Epidemiology of rhinovirus under the COVID-19 pandemic in Guangzhou, China, 2020

Jianyun Lu1 | Tiantian Wu2 | Qing Zeng3 | Yiyun Chen3 | Yanhui Liu3 | Di Wu3

1Director, Guangzhou Baiyun District Center for Disease Control and Prevention, Guangzhou, Guangdong, P. R. China
2Institute of Human Virology | Zhongshan School of Medicine | Key Laboratory of Tropical Disease Control of Ministry of Education, Sun Yat-sen University, Guangzhou, P. R. China
3Department of Biostatistics and Cancer Registration, Guangzhou Center for Disease Control and Prevention, Guangzhou, P. R. China

Correspondence
Di Wu, MPH, Department of Biostatistics and Cancer Registration, Guangzhou Center for Disease Control and Prevention, No. 1, Qide Rd, 510440 Guangzhou, P. R. China.
Email: wudi0729@126.com

Funding information
Natural Science Foundation of Guangdong Province, Grant/Award Number: 2019A1515011407; Guangdong Medical Science and Technology Research Project, Grant/Award Numbers: A2019379, A2020399, B2021244; Medical Science and Technology Project of Guangzhou, Grant/Award Numbers: 20201A011067, 20211A011059

Abstract

Background: To analyze the epidemic characteristics of the human rhinovirus (HRV) outbreaks in Guangzhou, China, in 2020.

Methods: Descriptive epidemiological methods were used to analyze the HRV-related outbreaks in Guangzhou, 2020.

Results: Seventeen outbreaks were reported in 2020 during the coronavirus disease 2019 (COVID-19) pandemic in Guangzhou, a total of 465 patients (290 males and 175 females) were enrolled, with a median age of 10. A total of 223 (47.96%) had been tested for HRV, 89 (39.91%) of which were positive; 344/465 (73.98%) had a fever, 138/465 (29.68%) had a runny nose, 139/465 (29.89%) had a sore throat, 86/465 (18.49%) had a cough, 41/465 (8.82%) had a headache, and 37/465 (7.96%) had a sneeze. Patients at age of 13–15 had the highest rate of sore throat and runny nose, patients aged 11–12 had the highest rate of sneezing, and patients at age of 12–14 had the highest rate of positive rate. Patients tested positive had a higher rate of fever ($\chi^2 = 11.271, p = .001$), cough ($\chi^2 = 6.987, p = .008$), runny nose ($\chi^2 = 7.980, p = .005$), and sneeze ($\chi^2 = 4.676, p = .031$).

Conclusion: The HRV was restored during the fighting of the COVID-19 pandemic. The conventional COVID-19 control measures were not effective enough in preventing rhinovirus. More appropriate control measures should be used to control HRV.

KEYWORDS
coronavirus disease 2019, human rhinovirus, outbreaks, pandemic, severe acute respiratory syndrome coronavirus 2

1 | BACKGROUND

Human rhinoviruses (HRV) are the most common pathogens of the “common cold,” and caused more than half of the “common cold” was caused by HRV.1 HRV was designated as A, B, and C groups, within the genus Enterovirus and the family Picornaviridae.2 The main symptoms of the “cold” caused by HRV infection are low fever, cough, runny nose, and so forth, and was a self-limited disease in most conditions.3 The coronavirus

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2022 The Authors. Immunity, Inflammation and Disease published by John Wiley & Sons Ltd.

Immun Inflamm Dis. 2022;10:e632.
https://doi.org/10.1002/iid3.632
disease 2019 (COVID-19) pandemic has led to an unprecedented level of concern about fever cases. The most common strategy for the control of the unexplained fever event during the COVID-19 pandemic was to test for the nucleic acid of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza virus (IFV); however, we detected and found both SARS-CoV-2 and influenza were negative and proved to be HRV infection finally. Studies have reported that interference among respiratory viruses could affect the infection of the host at a large scale population level,4–6 IFV was the most observed and studied respiratory virus, Wu et al.7 found that rhinovirus disrupted the 2019 influenza A virus (IAV) pandemic in Europe and indicated that the respiratory viral interference can potentially affect the seasonal influenza epidemics and ongoing COVID-19 pandemic. Piret and Boivin8 reported that HRV could reduce the likelihood of coinfection with IAV and reduce SARS-CoV-2 replication in human airway epithelial cells. We analyzed the outbreaks of the HRV infection in Guangzhou, China, during the fight against the COVID-19 pandemic, enhanced the understanding of the prevention and control of rhinovirus outbreaks, and thus provide better evidence for the interference of the respiratory virus during the COVID-19 pandemic, and thus control the pandemic.

2 | METHODS

2.1 | Data and specimen collection

We collected all the information on the fever events of unknown cause during the combatting of the COVID-19 pandemic in Guangzhou, 2020. Throat swabs or nasopharyngeal swabs were taken during all outbreaks of the fever events during the field investigation and were tested in the laboratory of the Guangzhou Center for Disease Control and Prevention.

2.2 | Case definition

The cases enrolled in the study are the ones with one of these symptoms since the first case and before the last case was reported: fever, cough, runny nose, sneezing, or sore throat. If there were more than five cases reported in 3 days in a class should be defined as an outbreak.

2.3 | Etiological detection

During the field investigation, throat swabs were collected from patients who did not take antiviral drugs within 3 days of onset and met the case definition. SARS-CoV-2 and influenza nucleic acid were tested by real-time quantitative polymerase chain reaction within 6 h after the samples were collected, and NxTAG Respiratory Pathogen Panel (LOT: XK051C-1045; Luminex) was used to test for the respiratory polyopathogen nucleic acid. IFV (subtype AH1, AH3), A (H1N1)pdm09, influenza B virus, respiratory syncytial virus (RSV), parainfluenza virus (PIV; 1, 2, 3, 4), bocavirus, human metapneumovirus (HMPV), HRV, adenovirus (ADV), coronavirus (OC43, 229E, HKU-1, NL63), legionella, mycoplasma pneumonia, and chlamydia pneumonia were included. All tests were followed by the manufacturers’ instructions.

2.4 | Statistical analysis

Excel 2019 was used to collect the basic information about the patients in the outbreaks during the field investigation. \( \chi^2 \) test was used for statistical analysis using SPSS statistics (version 13.0), \( p < .05 \) was considered to be significant.

3 | RESULTS

3.1 | General information

Guangzhou is the capital city of Guangdong Province, China, with an 18.6 million population. We have detected 17 outbreaks of HRV in 2020, a total of 465 cases have been reported, of which, 290 were male and 175 were female, with an average age of 11.9 and the median age was 10.

3.2 | Temporal and spatial epidemiology

Of all the 17 outbreaks, six were reported in June, three were reported in July, five were reported in September, one was reported in October, and two were reported in November. All outbreaks were reported in schools, 8 out of 17 were reported in primary school, six were reported in vocational education school, two were in kindergarten, and one in middle school (Table 1).

3.3 | Etiological detection

Of all the 465 cases, 223 (47.96%) had been taken specimens and tested, all negative for SARS-CoV-2 and influenza, of which, 89 (39.91%) were tested positive for HRV without genotyping.
3.4 | Clinical characteristics of the patients in the outbreaks

We collected all the core health indicators of the enrolled patients, such as age, sex, the temperature of the patients, and the symptoms of the patients: cough, sore throat, muscle pain, headache, conjunctival congestion, runny nose, sneezing, diarrhea, and vomit.

We analyzed and found the average age of all the patients is 11.9 ± 5.9 years, and the median age is 10. A total of 290 males and 175 females were enrolled, 344/465 (73.98%) had a record of temperature over 37.3°C, 138/465 (29.68%) had a runny nose, 139/465 (29.89%) had a sore throat, 86/465 (18.49%) had cough, 41/465 (8.82%) had a headache, 37/465 (7.96%) had sneezed, and we found the female patients had a higher rate of having fever and more likely to be tested positive for the HRV test (Table 2). Notably, 7/465 (1.51%) had muscle pain, 5/465 (1.08%) had diarrhea, 1/465 (0.22%) had conjunctival congestion, and 1/465 (0.22%) had vomiting.

We next analyzed the results by age group and found the patients less than 5 years old had the highest rate of having fever, and if the patients had an elder age will have less rate of having a fever, but the patients over 18 had the opposite trend. The patients aged 9–10 had the highest rate of cough. Patients at the age of 13–15 had the highest rate of sore throat and runny nose, patients at the age of 11–12 had the highest rate of sneezing, and patients at age of 12–14 had the highest rate of positive rate (Table 3).

We next found that the tested patients had a statistically lower rate of fever than that of the patients without test ($\chi^2 = 32.563, p < .001$), which might be due to our preference to take specimens of the cases with symptoms such as fever during field investigations. The rest of the clinical characteristics were no statistical difference between the tested and not tested ones (Table 4).

3.5 | Clinical characteristics of virus infections

We next analyzed the clinical characteristics of the patients we tested, and found that there was a higher rate of fever ($\chi^2 = 11.271, p = .001$), cough ($\chi^2 = 6.987, p = .008$), runny nose ($\chi^2 = 7.980, p = .005$), and sneeze ($\chi^2 = 4.676, p = .031$) in the positive ones of the infected (Table 5).

4 | DISCUSSION

The “common cold” was not generally concerned by the general public for the mild symptoms; however, there were more than 250 virus serotypes that could lead to the
As of February 2022, the WHO has identified the SARS-CoV-2 virus as the cause of the COVID-19 pandemic. The SARS-CoV-2 virus is a member of the family Coronaviridae, which is typically characterized by its spike proteins that allow it to attach to host cell receptors. The spike proteins of SARS-CoV-2 are highly conserved, allowing for cross-reactivity with other coronaviruses. However, the SARS-CoV-2 virus has unique characteristics that differentiate it from other coronaviruses, such as its high infectivity and ability to cause a wide range of clinical outcomes.

Primary care providers face numerous challenges in managing COVID-19 patients, including identifying those at risk for severe illness, managing symptoms, and managing comorbidities. The COVID-19 pandemic has also had a significant impact on mental health, with increased rates of anxiety, depression, and suicide.

The COVID-19 pandemic has also had a significant impact on the global economy. The pandemic has led to widespread economic shutdowns, as governments have implemented social distancing measures and lockdowns to control the spread of the virus. These measures have resulted in a significant decrease in economic activity, leading to widespread job losses and a decrease in GDP.

In conclusion, the COVID-19 pandemic has had a significant impact on global health and the economy. The pandemic has highlighted the need for improved global preparedness for future pandemics, as well as the importance of international collaboration in responding to such events.

Our previous studies have shown that the SARS-CoV-2 virus is highly contagious and can be transmitted through respiratory droplets. However, there is still much to learn about the transmission dynamics and the effectiveness of different control measures.

The COVID-19 pandemic has also highlighted the importance of research into new antiviral treatments and vaccines. While vaccines are currently available, there is still a need for new treatments to manage COVID-19 and prevent the spread of the virus.

In summary, the COVID-19 pandemic has had a significant impact on global health and the economy. The pandemic has highlighted the need for improved global preparedness for future pandemics, as well as the importance of international collaboration in responding to such events.

TABLE 3  Age-specific clinical characteristics of the patients.

| Age  | Total cases | Fever N (%) | Cough N (%) | Sore throat N (%) | Runny nose N (%) | Sneeze N (%) | HRV test |
|------|-------------|-------------|-------------|------------------|-----------------|-------------|----------|
| <5   | 54          | 49 (90.74)  | 4 (7.41)    | 4 (7.41)         | 0 (0)           | 0 (0)       | 36 (67)  |
| <8   | 82          | 62 (75.61)  | 7 (8.54)    | 20 (24.39)       | 28 (34.15)      | 5 (6.1)     | 50 (60)  |
| <10  | 79          | 56 (70.89)  | 28 (35.44)  | 32 (40.51)       | 35 (44.3)       | 13 (16.56)  | 30 (38)  |
| <12  | 47          | 32 (68.09)  | 6 (12.77)   | 21 (44.68)       | 20 (42.55)      | 9 (19.15)   | 17 (36)  |
| <15  | 25          | 15 (60.00)  | 7 (28.00)   | 13 (52.00)       | 13 (52.00)      | 4 (16.00)   | 12 (48)  |
| <18  | 42          | 21 (50.00)  | 16 (38.1)   | 12 (28.57)       | 18 (42.86)      | 3 (7.14)    | 14 (33)  |
| <20  | 72          | 53 (73.61)  | 10 (13.89)  | 16 (22.22)       | 14 (19.44)      | 0 (0)       | 35 (49)  |
| ≥20  | 64          | 56 (87.5)   | 8 (12.5)    | 21 (32.81)       | 10 (15.36)      | 3 (4.69)    | 48 (75)  |
| Total| 465         | 344 (73.98) | 86 (18.49)  | 139 (29.89)      | 138 (29.68)     | 37 (7.96)   | 242 (52) |

Abbreviation: HRV, human rhinovirus.

*The patients with a body temperature ≥37.3°C are defined as having fever.
*The percentage was the positive rate of the tested patients.
TABLE 4  The clinical characteristics of the patients in the outbreaks.

|               | HRV tested | Without HRV tested | $\chi^2$ | $P$  |
|---------------|------------|--------------------|----------|------|
| **Age**      |            |                    |          |      |
| Average      | 11.94      | 11.86              |          |      |
| **Sex**      |            |                    |          |      |
| Male         | 144 (64.6) | 146 (60.3)         | 0.890    | .345 |
| Female       | 79 (35.4)  | 96 (39.7)          |          |      |
| **Fever**    |            |                    |          |      |
| No           | 128 (38.1) | 36 (14.9)          | 32.563   | <.001|
| Yes          | 95 (61.9)  | 206 (85.1)         |          |      |
| **Cough**    |            |                    |          |      |
| No           | 188 (84.3) | 191 (78.9)         | 2.228    | .136 |
| Yes          | 35 (15.7)  | 51 (21.1)          |          |      |
| **Sore throat** |         |                    |          |      |
| No           | 165 (74.0) | 161 (66.5)         | 3.084    | .079 |
| Yes          | 58 (26.0)  | 81 (33.5)          |          |      |
| **Muscle pain** |        |                    |          |      |
| No           | 222 (99.6) | 236 (97.5)         | 3.228    | .072 |
| Yes          | 1 (0.4)    | 6 (2.5)            |          |      |
| **Headache** |            |                    |          |      |
| No           | 205 (91.9) | 219 (90.5)         | 0.296    | .586 |
| Yes          | 18 (8.1)   | 23 (9.5)           |          |      |
| **Conjunctival congestion** | |          |          |      |
| No           | 223 (100.0)| 241 (99.6)         | 0.923    | .337 |
| Yes          | 0 (0)      | 1 (0.4)            |          |      |
| **Runny nose** |         |                    |          |      |
| No           | 161 (72.2) | 166 (68.6)         | 0.722    | .396 |
| Yes          | 62 (27.8)  | 76 (31.4)          |          |      |
| **Sneeze**   |            |                    |          |      |
| No           | 202 (90.6) | 226 (93.4)         | 1.247    | .264 |
| Yes          | 21 (9.4)   | 16 (6.6)           |          |      |
| **Diarrhea** |            |                    |          |      |
| No           | 221 (99.1) | 239 (98.8)         | 0.128    | .720 |
| Yes          | 2 (0.9)    | 3 (1.2)            |          |      |
| **Vomit**    |            |                    |          |      |
| No           | 222 (99.6) | 242 (100)          | 1.088    | .297 |
| Yes          | 1 (0.4)    | 0 (0)              |          |      |

Abbreviation: HRV, human rhinovirus.

---

TABLE 5  The clinical characteristics of the HRV-tested patients in the outbreaks.

|                | Negative | Positive  | $\chi^2$ | $P$  |
|----------------|----------|-----------|----------|------|
| **Age**        |          |           |          |      |
| Average        | 11.03    | 13.4      |          |      |
| **Sex**        |          |           |          |      |
| Male           | 91 (67.9)| 53 (59.6) | 1.634    | .201 |
| Female         | 43 (32.1)| 36 (40.4) |          |      |
| **Fever**      |          |           |          |      |
| No             | 63 (47.0)| 22 (24.7) | 11.271   | .001 |
| Yes            | 71 (53.0)| 67 (75.3) |          |      |
| **Cough**      |          |           |          |      |
| No             | 120 (89.6)| 68 (76.4) | 6.987    | .008 |
| Yes            | 14 (10.4)| 21 (23.6) |          |      |
| **Sore throat**|          |           |          |      |
| No             | 105 (78.4)| 60 (67.4) | 3.328    | .068 |
| Yes            | 29 (21.6)| 29 (32.6) |          |      |
| **Muscle pain**|          |           |          |      |
| No             | 133 (99.3)| 89 (100)  | 0.667    | .414 |
| Yes            | 1 (0.7)  | 0 (0)      |          |      |
| **Headache**   |          |           |          |      |
| No             | 125 (93.3)| 80 (89.9) | 0.831    | .362 |
| Yes            | 9 (6.7)  | 9 (10.1)   |          |      |
| **Conjunctival congestion** | |          |          |      |
| No             | 134 (100)| 89 (100)  |          |      |
| Yes            | 0 (0)    | 0 (0)      |          |      |
| **Runny nose** |          |           |          |      |
| No             | 106 (79.1)| 55 (61.8) | 7.980    | .005 |
| Yes            | 28 (21.9)| 34 (32.8) |          |      |
| **Sneeze**     |          |           |          |      |
| No             | 126 (94.0)| 76 (85.4) | 4.676    | .031 |
| Yes            | 8 (6.0)  | 13 (14.6)  |          |      |
| **Diarrhea**   |          |           |          |      |
| No             | 133 (99.3)| 88 (98.9) | 0.086    | .770 |
| Yes            | 1 (0.7)  | 1 (1.1)    |          |      |
| **Vomit**      |          |           |          |      |
| No             | 133 (99.3)| 89 (100)  | 0.667    | .414 |
| Yes            | 1 (0.7)  | 0 (0)      |          |      |

Abbreviation: HRV, human rhinovirus.
the patients had a cough, and 8% of the patients had sneezing, so the most typical symptom of HRV infection in our study was fever. By sampling and testing, we found that patients with the symptoms of fever, cough, runny nose, and sneezing were more likely to test positive for HRV in an HRV-related outbreak. Studies have proved that HRV infection in youngsters would be symptomatic while in adults often asymptomatic. However, as we illustrated in Table 4, the tested patients had a higher proportion of fever, which would sure be selection bias, because the strategy during the control of the outbreaks is to identify the pathogens and control the spreading, so we were more likely to take the specimens of the patients with obvious symptoms instead of collecting samples of all patients, to improve the detection success rate.

Diurnal temperature range (DTR) was reported to be one of the risk factors of the common cold, which gives the answer to the trend of the endemic of HRV in spring and winter of the year. Obesity was another risk factor reported to rise the possibility of HRV infection. While in our study, we did not collect the DTR, height, and weight data of the patients, which is a shortcoming of this study.

In summary, this study gives a glimpse of the endemic of HRV in Guangzhou, proved better evidence for the prevention and control of respiratory viruses, and indicated that the conventional COVID-19 control measures, such as wearing face masks or social distancing, are not effective enough in preventing rhinovirus, so new masks that filter nonenveloped viruses, including HRV, should be considered as a possible new approach to preventing HRV infection.

DATA AVAILABILITY STATEMENT
Raw data were generated during the field investigation. Derived data supporting the findings of this study are available from the corresponding author on request.

AUTHOR CONTRIBUTIONS
Di Wu, Jianyun Lu and Tiantian Wu: Conceptualization and investigation of the original draft. Tiantian Wu, Qing Zeng, and Yiyun Chen: Methodology. Yanhui Liu: Data curation. Di Wu and Jianyun Lu: Review and editing.

ACKNOWLEDGMENTS
This study was supported by the Natural Science Foundation of Guangdong Province (2019A1515011407), the Medical Science and Technology Project of Guangzhou (20201A011067 and 20211A011059), and the Guangdong Medical Science and Technology Research Project (A2019379, A2020399, and B2021244).

CONFLICT OF INTEREST
The authors declare no conflict of interest.
15. Hung IF, Zhang AJ, To KK, et al. Unexpectedly higher morbidity and mortality of hospitalized elderly patients associated with rhinovirus compared with influenza virus respiratory tract infection. *Int J Mol Sci*. 2017;18:259.

16. Park S, Michelow IC, Choe YJ. Shifting patterns of respiratory virus activity following social distancing measures for COVID-19 in South Korea. *J Infect Dis*. 2021;224:1900-1906.

17. Zhang RX, Chen DM, Qian Y, et al. Surges of hospital-based rhinovirus infection during the 2020 coronavirus disease-19 (COVID-19) pandemic in Beijing, China. *World J Pediatr*. 2021;17:590-596.

18. Jia R, Lu L, Li S, et al. Human rhinoviruses prevailed among children in the setting of wearing face masks in Shanghai, 2020. *BMC Infect Dis*. 2022;22:253.

19. Maison N, Peck A, Illi S, et al. The rising of old foes: impact of lockdown periods on "non-SARS-CoV-2" viral respiratory and gastrointestinal infections. *Infection*. 2022;50:519-524.

20. Jiang H, Yang T, Yang C, et al. Molecular epidemiology and clinical characterization of human rhinoviruses circulating in Shanghai, 2012-2020. *Arch Virol*. 2022;167:1111-1123.

21. Uhteg K, Amadi A, Forman M, Mostafa HH. Circulation of non-SARS-CoV-2 respiratory pathogens and coinfection with SARS-CoV-2 amid the COVID-19 pandemic. *Open Forum Infect Dis*. 2022;9:ofab618.

22. Poole S, Brendish NJ, Tanner AR, Clark TW. Physical distancing in schools for SARS-CoV-2 and the resurgence of rhinovirus. *Lancet Resp Med*. 2020;8:e92-e93.

23. Perry Markovich M, Glatman-Freedman A, Bromberg M, et al. Back-to-school upper respiratory infection in preschool and primary school-age children in Israel. *Pediatr Infect Dis J*. 2015;34:476-481.

24. Leung NHL, Chu DKW, Shiu EYC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nature Med*. 2020;26:676-680.

25. Wu D, Ma X, Geng H, et al. Reduction in mumps during the fight against the COVID-19 pandemic. *Asia Pac J Public Health*. 2021;33:171-173.

26. Wu D, Lu J, Liu Y, Zhang Z, Luo L. Positive effects of COVID-19 control measures on influenza prevention. *Int J Infect Dis*. 2020;95:345-346.

27. Wu D, Liu Q, Wu T, Wang D, Lu J. The impact of COVID-19 control measures on the morbidity of varicella, herpes zoster, rubella and measles in Guangzhou, China. *Immun Inflamm Dis*. 2020;8:844-846.

28. Wu D, Lu J, Sun Z, et al. Rhinovirus remains prevalent in school teenagers during fight against COVID-19 pandemic. *Immun Inflamm Dis*. 2020;9:76-79.

29. Peltola V, Waris M, Osterback R, Susi P, Ruuskanen O, Hyypia T. Rhinovirus transmission within families with children: incidence of symptomatic and asymptomatic infections. *J Infect Dis*. 2008;197:382-389.

30. Ma Y, Yang S, Yu Z, et al. Effect of diurnal temperature range on outpatient visits for common cold in Shanghai, China. *Environ Sci Pollut Res Int*. 2020;27:1436-1448.

31. Orozco-Hernandez JP, Montoya-Martinez JJ, Pacheco-Gallego MC, Cespedes-Roncancio M, Porras-Hurtado GL. SARS-CoV-2 and rhinovirus/enterovirus co-infection in a critically ill young adult patient in Colombia. *Biomedica*. 2020;40:34-43.

**How to cite this article:** Lu J, Wu T, Zeng Q, Chen Y, Liu Y, Wu D. Epidemiology of rhinovirus under the COVID-19 pandemic in Guangzhou, China, 2020. *Immun Inflamm Dis*. 2022;10:e632. doi:10.1002/iid3.632