

SHORT COMMUNICATION

Epidemiologic and Seasonal Trends of Four Endemic Human Coronaviruses in Korea from 2018 to 2024

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ABSTRACT

Background: Human coronaviruses (HCoVs) 229E, NL63, OC43, and HKU1 are globally endemic causes of respiratory tract infections. However, long-term epidemiological data from Korea, particularly after the emergence of COVID-19, remain limited.

Methods: We retrospectively analyzed multiplex real-time reverse transcription PCR (RT-PCR) results for respiratory viruses obtained at a single university hospital between November 2018 and April 2024. The epidemiological patterns of the four common HCoVs were evaluated according to age group and seasonality.

Results: Among 6,914 respiratory samples, HCoVs were detected in 184 patients (101 adults and 83 children). HCoV-OC43 was the most frequently identified subtype in both adults (34.7%) and children (49.4%). Pediatric cases peaked in November-December, whereas adult cases peaked in December-January. A resurgence of HCoV circulation was observed in November 2023, following the COVID-19 pandemic.

Conclusions: Endemic HCoVs continue to circulate in Korea with distinct seasonal and age-related patterns. The reemergence of HCoVs after the COVID-19 pandemic highlights the need for accurate nationwide surveillance and analysis in relation to endemic SARS-CoV-2 to guide respiratory disease management.

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KEYWORDS

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INTRODUCTION

Coronaviruses are single-stranded positive-sense RNA viruses found in humans and various animal species. These viruses are the primary causes of respiratory infections in humans. The seven recognized human coronaviruses (HCoVs) are HCoV-229E, HCoV-NL63, HCoV-OC43, HCoV-HKU1, Middle East respiratory syndrome coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV), and SARS-CoV-2 [1]. HCoV-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1 were the four most common

endemic HCoVs prior to the emergence of SARS-CoV-2, which later became endemic. These four HCoVs generally cause mild upper respiratory tract infections [2]. Common HCoVs can be detected in hospitals using multiplex real-time reverse transcription polymerase chain reaction (RT-PCR) kits for respiratory viruses on nasopharyngeal swab (NPS) specimens. Many studies conducted across countries have reported the detection frequencies and seasonal patterns of these four common HCoVs using multiplex RT-PCR [2-4], and have shown HCoV-OC43 to exhibit the highest prevalence among the four HCoVs, predominantly in winter. The other three viruses (HCoV-NL63, HCoV-229E, and HCoV-HKU1) showed variable frequencies and seasonality, influenced by geographic and epidemiological factors specific to each study location.

As of 2025, in Korea, HCoV-HKU1 can be identified only by the FilmArray Respiratory Panel assay (BioMérieux, Paris, France) among the routinely used clinical RT-PCR kits [5,6]. The most commonly used multiplex RT-PCR kits for respiratory viruses in Korea do not target HCoV-HKU1 but detect only HCoV-OC43, HCoV-NL63, and HCoV-229E [5]. Few studies have investigated the epidemiology of all four common HCoVs in Korea. In this study, we investigated the epidemiology and seasonal patterns of the four common HCoVs spanning both pre- and post-pandemic periods (November 2018 to April 2024) by retrospectively analyzing clinical data from a multiplex RT-PCR assay supplemented with our previous experimental data for HCoV-HKU1 detection [7].

MATERIALS AND METHODS

Patients admitted to Hanyang University Guri Hospital in the capital region of Korea with acute respiratory symptoms between November 1, 2018, and April 30, 2024, were included in this study. These patients underwent multiplex RT-PCR for respiratory viruses to identify the cause of their symptoms. NPS specimens were collected using flocked swabs and transported in 3.0 mL of universal transport medium (Copan Diagnostics, Brescia, Italy). Nucleic acid extraction from the specimens was performed using the EMAG system (BioMérieux, Paris, France), and amplification and detection were performed using the Allplex Respiratory Panel assay kit (Seegene, Seoul, Korea) on a CFX96 Real-Time PCR Detection System (Bio-Rad Laboratories, CA, USA). The Allplex Respiratory Panel assay, the most commonly used multiplex RT-PCR assay for respiratory viruses in Korea, consists of three individual panels that collectively detect 16 respiratory viruses and three distinct subtypes of influenza A virus (H1, H3, and H1pdm09). Among these panels, Respiratory Panel 3 detects and identifies five causative viral pathogens of respiratory tract infection, including HCoV-OC43, HCoV-NL63, HCoV-229E, human bocavirus, and human rhinovirus. However, HCoV-HKU1 was not included in any panel

of the Allplex assay [8]. Allplex assay results, test dates, and patient ages were retrieved from the laboratory information system and analyzed in conjunction with data from the HCoV-HKU1 detection assay.

The frequency of HCoV-HKU1 infection was determined based on data from our previous study, which comprehensively demonstrated that the Allplex assay misidentified HCoV-HKU1 as HCoV-OC43 [7]. The study targeted all cases labeled as HCoV-OC43 by the Allplex assay among patients with acute respiratory symptoms who were admitted to Hanyang University Guri Hospital and tested between November 1, 2018, and April 30, 2024. The Allplex assay results were validated using the PowerChek Coronavirus 229E/OC43/NL63/HKU1 real-time PCR kit (KogeneBiotech, Seoul, Korea) and pan-coronavirus sequencing targeting the RNA-dependent RNA polymerase (RdRp) gene region [8]. Based on the experimental results, cases initially identified as HCoV-OC43 by the Allplex assay were reclassified as either HCoV-OC43 or HCoV-HKU1. The Institutional Review Board of Hanyang University Guri Hospital approved the study protocol (Approval No. 2024-11-018) and waived the requirement for informed consent owing to the retrospective nature of the study. Statistical analyses were performed using Microsoft Excel (version 2021; Microsoft Corporation, Redmond, WA, USA). Monthly epidemiological trends and seasonal patterns were analyzed based on the frequencies of HCoV-NL63 and HCoV-229E from the clinical data, as well as the reclassified frequencies of HCoV-OC43 and HCoV-HKU1.

RESULTS

A total of 6,914 Allplex assays were performed during the study period. Of these, 4,872 were from adult patients and 4,172 were from male patients. The median age of pediatric patients was 2 years (range, 0 - 17 years), whereas the median age of adult patients was 74 years (range, 18 - 106 years). Among the 6,914 tested cases, common HCoVs were detected in 184 patients (101 adults and 83 pediatric patients). The monthly distribution of the four common HCoV species was analyzed (Figure 1). Throughout the study period, HCoV-OC43 was the most frequently identified species in both adult (34.7%, 35/101) and pediatric (49.4%, 41/83) patients. The second most common species was HCoV-NL63 in pediatric patients (32.5%, 27/83) and HCoV-229E in adult patients (31.7%, 32/101). In pediatric patients, the peak frequencies of HCoV-OC43 and HCoV-NL63 were observed from November to December (winter in Korea). Similarly, in adult patients, the peak frequencies were observed from December to January for HCoV-OC43 and HCoV-229E. Comparable frequencies of HCoV-HKU1 were observed in both pediatric and adult patients in the study dataset (10.8% and 9.9%, respectively). During the pandemic, all HCoVs exhibited a decline in frequency and lacked a clear sea-

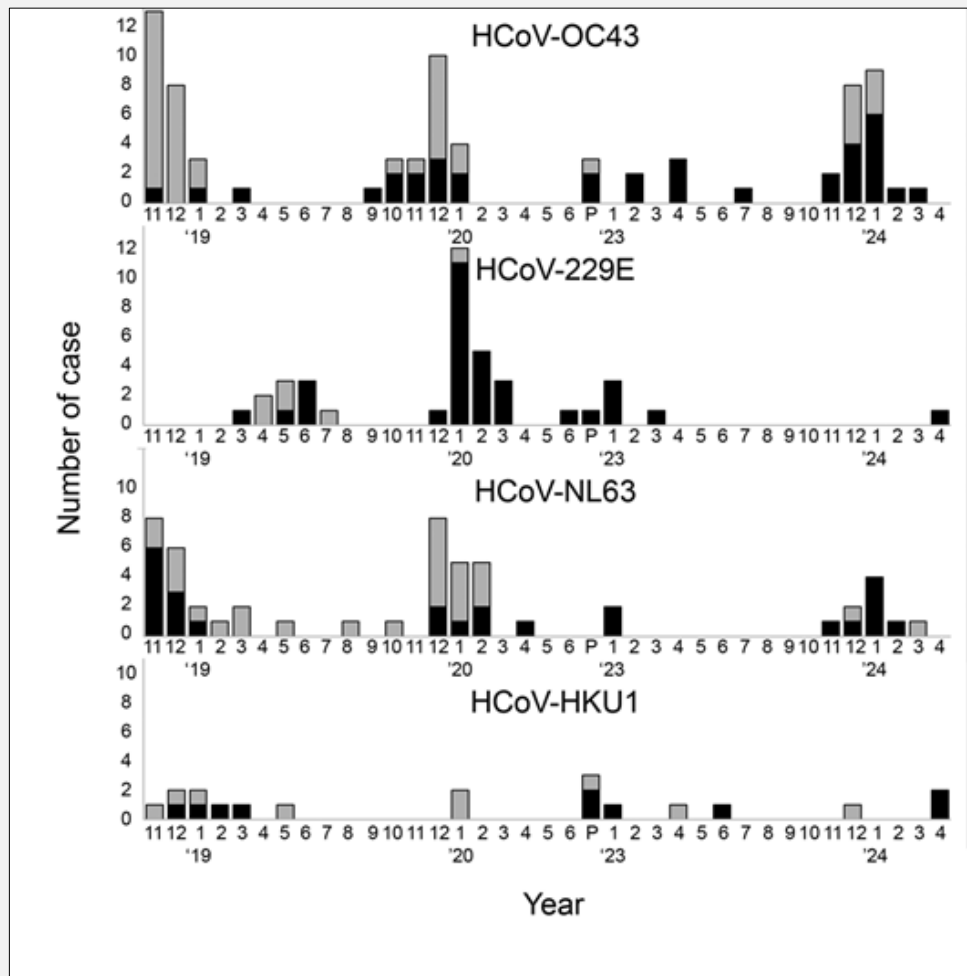


Figure 1. Monthly distribution of four common human coronaviruses among pediatric patients (gray, n = 83) and adult patients (black, n = 101).

Frequencies during the COVID-19 pandemic (July 2020 to December 2022) are condensed into the time interval labeled as 'P'.

sonal pattern. Subsequently, a peak in HCoV-OC43 was observed in both pediatric and adult patients between December 2023 and January 2024, whereas HCoV-NL63 peaked specifically in adult patients. Co-detection of HCoV-OC43 and HCoV-NL63 was observed in one adult patient in January 2024.

DISCUSSION

This study provides updated epidemiological data on the four common HCoVs in Korea, covering both the pre- and post-pandemic periods.

In Korea, one study analyzed the epidemiology and clinical features of common HCoVs in pediatric and

adult patients at five hospitals between January 2018 and March 2020 [9]. HCoV-OC43 and HCoV-NL63 peaked in December 2018 and 2019, respectively. This study analyzed the data obtained using the AdvanSure assay (Invitrogen, Seoul, Korea), the second most commonly used multiplex RT-PCR kit for respiratory viruses in Korea. However, because the assay did not detect HCoV-HKU1, patients infected with HCoV-HKU1 were excluded. During the period overlapping with the present study, our findings were similar, with HCoV-OC43 being the most common species, peaking in November 2018. Although a previous study reported HCoV-NL63 as the most prevalent strain during the winter season of 2019, our study identified HCoV-229E as having the highest peak during the same period, sug-

gesting epidemiological variability even among institutions in Korea.

Another study in Korea investigated four common HCoV using multiplex RT-PCR in pediatric patients from five hospitals between 2015 and 2019 [10]. In that study, the frequency of HCoV-HKU1 was determined using the FilmArray assay, which was performed at only two of the five participating research institutions between September 2018 and November 2019. That study reported 33 cases of HCoV-HKU1, with a peak frequency in April 2019. In comparison, our study detected five pediatric cases of HCoV-HKU1 during the same period but did not observe a distinct seasonal peak.

Multiplex RT-PCR for respiratory viruses is routinely performed in hospitals and is highly effective for generating extensive epidemiological data without incurring additional costs. However, in Korea, the detection of HCoV-HKU1 is limited to less commonly used reagents, and in most hospitals, its frequency can only be determined through additional experiments, making it difficult to generate timely epidemiological data. In this study, the frequency of HCoV-HKU1 used for analysis was based on data from a previous study that identified HCoV-HKU1 in specimens initially labeled as HCoV-OC43-positive using the Allplex assay. However, this approach overlooks HCoV-HKU1 cases that may have been present in HCoV-OC43-negative specimens. Although testing all specimens would yield more accurate data, it would require substantial costs and resources, posing a significant hurdle to the practical implementation of such research. Furthermore, the most widely used RT-PCR assay may overestimate HCoV-OC43 cases, as HCoV-HKU1 accounted for 20% of these cases [7], contributing to the lack of precision in Korea's current epidemiological data. Although common HCoVs do not differ significantly in clinical features, treatment, or prognosis, obtaining accurate nationwide epidemiological data on HCoVs and analyzing them in relation to the now-endemic SARS-CoV-2 may help restructure the healthcare system for better management of respiratory infections in the complex post-COVID-19 era [11].

One limitation of this study is that the frequency of HCoV-HKU1 was assessed only in cases that were initially misidentified as HCoV-OC43. Therefore, the true frequency of HCoV-HKU1 infection is likely to be underestimated. In addition, the clinical characteristics of the patients were not analyzed. As this study was conducted at a single center, further research involving a larger cohort would be valuable for generating more accurate epidemiological data on HCoVs in Korea.

In conclusion, this study provides updated epidemiological and seasonal trends for four endemic HCoVs in Korea. Obtaining accurate nationwide epidemiological data on HCoVs and analyzing them in relation to the now-endemic SARS-CoV-2 are essential for guiding the restructuring of the healthcare system to manage respiratory infections in the post-COVID-19 pandemic era.

Declaration of Interest:

The authors declare no conflict of interest.

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