

Commentary

Clinical characteristics of patients with multiple respiratory viruses during the COVID-19 pandemic period

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Abstract: Respiratory virus co-infections have been suggested to happen frequently and exacerbate patients' conditions, but little is known about the detailed rates and the combinations of viruses during the COVID-19 pandemic period. A total of 255 symptomatic patients who underwent multiplex PCR tests were analyzed, and it was found that 6 (6/255=2.4%) patients were infected with multiple viruses. The patients ranged in age from 1 to 38 years, and one female patient was pregnant. Of the 6 patients, 4 had fever, and 5 had human rhinovirus/enterovirus and another virus. These data suggested that the rate of respiratory virus co-infection was low, and the combination of SARS-CoV-2 and other viruses was rare even during the COVID-19 pandemic.

Keywords: SARS-CoV-2, Influenza Virus, Co-Infection, Human Rhinovirus/Enterovirus, Parainfluenza Virus 3, Huma Metapneumovirus

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1. Commentary

SARS-CoV-2 appeared in 2019, with COVID-19 becoming a pandemic and a major issue worldwide [1, 2]. During the COVID-19 surge period from December 2019, it was expected that SARS-CoV-2 might circulate with other respiratory viruses, increasing the probability of co-infections, and the clinical outcome of respiratory viral co-infections with SARS-CoV-2 was considered to be worse [3, 4].

In the UK, co-infection with influenza viruses (Flu), respiratory syncytial virus (RSV), or adenoviruses (ADVs) was analyzed in 6965 adults with SARS-CoV-2 infection who were admitted to hospital between February 6, 2020, and December 8, 2021, and co-infection was detected in 583 (8.4%) patients: 227 (3.2%) patients had Flu, 220 (3.2%) patients had RSV, and 136 (2.0%) patients had ADV. [5] Co-infection with influenza viruses was associated with increased odds of receiving invasive mechanical ventilation compared with SARS-CoV-2 infection alone. In addition, SARS-CoV-2 co-infections with Flu were each significantly associated with increased odds of death [5].

In Japan, we also analyzed the cases of co-infection of SARS-CoV-2 with other respiratory viruses during a similar COVID-19 pandemic period, from January 2023 to January 2024, and we found six cases (2.4%) from among the 255 patients who had respiratory symptoms and/or fever and confirmed respiratory virus infection by multiplex polymerase chain reaction (PCR) tests (BIOFIRE® FILMARRAY® Respiratory 2.1, bioMerieux, Lyon, France) (Table 1). There were no cases of co-infection of SARS-CoV-2 with other respiratory viruses, and all six cases survived.

Table 1. Clinical features of six patients co-infected with multiple respiratory viruses

Patient	Age (y.o.)	Male/Female	Underlying diseases	Symptoms	Detected Viruses
1	27	Female	Pregnancy	Fever, Cough, Sore throat	Human Rhinovirus/Enterovirus Parainfluenza virus 3
2	38	Female	None	Nasal discharge, Sore throat	Human Rhinovirus/Enterovirus Parainfluenza virus 3 Influenza A H3
3	12	Male	None	Cough, Headache, Stridor	Human Rhinovirus/Enterovirus Parainfluenza virus 3
4	4	Male	None	Fever, Cough, Sore throat, Fatigue	Influenza A H3 Coronavirus NL63
5	1	Female	None	Fever, Cough, Nasal discharge	Human metapneumovirus Coronavirus HKU1 human
6	15	Male	None	Fever, Cough, Sore throat	Human Rhinovirus/Enterovirus Parainfluenza virus 3

The patients were 1-38 years old; two were over 18 years old, and the other four patients were under 18 years old. The male to female ratio was 3:3, and only one patient had an underlying condition (pregnancy). Most patients were basically healthy; four of six patients had a fever, but all patients had respiratory symptoms. Five of six patients had human rhinovirus (HRV)/enterovirus (HEV) infection and were co-infected with other respiratory viruses, including four parainfluenza 3 (PIV3), two Flu A H3, one Coronavirus NL63, one Coronavirus HKU1 human, and one Human metapneumovirus (HMPV). One case (Case 2) had three viruses, HRV/HEV, PIV3, and Flu A H3. These data suggested that rates of co-infection of respiratory viruses were low, the same as or lower than the results from the UK, and the combination of SARS-CoV-2 with another virus was rare during the COVID-19 pandemic. The most common viruses combined with another respiratory virus were HRV and HEV.

Virus-virus interactions have been analyzed etiologically and experimentally, and it has been suggested that there is no significant relationship between the coronavirus and Flu, but interference was found between HRV/HEV and Flu [6]. Furthermore, there was a synergistic interaction between HRV/HEV and either RSV or PIV3 [6]. These data supported the present data that HRV/HEV increased during the COVID-19 pandemic period, although Flu decreased, and combinations with HRV/HEV and PIV3 dominated in our six co-infection cases. Coronavirus NL63 and Coronavirus HKU1 human were detected with either Flu A H3 (Case 4) or HMPV (Case 5). Flu and HMPV infections were suggested to be independent of coronavirus infections [6] and these co-infection cases might have happened by chance because HRV/HEV [7] and PIV3 [8] were actually increased from our previous etiological studies' data during the COVID-19 pandemic period. Furthermore, it was reported that surges of COVID-19 and influenza were slightly shifted in area and time, and an actual 'twindemic' did not happen all over the world, especially in European countries [9]. These data also supported our study data that there were no co-infection cases of SARS-CoV-2 with Flu.

As a limitation, the present sample was small, and showed a slight difference compared with the UK data. These differences might be affected by the study period: the UK study was performed during the period that the original SARS-CoV-2 Wuhan strains were dominant, but the present data were collected during the Omicron strain-dominant

period. These differences in pathogenesis and infectivity between the original Wuhan and Omicron strains may have led to lower mortality and no cases of SARS-CoV-2 and other respiratory virus co-infections in our study [10].

In conclusion, of the 255 symptomatic patients who underwent multiplex PCR tests during the COVID-19 pandemic era, cases of virus-virus co-infection were analyzed. Only six patients were infected with multiple viruses. Most patients were young and healthy, and combinations of HRV/HEV and other respiratory viruses, such as PIV3, RSV, and Flu, were dominant. These data suggest that co-infections of respiratory viruses were not very common, and there might be no significant synergy/interference between SARS-CoV-2 and other respiratory viruses. A further large study is needed.

Ethics: This study and related analysis were approved by the Institutional Review Board of Saitama Medical University International Medical Center (Hidaka City, Saitama, Japan) on July 06 and December 27, 2022 as #2022-032 and #2022-146, and registered as UMIN000047691. The patients whose specimens were analyzed provided written, informed consent to have any accompanying images and their case details published. This study was performed according to the Declaration of Helsinki.

COI: None

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References

- [1] Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*, 2020. 323: 1061-1069
- [2] Seki M. Trends in the management of infectious disease under SARS-CoV-2 era: From pathophysiological comparison of COVID-19 and influenza. *World J Virol*, 2021.10(2): 62-68.
- [3] Chekani-Azar S, Gharib Mombeni E, Birhan M, Yousefi M. CRISPR/Cas9 gene editing technology and its application to the coronavirus disease (COVID-19). *Journal of Life Science and Biomedicine*. 2020. 10(1): 1-9.
- [4] Gharib Mombeni E, Yousefi M, Chekani-Azar S, Abousenna MS, Arnin K, Shavano F, Emami E, Bahrami Y. Recent drugs and vaccine candidates to tackle COVID-19. *Journal of Life Science and Biomedicine*. 2020. 10(6): 70-9.
- [5] Swets MC, Russel C, Harrison EM, et al. SARS-CoV-2 co-infection with influenza viruses, respiratory syncytial virus, or adenoviruses. *Lancet*, 2022. 399(10334): 1463-1464.
- [6] Nickbakhsh S, Mair C, Matthews, et al. Virus-virus interactions impact the population dynamics of influenza and the common cold. *Proc Natl Acad Sci U S A*, 2019. 116: 27142-27150.
- [7] Watanabe Y, Kamioka Y, Seki M. Rhinovirus-Infected Patients in the COVID-19 Pandemic Period. *Infect Drug Resist*, 2021. 14: 609-611.
- [8] Suzuki J, Endo S, Mizuno T, et al. Use of a multiplex polymerase chain reaction assay for the early detection of an outbreak of human parainfluenza virus type 3 infection in a nursery school during the COVID-19 pandemic. *Infect Prev Pract*, 2022. 4(3): 100221.
- [9] Takashita E, Watanabe S, Hasegawa H, Kawaoka Y. Are twindemics occurring? *Influenza Other Respir Viruses*, 2023. 17(1): e13090.
- [10] Menni C, Valdes AM, Polidori L, et al. Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of omicron and delta variant dominance: a prospective observational study from the ZOE COVID Study. *Lancet*, 2022. 399(10335): 1618-1624.