



Rates of Coinfection Between SARS-CoV-2 and Other Respiratory Viruses in Korea

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Dear Editor,

While the pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has posed an unprecedented challenge to the global healthcare system, the concern about epidemics caused by other pathogens, such as influenza, is increasing [1]. It is well established that infection with one respiratory pathogen makes a patient vulnerable to secondary infections via several mechanisms, including epithelial damage [2]. As coinfection leads to severe clinical manifestations and longer treatment duration, its risks should be accurately estimated. Previous studies have estimated the coinfection rates of other respiratory pathogens in coronavirus disease (COVID-19) patients [3-7]. We estimated the coinfection rates of respiratory viruses in COVID-19 patients in Korea.

This study was approved by the Institutional Review Boards (IRBs) of all four participating institutions in Seoul, Korea: Seoul National University Hospital (SNUH, IRB No. 2009-166-1160), Seoul National University Boramae Medical Center (SNUBM, IRB No. 30-2020-233), National Medical Center (NMC, IRB No. NMC-2012-091), Seoul Medical Center (SMC, IRB No. 2020-04-035-005). Informed consent from patients was not obtained, as this was a retrospective study performed using residual samples. We performed respiratory virus panel testing on residual

samples collected from 504 patients who tested positive for SARS-CoV-2 using emergency use authorization (EUA) assays in Korea (SNUH, NMC, SMC: PowerChek 2019-nCoV Real-time PCR Kit, KogeneBiotech Co., Seoul, Korea; SNUBM: Allplex 2019-nCoV Assay, Seegene Inc., Seoul, Korea) [8]. The number of patients included, sample types collected, and types and numbers of coinfecting viruses are described in Table 1. As both upper and lower respiratory tract samples were available from all patients at NMC and SMC, the total number of samples tested in our study was 748, including 374 each from the upper and lower respiratory tract. The DNA extracted from these samples was stored at 4°C until further use. The average storage duration was 2.8 months (1-5 months). Each sample was tested using the Allplex RV-Essential Assay (Seegene) following the manufacturer's instructions. This assay can detect seven respiratory viruses, including adenovirus, influenza A virus, influenza B virus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, and human rhinovirus.

Adenovirus, human rhinovirus, and metapneumovirus were detected in this study. The coinfection rates determined in the four institutions ranged from 1.3% to 3.3%. Among the 504 patients, coinfection with other respiratory viruses was detected in 11 patients (2.2%). Adenovirus was the most frequently detected

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Table 1. Sample characteristics and SARS-CoV-2 coinfection with other respiratory viruses detected in this study

Institution	Collection period in 2020	Patients N	Patients with coinfection N (%)	Type of sample	Samples collected N	Coinfecting virus N
SNUH	March	37	1 (2.7)	URT	10 (10/0)	
				LRT	27	HRV (1)
SNUBM	June-July	223	3 (1.3)	URT	120 (0/120)	
				LRT	103	AdV (3)
NMC*	March-July	121	3 (2.5)	URT	121 (121/0)	AdV (2) [†] , MPV (1)
				LRT	121	AdV (1) [†]
SMC*	March-July	123	4 (3.3)	URT	123 (81/42)	HRV (2)
				LRT	123	HRV (1), AdV (1)
Total	March-July	504	11 (2.2)	URT	374 (212/162)	AdV (2) [†] , HRV (2), MPV (1)
				LRT	374	AdV (5) [†] , HRV (2)

All URT samples included NPS/NPS+OPS samples, and all LRT samples included sputum samples.

*Both URT and LRT samples were available from all patients; [†]In one patient, adenovirus was identified from both URT and LRT samples.

Abbreviations: SNUH, Seoul National University Hospital; SNUBM, Seoul National University Boramae Medical Center; NMC, National Medical Center; SMC, Seoul Medical Center; URT, upper respiratory tract; LRT, lower respiratory tract; NPS, nasopharyngeal swab; OPS, oropharyngeal swab; AdV, adenovirus; HRV, human rhinovirus; MPV, metapneumovirus.

coinfecting virus and was detected in six patients. Human rhinovirus and metapneumovirus were detected in four patients and one patient, respectively. Adenovirus was detected in both the upper and the lower respiratory tract samples from one patient, where in other patients, coinfections were detected in only one sample. Furthermore, 1.3% (5/374) and 1.9% (7/374) of upper respiratory tract and lower respiratory tract samples were positive for the coinfection, respectively.

Previous studies have reported viral coinfection rates of 0–6.5% [5-7]. Frequently coinfecting viruses were respiratory syncytial virus, human rhinovirus, metapneumovirus, parainfluenza virus, influenza virus, and non-SARS-CoV-2 coronavirus. The coinfection rate in our study was within the reported range [5-7]. However, three factors might have led to an underestimation of the coinfection rate in our study. First, all samples were collected in spring and summer, which follow the outbreak peak of respiratory pathogens, such as seasonal influenza and respiratory syncytial virus. Second, we used a limited target panel due to limited residual sample volumes, which may have contributed to the low coinfection rate, as non-SARS-CoV-2 coronaviruses, which are frequently reported coinfecting viruses in COVID-19 patients [5-7], were not included in the panel. Finally, the nucleic acids may have degraded during storage.

The Korea Disease Control and Prevention Agency compared reported infection rates of respiratory viruses before and after the COVID-19 pandemic [9]. According to the report, the influenza infection rate decreased after the pandemic, probably as a

result of social distancing, whereas the human rhinovirus infection rate increased. The authors reasoned that it was because human rhinoviruses, as non-enveloped viruses, are resilient to environmental changes and because they have a long shedding period. According to the report, the two most frequently detected non-SARS-CoV-2 respiratory viruses during the pandemic were adenovirus and human rhinovirus, which were the most and second-most frequently identified causes of co-infection, respectively.

As coinfection with other viruses is associated with more severe clinical manifestations in COVID-19 patients, the possibility of coinfection should be carefully considered in COVID-19 patient management [3]. In addition, as COVID-19 and other viral illnesses, such as influenza infection, cannot be distinguished based on clinical manifestations, non-SARS-CoV-2 pathogens should be comprehensively considered in the diagnosis of patients with acute respiratory illnesses [10].

In conclusion, we evaluated the rates of coinfection with other respiratory viruses in Korean COVID-19 patients in spring and summer 2020 by testing residual samples. Despite the low coinfection rates, the possibility of coinfection should be carefully considered, and appropriate tests should be instantly performed when deemed necessary.

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AUTHOR CONTRIBUTIONS

Kim YG and Park H performed the experiments and drafted the manuscript. Kim SY and Hong KH analyzed the data. Kim MJ and Lee JS interpreted the data and contributed to the revision of the manuscript. Park SS and Seong MW supervised the study and performed the final revision of the manuscript.

CONFLICTS OF INTEREST

None declared.

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