

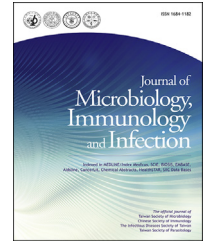


Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

journal homepage: [www.e-jmii.com](http://www.e-jmii.com)

Short Communication

# An outbreak of human Rhinovirus-A21 infection in a psychiatric ward during COVID-19 pandemic

Lung-Chiung Chen <sup>a,c</sup>, Chih-Chien Chiu <sup>b,c</sup>, Fu-Mei Chang <sup>b</sup>,  
 Pei-Yuan Wu <sup>d</sup>, Shu-Li Yang <sup>e,f</sup>, Chung-Guei Huang <sup>e,f</sup>,  
 Yhu-Chering Huang <sup>f,g,\*</sup>

<sup>a</sup> Department of Pediatrics, Taoyuan Armed Forces General Hospital, 325, Taoyuan, Taiwan

<sup>b</sup> Infection Control Office, Taoyuan Armed Forces General Hospital, 325, Taoyuan, Taiwan

<sup>c</sup> Department of Internal Medicine, Taoyuan Armed Forces General Hospital, 325, Taoyuan, Taiwan

<sup>d</sup> Centers for Disease Control, Northern Regional Center, Taoyuan, Taiwan

<sup>e</sup> Department of Laboratory Medicine, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan

<sup>f</sup> School of Medicine, Chang Gung University, 333, Taoyuan, Taiwan

<sup>g</sup> Division of Pediatric Infectious Diseases, Chang Gung Memorial Hospital, 333, Taoyuan, Taiwan

Received 1 November 2021; received in revised form 2 July 2022; accepted 26 July 2022

Available online ■ ■ ■

## KEYWORDS

Outbreak;  
 Rhinovirus-A21;  
 Psychiatric ward;  
 COVID-19

**Abstract** A cluster of acute respiratory illnesses involving 12 inpatients and 3 healthcare workers occurred in a psychiatric ward. Eight of them were identified as HRV-A21. Fever and cough were the most common symptoms. The study also provides further evidence of the impact of HRV on lower respiratory tract illness.

Copyright © 2022, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Human rhinovirus (HRV) causes respiratory illnesses in all age groups throughout the world, and throughout the year,

although most prevalent in the fall and spring in temperate climates.<sup>1</sup> More than 150 serotypes of HRVs have been identified and now divided into three phylogenetic species, HRV-A, HRV-B and HRV-C.<sup>2</sup> The major clinical syndrome

\* Corresponding author. Division of Pediatric Infectious Diseases, Department of Paediatrics, Chang Gung Memorial Hospital, Linkou, No. 5, Fu-Shin Street, Kweishan, 333, Taoyuan, Taiwan. Fax: +886 3 3288957.

E-mail address: [ychuang@cgmh.org.tw](mailto:ychuang@cgmh.org.tw) (Y.-C. Huang).

<https://doi.org/10.1016/j.jmii.2022.07.007>

1684-1182/ Copyright © 2022, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

associated with HRV infection is an upper respiratory illness that is traditionally called as "common cold." Occasionally, HRVs do cause community-acquired pneumonia (CAP) in both children and adults.<sup>3</sup> Hospital outbreaks of HRV infections have been reported in various institutions, including neonatal intensive care units and long-term care facilities.<sup>4,5</sup> However, these outbreaks usually occurred insidiously and continued for a period of weeks and even months.

Since identified in late 2019, coronavirus disease-19 (COVID-19) spread rapidly worldwide soon later in most countries and territories. In Taiwan, a series of strict control policies, strategies as well as infection control measures were implemented by the public health authorities and the hospital settings to contain the pandemic, including strict contact tracing, strict contact isolation regulations, and mandatory mask-wearing when using public transportation, when mass gathering, and in a closed indoor space etc.<sup>6</sup> The measures were even more strict in hospital settings. Thus, as of April 22, 2021, the total laboratory-confirmed case number of COVID-19 was 1086 in Taiwan, among which less than one hundred cases were domestically infected among 24 million citizens.

In March–April 2020, during COVID-19 pandemic, a cluster of respiratory illnesses occurred in the psychiatric wards of a general hospital in northern Taiwan, which was reported to Taiwan Centers for Diseases Control (Taiwan-CDC) once recognized. An investigation was conducted, a series of infection control measures were soon implemented to control the outbreak and the outbreak was turned out to be caused by HRV-A21.

## Methods

### The outbreak

Taoyuan Armed Forces General Hospital is a >700-bed, regional teaching hospital in northern Taiwan. The hospital has one 100-bed ward for chronic diseases and the ward's bed occupancy rate is usually greater than 90%. In March–April 2020, a cluster of acute respiratory illness occurred in the ward. Initially, two female patients suffered from fever and productive cough since March 31 and April 6, respectively, and both of them were subsequently diagnosed as pneumonia. They were immediately transferred to an observation room of the ward, respectively, and received empiric antibiotics. Afterwards, additional 10 patients hospitalized in the same ward developed respiratory symptoms with or without fever between April 8 and April 9. Due to the concern of an outbreak of COVID-19 in this ward, the hospital administrator reported the cluster to the regional authority of Taiwan-CDC on April 9.

### Clinical investigation and intervention

On the same day of notification, the infection control practitioners conducted an investigation for this outbreak. Till April 9, twelve patients and two healthcare workers (HCWs) in the psychiatric ward developed one or more of the following symptoms and/or signs: fever, cough, rhinorrhea, stuffy nose and sore throat since March 31. All of

the patients were isolated in place for droplet and contact precautions immediately. Clinical features including symptoms/signs, results of influenza rapid test and bacterial culture, chest radiography, and antibiotic use were retrospectively extracted from electronic medical records.

### Laboratory investigations

On April 11, the epidemic investigating team from Taiwan-CDC entered the hospital to investigate the outbreak. Two sets of pharyngeal swabs were collected from twelve affected patients for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) screening and testing for a wide range of respiratory viruses, respectively. SARS-CoV-2 screening were performed to detect the nucleic acid of SARS-CoV-2 with real-time reverse transcription-polymerase chain reaction (RT-PCR) in the laboratory designated by Taiwan-CDC.

The Biofire® Filmarray® Respiratory panel (Biomérieux, Marcy l'Etoile, France) was also used for respiratory pathogens detection.

### RT-PCR and sequencing

Consensus-Degenerate Hybrid Oligonucleotide Primer (CODEHOP) PCR primers derived from amino acid sequence motifs which are highly conserved between members of a protein family have proven to be highly effective in the identification and characterization of distantly related family members of some pathogens. The assay was developed for the detection and identification of enterovirus (EV) RNA. A product of the expected size was successfully amplified and sequenced from the prototype EV strains appeared in Taiwan.<sup>7</sup> The assay could also detect and identify other picornaviruses such as human rhinovirus.

### Ethics approval

The study design was approved by the Institutional Review Board of the medical ethical committee of the Tri-Service General Hospital (application no. B202205061). Informed consent was waived because it was an investigation for outbreak of respiratory illnesses and retrospective chart review.

## Results

The manifestations of all 15 affected cases are shown in [Table 1](#). Six were male and 9 were female. Age ranged from 24 to 67 years with a median age of 46.7 years. Cough (N = 11, 73.3%) was the most common symptom. Other common symptoms included fever (N = 7, 46.7%) and rhinitis (N = 6, 40%). Three cases (20%) experienced 3 or more symptoms. Twelve patients underwent influenza rapid test and all results were negative. Ten patients presented new abnormalities in chest X-ray films, and two of them with patch infiltrates were diagnosed as pneumonia and prescribed antibiotics. No bacterial pathogen was identified from sputum culture of these two patients. All the blood cultures obtained were negative for bacteria.

**Table 1** Characteristics of 15 affected cases.

Characteristic	No. (%)
Male, n (%)	6 (40)
Average age in years (range)	46.7 (24–67)
Symptoms, n (%)	
Fever	7 (46.7)
Rhinitis	6 (40)
Pharyngitis	1 (6.7)
Cough	11 (73.3)
Sputum production	3 (20)
3 or more symptoms, n (%)	3 (20)
Patients who had influenza rapid test, n (%)	12 (80)
Number of negative influenza rapid test (%)	12 (100)
Patients who had specimens submitted for any bacterial culture, n (%)	5 (33.3)
Number of positive bacterial cultures	0
Patients who underwent chest radiography, n (%)	14 (93.3)
Number of chest X-rays with new abnormalities <sup>a</sup> (%)	10 (71.4)
Patients who received antibiotics, n (%)	2 (13.3)

<sup>a</sup> Including pulmonary edema, bronchitis, pleural effusion, opacities, and consolidation.

## Laboratory investigations

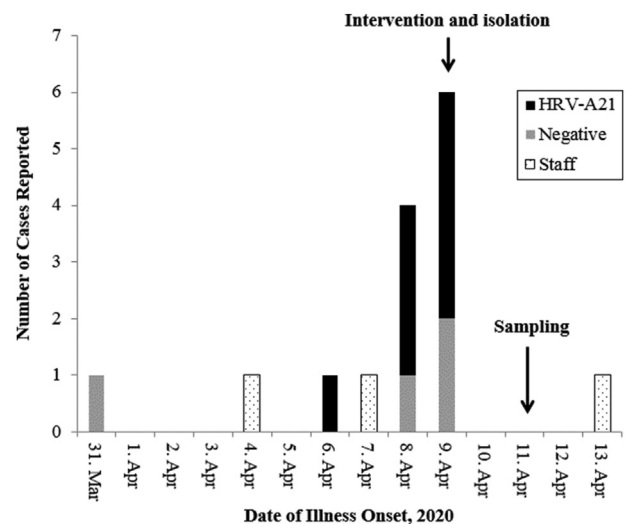
All affected patients screened for SARS-CoV-2 tested negative. Of 12 screened, 8 patients were positive for enterovirus/rhinovirus by the Biofire® Filmarray® Respiratory Panel. Further analysis of the 8 specimens by CODEHOP were performed and demonstrated that the eight specimens were positive for HRV and turned out to be HRV-A21. The other 4 specimens were negative for the designated respiratory pathogens.

## Epidemiological investigation and interventions

Fig. 1 illustrates the epidemiologic curve indicating the dates of onset of HRV-A21 infections, and the dates of intervention and sampling. After infection control interventions were conducted on April 9, no further cases of respiratory symptoms were identified in these wards except one additional nurse student interning in this ward, who presented respiratory symptoms on April 13. The interventions of infection control measures were terminated on April 27, which was the date of identification of the last probable case plus two weeks.

## Discussion

In this report, we described an outbreak of respiratory illnesses caused by HRV-A21 that occurred in a 100-bed psychiatric ward for chronic diseases in northern Taiwan. The outbreak spanned two weeks and consisted of 8 laboratory-confirmed cases and 7 probable cases. The contributing pathogen of confirmed cases was identified as HRV-A21 by



**Figure 1.** Epidemic curve of human rhinovirus-A21 outbreak in a psychiatric ward. Nasopharyngeal swabs were not obtained from the staffs.

RT-PCR and partial viral sequencing. Although the specimens were not obtained from three HCWs, the period of illness onset between confirmed cases and them all corresponded with the incubation period for HRV. Though not virologically confirmed, the seven probable cases, including three cases without samplings and four with negative results, could also be presumed to be caused by HRV-A21, due to the strong epidemiological linkage.

The illness with HRV infection is usually self-limited in healthy people, but can be associated with severe complications in immunocompromised hosts and individuals with underlying heart or lung diseases.<sup>8</sup> The role of specific HRV genotypes in patients with acute respiratory tract infections (RTIs) has been scanty reported. Ren et al.<sup>9</sup> conducted a study in China in 2013 and recruited 147 adult inpatients with community-acquired pneumonia (CAP) and 291 adult outpatients with upper RTIs. HRV was detected in 42 patients and seventeen genotypes were identified. HRV-A21 was detected in four patients with CAP and in five with upper RTIs, the most frequently genotype detected, and was more frequently detected in patients with severe CAP than in those with non-severe CAP and upper RTIs. In current study, the median age of patients with new abnormalities in chest X-ray was 50.5 years and it was older than that of affected cases with upper RTIs. There was no underlying chronic lung disease in these cases with lower RTIs. Both cases with pneumonia recovered without evidence of bacterial complication.

Although some clinical features, particularly loss of smell or taste, are more common in infections with SARS-CoV-2 than with other viruses, there are no specific symptoms or signs that can reliably distinguish COVID-19 from other viral respiratory infections.<sup>10</sup> Recommended infection prevention and control practices are stricter when caring for a patient with suspected or confirmed SARS-CoV-2 infection than other viruses of common colds, including placing patients suitably and using personal protective

equipment at all times. Therefore, immediate intervention and applying a sensitive diagnostic testing for a variety of respiratory viruses should be taken in order to guide more effective control measures when an outbreak of acute respiratory illness is suspected during the pandemic of COVID-19.

## Conclusions

We described an outbreak of HRV-A21, a rarely reported type of HRV, which was rapidly detected by the vigorous interventions because of COVID-19 pandemic. Human rhinovirus is a common cause of mild upper respiratory tract infections and can also result in severe lower respiratory tract illness. The study provided further evidence of the impact of HRV on lower respiratory tract illness.

## Funding

The work was partly supported by grants from Chang Gung Memorial Hospital (CMRPG3K2081, CMRPG3F1372). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

## Declaration of competing interest

The authors declare that they have no competing interests.

## Acknowledgement

Not applicable.

## References

1. Arruda E, Pitkäranta A, Witek Jr TJ, Doyle CA, Hayden FG. Frequency and natural history of rhinovirus infections in adults during autumn. *J Clin Microbiol* 1997;35:2864–8.
2. Kuroda Makoto, ShoichiNiwa, Sekizuka Tsuyoshi, Tsukagoshi Hiroyuki, Yokoyama Masaru, Ryo Akihhide, et al. Molecular evolution of theVP1, VP2, and VP3 genes in human rhinovirus species C. *Sci Rep* 2015;5:8185.
3. Marcos MA, Esperatti M, Torres A. Viral pneumonia. *Curr Opin Infect Dis* 2009;22:143–7.
4. Reid AB, Anderson TL, Cooley L, Williamson J, Mcgregor AR. An outbreak of human rhinovirus species C infections in a neonatal intensive care unit. *Pediatr Infect Dis J* 2011;30. 1096–1068.
5. Longtin J, Winter AL, Heng D, Marchand-Austin A, Eshaghi A, Patel S, et al. Severe human rhinovirus outbreak associated with fatalities in a long-term care facility in Ontario, Canada. *J Am Geriatr Soc* 2010;58:2036–8.
6. Yen MY, Schwartz J, Chen SY, King CC, Yang GY, Hsueh PR. Interrupting COVID-19 transmission by implementing enhanced traffic control bundling: implications for global prevention and control efforts. *J Microbiol Immunol Infect* 2020;53:377–80.
7. Rose Timothy M, Henikoff Jorja G, Henikoff Steven. CODEHOP (COnsensus-DEgenerate Hybrid Oligonucleotide primer) PCR primer design. *Nucleic Acids Res* 2003;31:3763–6.
8. El-Sahly HM, Atmar RL, Glezen WP, Greenberg SB. Spectrum of clinical illness in hospitalized patients with “common cold” virus infections. *Clin Infect Dis* 2000;31:96–100.
9. Ren L, Yang D, Ren X, Li M, Mu X, Wang Q, et al. Genotyping of human rhinovirus in adult patients with acute respiratory infections identified predominant infections of genotype A21. *Sci Rep* 2017;7:41601. <https://doi.org/10.1038/srep41601>.
10. Struyf T, Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Leeflang MM, et al. Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19 disease. *Cochrane Database Syst Rev* 2020;7: CD013665.