinfection with CoV-HKU1 (Table S1), which is a β -coronavirus A strain and has a genome structure that is similar to that of other coronaviruses of the β group, and has been previously reported.^{4,9} This indicates that this subject was simultaneously infected with two different β -group coronaviruses. Ten patients with COVID-19 (31%) were infected with opportunistic pathogenic bacteria, including gram-negative bacteria *Staphylococcus epidermidis*, and *Acinetobacter baumannii*. *Candida albicans* infection was also common among these patients (Table S1). This finding suggests that we need to pay additional attention to the possibility of secondary infections in severe patients and take appropriate measures to prevent the occurrence of this situation.

Our results showed that the proportion of intensive care unit (ICU) patients in patients with COVID-19 with other respiratory pathogen infections was significantly higher than those without other respiratory pathogen infections ($P < .05$) (Table 1). The differences of symptoms between the two groups were manifested mainly in the breathing of patients, and patients with COVID-19 with coinfections presented with more severe difficulty in breathing ($P < .05$) (Table 1). In addition, patients with COVID-19 with coinfection were more likely to have complications such as acute respiratory distress syndrome and shock ($P < .05$) (Table 1). The computed tomography images of patients with COVID-19 with coinfection were more complicated and diverse and were different from those of patients without coinfection.

Further comparison of laboratory results between patients with COVID-19 with and without coinfection showed that lymphocyte and platelet counts of coinfecting patients with the novel coronavirus were significantly lower than those of patients without coinfection ($P < .05$) (Table S2), and lymphocytopenia was identified as a risk factor for coinfection during COVID-19 (Table S3). Since the

outbreak of COVID-19, a significant reduction in lymphocyte counts in peripheral blood has been clinically observed in many cases of COVID-19, which has been listed as one of the laboratory indicators by clinical guidelines.¹⁰⁻¹² A study of 1099 patients with COVID-19 showed that lymphocytopenia was present in 83.2% of the patients on admission.¹³ Lymphocytes play an important role in the body's adaptive immunity against a variety of pathogens. The emergence of lymphocytopenia in patients with COVID-19 results in a state of immunodeficiency, which makes it easier to be coinfecting with other respiratory pathogens, including viruses, bacteria, and even fungi. A recent preprint study showed that human primary peripheral blood monocytes are not susceptible to SARS-CoV-2 because viral replication was not detected in human immune cells. Interestingly, SARS-CoV-2 virus-like particles were observed in primary CD4+ T cells by electron microscopy.¹⁴ Sepsis leads to large amounts of proinflammatory and anti-inflammatory cytokines, which induce reduced lymphocyte apoptosis and chronic immune responses.¹⁵ The cause of the lymphocytic reduction in patients with COVID-19 may be related to the excessive immune response and cytokine storm.

In summary, we must be alert to the occurrence of coinfection in patients with COVID-19, especially in severe ICU patients. Lymphocytopenia may play an important role in the occurrence of coinfection, which deserves additional research to explore its potential mechanisms and the impact on the pathogenesis of patients with COVID-19.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.