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Contact tracing period and epidemiological characteristics of an outbreak of the SARS-CoV-2 Delta variant in Guangzhou

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A B S T R A C T

Objectives: An outbreak of the SARS-CoV-2 Delta variant occurred in Guangzhou in 2021. This study aimed to identify the transmission dynamics and epidemiological characteristics of the Delta variant outbreak to formulate an effective prevention strategy.

Methods: A total of 13102 close contacts and 69 index cases were collected. The incubation period, serial interval, and time interval from the exposure of close contacts to the symptom onset of cases were estimated. Transmission risks based on the exposure time and various characteristics were also assessed.

Results: The mean time from exposure to symptom onset among non-household presymptomatic transmission was 3.83 ± 2.29 days, the incubation period was 5 days, and the serial interval was 3 days. The secondary attack rate was high within 4 days before onset and 4–10 days after symptom onset. Compared with other contact types, household contact had a higher transmission risk. The transmission risk increased with the number and frequency of contact with index cases. Cycle threshold (Ct) values were associated with lower transmission risk (adjusted odds ratio [OR] 0.93 [95% CI 0.88–0.99] for *ORF 1ab* gene; adjusted OR 0.91 [95% CI 0.86–0.97] for *N* gene).

Conclusion: The contact tracing period may need to be extended to 4 days before symptom onset. The low Ct value of index cases, the high number and frequency of contact with index cases, and household contacts were associated with a higher transmission risk of SARS-CoV-2 Delta.

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Introduction

Since the B.1.617.2 (Delta) variant of SARS-CoV-2 was first identified in India in October 2020, it has become the main epidemic strain in many countries (Alizon et al., 2021; Del et al., 2021; Lauring and Malani, 2021; Lopez et al., 2021). As of September 21, 2021, the variant had spread to 185 countries and regions (WHO, 2021). The Delta variant has increased transmissibility owing to its increased fitness, and it could be able to escape from host immunity (Hoffmann et al., 2021; Planas et al., 2021). Thus, it poses a great threat to global public health.

Contact tracing and isolation of confirmed and suspected cases are crucial measures to control infectious diseases (Liu et al., 2020) and have been implemented in the prevention of COVID-19. However, these measures will become less effective if the reproduction number is high or if infectiousness occurs in the presymptomatic period (Hellewell et al., 2020). A study using mathematical modeling demonstrated that in higher transmission scenarios, tracing and isolating a larger proportion of close contacts are needed to bring the median effective reproductive number

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below 1 and, therefore, prevent the transmission of COVID-19 (Hellewell et al., 2020). Compared with the wild-type virus, the Delta variant has higher transmissibility. The basic reproduction number and viral load in a person infected with the Delta variant are higher than those of the wild-type virus (Luo et al., 2021; Liu and Rocklov, 2022). This finding indicates that a higher level of contact tracing may be needed to contain the transmission of the Delta variant.

The presymptomatic transmission of COVID-19 has been found in previous studies (Liu et al., 2020; Huang et al., 2020; Ren et al., 2021), and some studies indicated that the proportion of the presymptomatic transmission of the Delta variant is higher than those of other variants (Min et al., 2021; Zhang et al., 2021). Tracing the contacts of confirmed cases and testing (and isolating) the contacts before symptom onset are the ideal way to prevent disease transmission (Hellewell et al., 2020). Therefore, effectively searching and isolating contacts before the infected cases show symptoms are extremely important in the prevention of the Delta variant.

In China, according to "The New Coronavirus Pneumonia Prevention and Control Plan (Eighth Edition)," close contacts are defined as those who had contact, without effective protective measures (such as without wearing proper personal protection equipment), with suspected and confirmed cases within 2 days before the onset of symptoms or within 2 days before the sampling of asymptomatic infected persons (China State Council, 2021). Tracing close contacts according to the scale of this definition was able to control the spread of COVID-19 caused by wild-type SARS-CoV-2 (Lai et al., 2020). Nevertheless, the criteria of contact tracing may need to be more inclusive (such as expanding contact tracing to a longer time frame) for the prevention of variants with higher transmissibility, such as the Delta variant. On May 21, 2021, a local case of the Delta variant was detected in Guangzhou, China. It then caused a local outbreak in the following days and weeks. This epidemic provides an opportunity to estimate transmission parameters, such as the incubation period and serial interval of the epidemic, as well as the transmission dynamics among the close contacts of index cases infected with the Delta variant. Other epidemical characteristics of the Delta variant can also be observed. Cycle threshold (Ct) value is an important indicator when studying the epidemical characteristics of COVID-19, as it may be associated with mortality (Huang et al., 2020), disease severity (Liu et al., 2021; Liu et al., 2020; Zheng et al., 2020), and biochemical and hematological markers (Azzi et al., 2020; Liu et al., 2020; Shi et al., 2020). However, whether Ct values will affect the transmission risk of the Delta variant is still unclear.

In this study, we aimed to investigate the epidemiological characteristics and transmission dynamics of COVID-19 caused by the Delta variant. We also evaluated the transmission risk by different exposure windows and various characteristics.

Methods

Data collection

Since the first local case was confirmed in Liwan District of Guangzhou City on May 21, 2021, the Guangzhou Center for Disease Control and Prevention (CDC) immediately carried out case searches and strengthened disease surveillance. Index cases were detected through screening in fever clinics, tracing and screening of close contacts, and community screening. Nasopharyngeal swabs were collected for reverse transcription-polymerase chain reaction (RT-PCR) test to quickly screen suspected cases. The PCR-positive samples were sent to the Guangzhou CDC for review, and those confirmed to have a positive PCR result were sent to designated hospitals for diagnosis, isolation, and treatment. All the close contacts were identified and quarantined according to the epidemiology investigations of confirmed cases and big data technology screening through multisectoral collaboration.

From May 21, 2021, to June 18, 2021, 69 index cases and 13102 close contacts were identified by the Guangzhou CDC. The index cases and close contacts were people living in Guangzhou during the epidemic period. The information of index cases included demographic characteristics, epidemiological history, and clinical data. Close contacts were quarantined for 14 days from the last contact with index cases and were subjected to regular PCR testing and physical condition monitoring.

Procedures and definitions

The incubation period and serial interval of the COVID-19 epidemic caused by the Delta variant were estimated to investigate its epidemiological features. The incubation period is defined as the time from exposure to symptom onset. For asymptomatic cases, the incubation period is the time between exposure and the first PCR-positive test result. We excluded cases of household contact because their exposure time was difficult to determine. As a result, 65 cases were included in the estimation of the incubation period. Serial interval is defined as the period of time from the onset of symptoms in the index case to the onset of symptoms in an associated secondary case. For asymptomatic cases, the serial interval is the time difference between the first PCR-positive test of the index case and the secondary case. We identified 35 non-household infector–infectee pairs to investigate the epidemiological characteristics of the presymptomatic transmission. Each infectee was the earliest confirmed case among close contacts exposed to the infectors in the presymptomatic period. Then, the time period between the exposure of infectees and the symptom onset of infectors was estimated. For symptomatic index cases, the time interval from the exposure of infected cases to symptom onset was used. For asymptomatic index cases, the time interval from the exposure of infectees to the first positive PCR test was used.

Contact types and frequency

The relationships between index cases and close contacts were divided into 5 contact types: household (family or living together), dine together, socially interacting (including colleagues, classmates, and those who had a relationship and interaction), casual contact (including public places, community contact, and those who had no relationship and interaction), and multiple types (more than 1 contact type). Contact frequency was categorized as "occasional," "moderate," and "often."

Ct values

Ct value is the number of cycles experienced when the fluorescent signal in each reaction tube reaches the set threshold in real-time fluorescence quantitative PCR detection. Ct values can be used as a semi-quantitative proxy of viral load, in which a high Ct value corresponds to a low viral load. The PCR detection method targets the open reading frame 1ab (*ORF lab*) and nucleocapsid protein (*N*) genes in the SARS-CoV-2 genome.

Outcomes and definitions

The main outcome was transmission, which means that a confirmed infection appeared among close contacts under quarantine. The secondary attack rate is defined as the ratio of the number of confirmed cases among close contacts. Asymptomatic cases are those who had no relevant clinical symptoms but had a positive etiological test result of the respiratory specimen. Symptomatic

Table 1
Demographic and epidemiological characteristics of 13102 close contacts.

Characteristic	Close contacts (n=13102)
Age group, years	
< 20	1497(11.43)
20 ~ 59	9516(72.63)
≥ 60	2089(15.94)
Sex (n, %)	
Male	7363(56.20)
Female	5739(43.80)
Number of index cases	
1	10236(78.13)
2	1725(13.17)
≥ 3	1140(8.70)
Unknown	1(0.00)
Contact type (n, %)	
Household	162(1.24)
Dine together	752(5.74)
Socially interact	2695(20.57)
Casual contact	7086(54.08)
Multiple types	8(0.06)
Unknown	2399(18.31)
Frequency (n, %)	
Occasional	5406(41.26)
Moderate	4363(33.30)
Often	427(3.26)
Unknown	2906(22.18)
Time from onset to exposure, median (range), days [a]	-1(-3,1)
Time from onset to exposure, days [a]	
≤ -5	1408(13.92)
-4 ~ -1	5077(50.18)
0 ~ 3	2147(21.22)
4 ~ 6	487(4.81)
7 ~ 10	799(7.90)
> 10	200(1.98)

[a] Defined as the time period between the symptom onset of index cases and the exposure time of close contacts, the negative value means the close contacts have exposed to the index cases before the case had symptoms. The time from onset to exposure was estimated from those non-household close contacts linked to only 1 index case, thus the number of close contacts was 10118.

confirmed cases were classified into mild, moderate, severe, and critical according to the "COVID-19 diagnosis and treatment protocol." Details are shown in the Supplementary text. Vaccination status was categorized as unvaccinated, vaccinated with 1 dose, and vaccinated with 2 doses. Close contacts need to be paired with their indicator cases to analyze the relationship between the Ct values of index cases and disease transmission. Therefore, the close contacts linked to only 1 index case were selected for analysis.

Statistical analysis

The incubation period, serial interval, and time period from exposure to symptom were estimated using the data obtained from epidemiological investigations. The median Ct values of the first positive PCR test of the *ORF 1ab* and *N* genes were separately calculated. Continuous variables with normal distribution were calculated as mean (standard deviation [SD]), and those with skewed distribution were calculated as median (interquartile range [IQR]). Categorical variables were calculated as frequency (percentages).

We compared the secondary attack rate using the chi-square test and used multivariable logistic regression models to estimate transmission risk using the characteristics of close contacts (age, sex, number of index cases, contact types, and frequency) and the time of exposure (using non-household contacts linked to only 1 index case). We also explored the association between the transmission risk of close contacts and the Ct values of index cases, as well as between vaccination status and Ct values. The missing data of covariates were imputed using multiple imputations with chained equations. All analyses were performed by STATA Statistical Software Version 15.0 with a two-sided $P < 0.05$ as statistically significant.

The data in this study were obtained from the Guangzhou CDC from a work for preventing and controlling the COVID-19 outbreak as required by the public health policy of the National Health Commission of China. According to the law on the prevention and control of infectious diseases, cases should truthfully provide relevant information. Hence, individual informed consent was waived, and after consultation with the ethics committee of the Guangzhou CDC, this study was considered that ethical approval is not required. The analytical datasets were constructed anonymously.

Results

A total of 69 index cases and 13102 close contacts in Guangzhou were collected. Among the 13102 contacts, 84 developed secondary cases. Therefore, 153 cases were identified in this epidemic. **Table 1** lists the demographic and epidemiological characteristics of all close contacts. Of the 13102 close contacts, 1.62% were household contacts, 20.57% were socially interacting, and 54.08% were casual contacts. The median time from exposure to symptom onset of index cases was −1 day, and most of the close contacts were exposed to index cases before the symptom onset of index cases. The median age of index cases was 51 years (IQR 32–67), and the median age of the secondary cases was 46 years (IQR 24–68). Most of the cases were males, most of whom had not been vaccinated and often wore masks when going out. Of the 153 cases, 11 (7.19%) were asymptomatic, and most of the symptomatic cases presented mild and moderate symptoms with fever and dry cough as the main symptoms (**Table A.1**).

The median incubation period for all cases was 5 days (IQR 3–7), and the median serial interval was 3 days (IQR 1–5). The mean time from exposure to symptom onset among presymptomatic

Table 2
Secondary attack rate of COVID-19 caused by SARS-CoV-2 Delta variant among close contacts by different characteristics and time.

Characteristics	Number of contacts	Number of secondary cases	Secondary Attack Rate, % (95% CI)	Adjusted odds ratio (95% CI)
Age group, years (n=13102)				
< 20	1497	16	1.07 (0.63-1.77)*	1.60 (0.86-3.00)
20∼59	9516	39	0.41 (0.30-0.57)	1.00 (Reference)
≥ 60	2089	29	1.39 (0.95-2.02)	2.74 (1.65-4.58)
Sex (n=13102)				
Male	7363	34	0.46 (0.32-0.65)*	1.00 (Reference)
Female	5739	50	0.87 (0.65-1.16)	1.79 (1.14-2.84)
Contact types (n=13102)				
Household	162	15	9.26 (5.69-14.72)*	1.00 (Reference)
Dine together	752	9	1.20 (0.59-2.35)	0.49(0.17-1.41)
Socially interacting	2695	19	0.71 (0.44-1.13)	0.24 (0.10-0.57)
Casual contact	7086	36	0.51 (0.36-0.71)	0.30 (0.12-0.76)
Multiple types	8	3	37.50 (10.24-74.11)	13.97 (1.78-109.51)
Unknown	2399	2	0.08 (0.01-0.33)	0.05(0.01-0.26)
Frequency (n=13102)				
Occasional	5406	20	0.37 (0.23-0.58)*	1.00 (Reference)
Moderate	4363	32	0.73 (0.51-1.04)	2.23 (1.25-4.00)
Often	427	24	5.62 (3.71-8.36)	12.86 (5.45-30.34)
Unknown	2906	8	0.28 (0.13-0.57)	1.63 (0.66-4.04)
Time from symptoms onset to exposure, days (n=10118) [a]				
≤ -5	1408	1	0.07 (0.00-0.46)	1.00 (Reference)
-4 ∼ -1	5077	19	0.37 (0.23-0.59)	4.65 (0.60-35.82)
0∼3	2147	2	0.09(0.01-0.37)	1.13 (0.10-12.15)
4∼6	487	2	0.41 (0.07-1.64)	6.93 (0.60-80.14)
7∼10	799	2	0.25 (0.04-1.00)	5.50 (0.46-60.35)
> 10	200	0	0.00	*NA*
Number of index cases (13102)				
1	10235	36	0.35 (0.25-0.49)*	1.00 (Reference)
2	1726	17	0.99 (0.59-1.60)	3.00 (1.62-5.52)
≥ 3	1140	31	2.72 (1.89-3.89)	7.48 (4.48-12.49)
Unknown	1	0	0.00	*NA*

* $P < 0.05$.
[a] Defined as the time period between the symptom onset of index cases and the exposure time of close contacts, contacts were non-household contact those who linked to only 1 case. The negative value means the close contacts have exposed to the index cases before the case had symptoms.

Table 3
Association between Ct values and transmission risk among close contacts linked to 1 index case.

Ct values	Univariable analysis Odds Ratio (95% CI)	*P* value	Multivariable analysis [a] Odds Ratio (95% CI)	*P* value
ORF1ab gene*N* gene	0.93 (0.88-0.99)0.93 (0.88-0.99)	0.0180.017	0.92(0.86-0.98)0.91 (0.85-0.97)	0.0090.004

[a] Multivariable analysis adjusted for age, sex, contact types and contact frequency.

transmission was 3.83 ± 2.29 days (95% CI 3.04–4.62). The median Ct values of the first positive PCR test were 26.50 (IQR 21.33–33.44) for the *ORF 1ab* gene and 25.50 (IQR 19.87–32.00) for the *N* gene, respectively.

The total secondary attack rate was 0.64% (95% CI 0.51%–0.80%). Contacts aged <20 years (1.07% [95% CI 0.63%–1.77%]) and ≥60 years (1.39% [95% CI 0.95%–2.02%]) had a higher secondary attack rates than those aged 20–50 years (0.41% [95% CI 0.30%–0.57%]). Compared with the close contacts whose exposure to the index case was 10 days after symptom onset (zero transmission of 200 contacts [95% CI 0.00%–2.35%]), those who were exposed 4 days before symptom onset (0.37% [95% CI 0.23%–0.59%]) and 4–10 days after symptom onset (4–6 days: 0.41% [95% CI 0.07%–1.64%] and 7–10 days: 0.25% [95% CI 0.04%–1.00%]) had higher secondary attack rates. In multivariable logistic models, females were more likely to be secondary cases than males (adjusted OR 1.79, 95% CI 1.14–2.84). The transmission risk increased with the number (1: adjusted OR, 3.00 [95% CI 1.62–5.52] to ≥ 3: adjusted OR, 7.48 [95% CI 4.48–12.49]) and frequency (occasional: adjusted OR, 2.25 [95% CI 1.25–4.00] to often: adjusted OR, 12.86 [5.45–30.34]) of contact with index cases. In terms of contact types, household contact showed a higher transmission risk than other types, and the secondary attack rate of household contact (9.26% [95% CI 5.69%–14.72%]) was higher than the total secondary attack rate (**Table 2**).

In close contacts linked to 1 index case, high Ct values were associated with lower transmission risk (*ORF 1ab* gene: adjusted OR, 0.93 [95% CI 0.88–0.99]; *N* gene: adjusted OR, 0.91 [95% CI 0.86–0.97]; **Table 3**). The Ct values of the *N* gene were higher in those who received 2 doses of vaccine after adjusting for age and sex (**Table A.2**).

Discussion

In this study, we found that the median incubation period and serial interval were 5 days and 3 days, respectively. The mean time from exposure to symptoms onset was 3.83 days among presymptomatic transmission cases. A higher secondary attack rate was found within 4 days before and 4–10 days after symptom onset, followed by a lower secondary rate at over 10 days after symptom onset. In terms of the risk factors for transmission, a lower Ct value in index cases was associated with a higher risk of SARS-CoV-2 transmission. Compared with other contact types, household contact had a higher infection risk. Close contacts exposed to a higher number of index cases and with a higher frequency of contact were more likely to be infected.

In the prevention of COVID-19, the presymptomatic transmission would hinder the effectiveness of control measures. Tracing the contacts of infected cases after symptomatic onset is relatively easier compared with contacts in the presymptomatic period, because presymptomatic transmission is hidden, and the onset time of infectiousness of cases is uncertain. Without sufficient contact tracing, those omitted contacts will then become a challenge in controlling the COVID-19 epidemic. In this study, the median serial interval (3 days) was shorter than the incubation period (5 days), which indicates that presymptomatic transmission is likely to have occurred and may even be more frequent than symptomatic transmission (Nishiura et al., 2020). The earliest presymptomatic transmission occurred 9 days before the symptom onset of the index case, and the average time of presymptomatic transmission was 3.83 days before the symptom onset of the index case. Moreover, the secondary attack rate was relatively high among those whose initial exposure to the index case was within 4 days before and 10 days after the symptom onset of index cases. This finding implies that presymptomatic transmission in this epidemic may reduce the effect of contact tracing based on the current criteria of close contacts. Actually, screening close contacts according to the current definition of close contacts has failed to contain the epidemic. The epidemic was finally effectively controlled by extending the screening time of close contacts to 4 days before the onset of the case tentatively, social distancing and community closure management in high-risk areas, and actively finding cases and close contacts through mass testing. The results suggest that expanding the time scale of contact tracing and taking more active actions to detect the contacts of infected persons before they develop symptoms can improve the effectiveness of control measures against the Delta variant.

Transmission and viral shedding before COVID-19 symptom onset were observed in previous studies (Jefferson et al., 2021; Cheng et al., 2020; Ge et al., 2021; He et al., 2020). High transmission risk and viral load were found around the time of symptom onset (between about −2 and 3 days from symptom onset) (Cheng et al., 2020; Ge et al., 2021). In this study, the secondary attack rate was high from 4 days to 1 day before symptom onset. Another study found a high viral load of the Delta variant at least 4 days before illness onset (Min et al., 2021). This finding suggests that the Delta variant may have transmissibility in an earlier period than the wild-type virus. Viral dynamics studies showed that the viral load decreased gradually within 7 days of symptom onset (He et al., 2020; Zou et al., 2020). A contact tracing study in Taiwan found that the risk of transmission declined after 1 week of symptom onset (Cheng et al., 2020). However, we observed in the present study that the transmission risk declined 10 days after the onset of symptoms, which indicates that the Delta variant may have a longer infection duration. This finding was supported by another study, which found a prolonged viral shedding of the Delta variant than the wild-type virus (Wang et al., 2021). Therefore, extending the contact tracing period to perhaps 4 days before symptom onset and strengthening the management of infected cases may be necessary.

Our results showed that the increased Ct values of index cases were associated with a lower transmission risk. The Ct value is an inversely proportional measure of viral load in the specimen (Trunfio et al., 2021). Thus, a lower viral load is associated with a lower transmission risk, which was consistent with a previous study (Marks et al., 2021). Compared with the 2020 epidemic, the Ct values of the first positive PCR test were lower (34.31, IQR 31.00–36.00 for *ORF 1ab* gene) (Li et al., 2021), which suggests that the viral load of the Delta variant was higher than that of the wild-type virus in infectious people. The peak viral load of the Delta variant is also higher than that of the wild-type virus (Wang et al., 2021). Therefore, the high viral load seems to contribute to the increased transmissibility of the Delta variant.

The secondary attack rate of COVID-19 in our study was 0.64% among all close contacts, and the secondary attack rate among household contacts was similar to the secondary attack rate in the 2020 epidemic (9.26% vs. 10.30%) (Luo et al., 2020). In this epidemic, household contact was the highest risk factor for SARS-CoV-2 transmission, which was in line with previous results (Ng et al., 2021; She et al., 2020). This finding implies that the prevention of family transmission remains the most important measure to control the COVID-19 epidemic. Compared with the male sex, the female sex was associated with a higher COVID-19 transmission risk. A national study in mainland China estimated a higher attack rate of COVID-19 in females than in males, which implies that females are more likely to be infected by SARS-CoV-2 than males (Qian et al., 2020). A potential reason may be that females have a higher angiotensin-converting enzyme 2 (ACE2) levels (Bhatia et al., 2013) because the *ACE2* gene is located in the X chromosome. Moreover, the ACE2 receptor is the channel through which SARS-CoV-2 viruses enter tissues (Batlle et al., 2020) and cause infection. In addition, we found that transmission risk increased with the increase in the number of index cases and frequency of exposure of close contacts. Gathering outside with people will increase the chance of contact with suspicious cases and increase the risk of infection. Considering the higher transmissibility and faster spread of the Delta variant, case isolations and contact tracing alone would be unlikely to control the transmission of the Delta variant. Aggressive social distancing and community closure management in high-risk areas may be essential to contain the spread of the COVID-19 epidemic caused by the Delta variant.

This study has several limitations. First, the symptom onset time of most cases was obtained retrospectively through epidemiological investigations; therefore, recall bias may occur. Second, we used Ct values as a proxy of viral load, but the precise correlation between Ct values and viral load may be influenced by many factors. Our results suggested a potential link between viral load and transmission risk. Third, we were unable to examine potential determinants for the secondary attack rate of household transmission, including the characteristics of index cases and household contacts. We were also unable to estimate the transmission risk of household contacts by the timing of exposure because the exposure time for intra-family transmissions was difficult to pinpoint. Finally, Guangzhou adopted strict prevention and control measures at the initial stage of the epidemic and carried out large-scale PCR test screening, which quickly contained the spread of the epidemic. These measures were different from other countries, and it may affect the representativeness of our results.

In conclusion, our results showed that the mean time from exposure to symptom onset of presymptomatic transmission cases was 3.83 days, and most COVID-19 cases caused by the transmission of the Delta variant occurred within 4 days before and 4–10 days after symptom onset. Low Ct values were associated with high transmission risk, and household contact was at higher risk of transmission than other contact types. Close contacts exposed to a large number of index cases and with higher frequency had a higher risk of being infected. The Delta variant was more transmissible, and the infectivity appeared earlier; thus, an expansion of the contact tracing period and more active control measures may be needed in the prevention of the transmission of the Delta variant.

Conflict of interest

The authors declare no conflict of interest.

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Ethical Approval

The data used in this study were obtained from a work for preventing and controlling the COVID-19 outbreak by the Guangzhou CDC as required by the public health policy of the National Health Commission of China. According to the law on the prevention and control of infectious diseases, cases should truthfully provide relevant information. Hence, individual informed consent was waived, and after consultation with the ethics committee of Guangzhou CDC, the study was considered that ethical approval is not required. The analytical data sets were constructed anonymously.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.01.034.

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