Clinical characteristics and viral shedding kinetics of 38 asymptomatic patients with coronavirus disease 2019

A retrospective observational study

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Abstract

This study aims to investigate the clinical characteristics and viral shedding kinetics of asymptomatic patients with coronavirus disease 2019 (COVID-19).

The data of 38 asymptomatic patients positive for SARS-CoV-2 nucleic acid were collected from February to March 2020 in Tuanfeng County, Huanggang, Hubei, China. The epidemiology, laboratory examination, chest imaging, viral nucleic acid test results, clinical characteristics, and viral shedding time were summarized in this retrospective study.

The study included 20 family members of patients with COVID-19, 10 medical personnel participating in COVID-19 treatment or working in a fever clinic, 6 personnel from quarantine places, 1 individual with a close contact history with confirmed patients, and 1 local epidemic prevention personnel. All were positive for SARS-CoV-2 nucleic acid. The white blood cell (WBC) count, the absolute value of lymphocytes, C-reactive protein (CRP), and D-dimer were normal. Pneumonia manifestations were not found in the chest computed tomography (CT) scan of 36 patients; the remaining 2 cases included a 1-year-old child and a pregnant woman, and they did not undergo chest CT. The viral shedding time was 6 days.

All asymptomatic patients with COVID-19 had a history of close contact or exposure. Laboratory tests were normal. Chest imaging did not show any pneumonia manifestation. The viral shedding time was <10 days, which is shorter than that of patients with COVID-19. A timely discovery of such asymptomatic infections is crucial for blocking the spread of the virus and strengthening the prevention and control measures.

Abbreviations: ALT = alanine transaminase, AST = aspartate transaminase, CDC = Center for Disease Control and Prevention, COVID-19 = coronavirus disease 2019, CRP = C-reactive protein, CT = computed tomography, ESR = erythrocyte sedimentation rate, PCT = procalcitonin, SD = standard deviation, TCM = traditional Chinese medicine, WBC = white blood cells, WHO = World Health Organization.

Keywords: asymptomatic infection, coronavirus disease 2019, SARS-CoV-2, viral shedding time
1. Introduction

The World Health Organization (WHO) reported a total of 823,626 confirmed cases of coronavirus disease 2019 (COVID-19) in 205 countries or regions, with 40,598 deaths by the end of the period covered by this study (April 1, 2020).\cite{1} On October 12, 2020, the WHO reported that over 37 million individuals were infected, with over 1 million deaths.\cite{2} During the pandemic of COVID-19, rapid tracking, isolation of infection sources, and cutting-off of the transmission routes are the fundamental methods to control the epidemic. Symptomatic infections are identified by visiting the doctors, but the diagnosis of asymptomatic infections is challenging but is a key link in epidemiological tracking and epidemic prevention and control. The accurate definition of asymptomatic infections needs to be standardized urgently to avoid bias in investigations due to broad and vague definitions. A number of asymptomatic infected patients ultimately present obvious clinical symptoms during medical observation, as well as abnormalities in chest imaging.\cite{3} Such patients should be regarded as viral nucleic acid positive and in the incubation period rather than asymptomatic.

Herein, we strictly defined “asymptomatic patient” as patients with positive SARS-CoV-2 nucleic acid test results but who do not present obvious self-perceived or observable clinical symptoms and signs throughout the follow-up period. Moreover, relevant clinical laboratory testing and chest imaging are negative. Thus, a strict definition can distinguish true asymptomatic infections from those patients who are in the incubation period.

This retrospective study analyzed 38 patients with asymptomatic positive SARS-CoV-2 in Tuanfeng County (Huanggang, Hubei, China), summarized the results of their epidemiology, laboratory examinations, chest imaging, and nucleic acid testing, discussed the viral shedding kinetics, and emphasized the strengthening of the tracking and monitoring of such patients to control the spread of the epidemic.

2. Materials and methods

2.1. Study subjects

The retrospective study was approved by the ethics committee of Tuanfeng County People’s Hospital. Informed consent was obtained from every patient. A total of 38 asymptomatic patients with a positive SARS-CoV-2 nucleic acid test were included in this study. They all were from Tuanfeng County People’s Hospital in Tuanfeng county, Huanggang, Hubei province, and were diagnosed in February and March 2020.

2.2. Epidemiological investigation

The 38 cases were evaluated with respect to epidemiology, including diagnosis of family members, close contact with confirmed patients except for family members, engaged in the treatment of patients with COVID-19, or directly in contact with patients with fever. Close contact indicated those who have not been effectively protected from close contact with suspected or confirmed cases since 2 days before presenting symptoms or specimens of asymptomatic infected persons from 2 days before sampling, without effective protection.\cite{4}

2.3. Laboratory examination and chest imaging

The levels of white blood cell count (WBC), D-dimer, C-reactive protein (CRP), procalcitonin (PCT), erythrocyte sedimentation rate (ESR), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) in the 38 asymptomatic patients were recorded. The chest computed tomography (CT) scans were reviewed.

2.4. Treatment

The treatments of the 38 patients after admission to the hospital were recorded. Since there is no standard for the diagnosis and treatment of asymptomatic patients with COVID-19, the treatment referred to the latest new coronavirus pneumonia diagnosis and treatment program issued by the National Health Commission. The empirical treatment of arbidol and traditional Chinese medicine (TCM) was administered. No drug intervention was given to children, pregnant women, or patients who did not agree with medication.

2.5. Nucleic acid testing

The specimens were pharyngeal swabs, and the first specimens were uniformly collected by personnel from the Tuanfeng County Center for Disease Control and Prevention (CDC). During hospitalization, the specimens were collected by the physicians. All specimens were transported to the CDC of Huanggang, Hubei, according to the transportation requirements for testing. The nucleic acid was extracted by an automatic extractor (Xi’an Tianlong Science and Technology Co., Ltd., Shunyi District, Beijing) and detected by a qRT- Polymerase Chain Reaction (PCR) kit (Beijing Genomics Institution, BGI). The expression of the highly conserved region of COVID-19 was normalized against that of the internal reference gene. The COVID-19 probe was labeled with a Carboxyfluorescein. The internal reference probe was labeled with a VIC/HEX. The probe 3’-end was labeled with the quencher. During PCR amplification, specific primers and probes bind the target sequence, and the formation of PCR products is assessed based on the accumulation of fluorescent signals through DNA polymerase activity and 5’-3’ exonuclease activity of Taq enzyme, thereby detecting the nucleic acids in the specimens qualitatively. In this study, the first nucleic acid-positive test was considered as positive. Two consecutive negative nucleic acid tests (interval of >24 hours) were judged as negative.\cite{5} Viral shedding is defined as the detachment of the virus from the body’s secretions, excreta, or surface, which might lead to the spread of the viral infection.\cite{6} In this study, the viral shedding time was defined as the time interval from the first positive nucleic acid testing to the consecutive negative test.

2.6. Data analysis

IBM SPSS statistics 22.0 Chinese version. was used for statistical analysis. Continuous data with a normal distribution are expressed as means ± standard deviations (SD) and were analyzed using Student’s t test. Continuous data with a skewed distribution are expressed as medians and interquartile distance (median [P25, P75]) and were analyzed by non-parametric tests.

3. Results

3.1. Epidemiological characteristics

The age of the cohort was 34 (27.0, 51.3) years. No obvious symptoms were reported by or detected in these patients from close contact to the discovery time of positive nucleic acid and to turning negative. Of these, 20 were family members of patients...
Table 1
Epidemiological characteristics and nucleic acid positive time.

| Patient ID | Sex   | Age, y | Combined underlying disease | Imported cases | History of close contact | How to find nucleic acid positive | First nucleic acid positive time |
|------------|-------|--------|------------------------------|----------------|--------------------------|----------------------------------|---------------------------------|
| P1         | Female| 49     | Chronic gastritis            | No             | Husband was diagnosed with COVID-19 | Nucleic acid detection           | 2020.02.24                     |
| P2         | Female| 60     | No                           | No             | Husband was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.21                     |
| P3         | Female| 56     | No                           | No             | Husband was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.19                     |
| P4         | Female| 37     | No                           | No             | Parent was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.19                     |
| P5         | Female| 21     | No                           | No             | Father was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.19                     |
| P6         | Male   | 63     | Chronic obstructive pulmonary disease | No | Wife was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.23                     |
| P7         | Male   | 20     | No                           | No             | COVID-19 was diagnosed in the patient who accompanied his father to bed during his stay in the hospital | Nucleic acid testing in quarantine place | 2020.02.22                     |
| P8         | Male   | 29     | No                           | No             | Mother was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.22                     |
| P9         | Male   | 56     | No                           | No             | Wife was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.22                     |
| P10        | Male   | 6      | No                           | No             | Grandmother was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.19                     |
| P11        | Male   | 12     | No                           | No             | Grandfather was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.24                     |
| P12        | Female | 1      | No                           | No             | Grandfather was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.19                     |
| P13        | Female | 15     | No                           | No             | Father was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.19                     |
| P14        | Male   | 43     | No                           | No             | Wife was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.26                     |
| P15        | Female | 31     | No                           | No             | Husband was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.24                     |
| P16        | Female | 55     | Coronary heart disease       | No             | Husband was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.24                     |
| P17        | Female | 36     | No                           | No             | Nurse in infection department of local county hospital | Physical examination | 2020.02.24                     |
| P18        | Female | 30     | No                           | No             | Nurse in infection department of local county hospital | Physical examination | 2020.02.23                     |
| P19        | Female | 30     | No                           | No             | Father was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.21                     |
| P20        | Female | 24     | No                           | No             | Grandfather was diagnosed with COVID-19 | Nucleic acid testing in quarantine place | 2020.02.19                     |
| P21        | Male   | 61     | Rheumatoid arthritis         | No             | local epidemic prevention and killing personnel | Physical examination | 2020.02.24                     |
| P22        | Male   | 40     | No                           | No             | Staff in quarantine place | Physical examination | 2020.02.22                     |
| P23        | Female | 24     | No                           | No             | Nurse in infection department of local county hospital | Physical examination | 2020.02.21                     |
| P24        | Female | 28     | No                           | No             | Nurse in infection department of local county hospital | Physical examination | 2020.02.14                     |
| P25        | Female | 41     | No                           | No             | Nurse in infection department of local county hospital | Physical examination | 2020.02.19                     |
| P26        | Female | 29     | No                           | No             | Nurse in infection department of local county hospital | Physical examination | 2020.02.19                     |
| P27        | Female | 36     | No                           | No             | Staff in quarantine place | Physical examination | 2020.02.24                     |
| P28        | Female | 27     | No                           | No             | Nurse in infection department of local county hospital | Physical examination | 2020.02.21                     |
| P29        | Male   | 57     | No                           | No             | Staff in quarantine place | Physical examination | 2020.02.24                     |
| P30        | Male   | 32     | No                           | No             | Staff in quarantine place | Physical examination | 2020.02.24                     |
| P31        | Male   | 30     | No                           | No             | Staff in quarantine place | Physical examination | 2020.02.24                     |
| P32        | Male   | 49     | No                           | No             | Staff in quarantine place | Physical examination | 2020.02.24                     |
| P33        | Female | 44     | No                           | No             | Physician in infection department of local county hospital | Physical examination | 2020.02.18                     |
| P34        | Female | 27     | No                           | No             | Nurse in local county hospital | Physical examination | 2020.02.15                     |
| P35        | Male   | 36     | No                           | No             | Physician in respiratory department of local county hospital | Physical examination | 2020.03.02                     |
| P36        | Male   | 55     | Chronic renal disease        | No             | Wife was diagnosed with COVID-19 | Positive nucleic acid testing in quarantine place | 2020.02.26                     |
| P37        | Female | 50     | No                           | No             | Husband was diagnosed with COVID-19 | Positive nucleic acid testing in quarantine place | 2020.02.22                     |
| P38        | Female | 73     | Chronic obstructive pulmonary disease | No | Husband was diagnosed with COVID-19 | Positive nucleic acid testing in quarantine place | 2020.02.22                     |
| M (QL, QL) |        | 34     | (27, 51.3)                  |                |                          |                                  |                                 |

3.2. Laboratory testing results

WBC $(5.7 \pm 1.5) \times 10^9/L$, lymphocyte count $(1.9 \pm 0.8) \times 10^9/L$, CRP $0.3 \ (0, 0.7) \text{mg/L}$, and D-dimer $0.2 \ (0.1, 0.4) \text{mg/L}$ were all normal in all patients. The ESR was $12.5 \ (7.0, 15.3) \text{mm/h}$; 32 cases were normal, and 6 showed a mild elevation. ALT was 19.2 $(13.8, 23.2) \text{U/L}$ and AST 18.5 $(14.9, 25.0) \text{U/L}$, that is, normal in 36 patients, while 2 patients had a history of self-medication, although the details were not clear. In addition, 37 patients showed a normal level of PCT at 0.01 $(0.01, 0.02) \text{ng/mL}$; 1 patient had PCT at 0.56 ng/mL, which is 10 times higher than the
normal upper limit, but this patient has chronic kidney disease (Table 2).

### 3.3. Chest CT examination

A chest CT examination was conducted within 1 week after admission. No signs of pneumonia were found in 36 patients. Two patients with chronic obstructive pulmonary disease showed emphysema. Suspicious malignant pulmonary nodules were found in 1 patient. Two patients did not undergo chest CT: a 1-year-old child and a pregnant woman (Table 3).

### 3.4. Treatments

A total of 30 patients were administered arbidol and TCM. The remaining 8 patients, including children, pregnant women, and those who refused medication, did not receive any drug intervention. Currently, there is no relevant study supporting that arbidol and TCM can shorten the time of viral shedding. Therefore, the influence of arbidol on viral shedding time was not considered, and the influence of TCM on viral shedding time is not supported by relevant data (Table 3).

### 3.5. Nucleic acid testing results

Daily nucleic acid tables were collected for statistics. Several factors, including the limited number of nucleic acid kits, patient compliance, hospital relocation, other objective or subjective factors, as well as non-standard sampling intervals, might be the underlying reasons for patients not being subjected to continuous nucleic acid test every alternate day. A total of 17 patients were tested every other day, 2 patients were tested every 2 days, 2 patients were tested every 3 days, 2 patients were tested every 4 days, and 3 patients were tested every 5 days. In addition, 3

| Table 2 |
|---|
| Laboratory examination of patients. |
| Patient ID | WBC (× 10^9/L) | LYM (× 10^9/L) | CRP, mg/L | PCT, ng/mL | ESR, mm/h | ALT, U/L | AST, U/L | D-dimer, mg/L |
| P1 | 3.5 | 1.4 | 0 | 0.01 | 8 | 29 | 15.6 | 0.21 |
| P2 | 5 | 1.6 | 0.6 | 0.02 | 10 | 12 | 13.3 | 0.11 |
| P3 | 4.5 | 1.7 | 0.8 | 0.08 | 21 | 158 | 78.4 | 0.31 |
| P4 | 4.9 | 1.2 | 0 | 0.01 | 11 | 20 | 14.6 | 0.05 |
| P5 | 6.7 | 2.5 | 0 | 0.02 | 15 | 14 | 15.3 | 0.10 |
| P6 | 7.1 | 2.0 | 0 | 0.01 | 12 | 21 | 26.4 | 0.90 |
| P7 | 7.1 | 2.6 | 0.6 | 0.04 | 20 | 12 | 15 | 0.17 |
| P8 | 6.1 | 2.4 | 0 | 0.01 | 10 | 16 | 19.6 | 0.05 |
| P9 | 5.1 | 1.5 | 0.6 | 0.01 | 13 | 15 | 18.2 | 0.10 |
| P10 | 7.3 | 3.0 | 0 | 0.01 | 15 | 14 | 15.5 | 0.06 |
| P11 | 3.7 | 1.7 | 0 | 0 | 13 | 13 | 16.9 | 0.08 |
| P12 | 7.7 | 4.8 | 0 | 0.01 | 14 | 26.1 | 18.8 | 0.05 |
| P13 | 6.5 | 2.5 | 4.1 | 0.02 | 15 | 23 | 13.8 | 0.40 |
| P14 | 4.3 | 1.4 | 0 | 0.01 | 7 | 36 | 22.7 | 0.01 |
| P15 | 3.6 | 1.4 | 0.7 | 0.01 | 4 | 19 | 14.5 | 0 |
| P16 | 4.1 | 1.1 | 0 | 0.02 | 21 | 17 | 22.1 | 0.18 |
| P17 | 5.6 | 1.7 | 0.3 | 0.01 | 18 | 23 | 16.4 | 0.21 |
| P18 | 4.9 | 1.5 | 0.3 | 0.01 | 12 | 8 | 12.5 | 0 |
| P19 | 4.6 | 1.9 | 0 | 0 | 3 | 15 | 20.9 | 0.1 |
| P20 | 4.2 | 1.7 | 0.4 | 0.02 | 6 | 352 | 192.5 | 0.54 |
| P21 | 8.6 | 2.8 | 1.9 | 0.01 | 8 | 29 | 19.2 | 0.21 |
| P22 | 3.5 | 1.4 | 0.5 | 0.02 | 4 | 23.1 | 12.9 | 0.67 |
| P23 | 4.3 | 1.5 | 0.1 | 0 | 7 | 6 | 12.5 | 0.87 |
| P24 | 5 | 1.6 | 0.5 | 0.01 | 4 | 22 | 24.5 | 0.11 |
| P25 | 6.1 | 1.4 | 0.4 | 0.02 | 28 | 17.9 | 26.8 | 0.2 |
| P26 | 3.6 | 0.9 | 6.9 | 0.01 | 14 | 20 | 20.1 | 0.13 |
| P27 | 5.7 | 1.8 | 0.5 | 0.01 | 14 | 19.4 | 31.3 | 0.24 |
| P28 | 8.6 | 1.7 | 0.2 | 0.02 | 13 | 12 | 16.2 | 0.23 |
| P29 | 7.3 | 3.6 | 0.1 | 0.01 | 11 | 34 | 21.7 | 0.33 |
| P30 | 7.1 | 1.7 | 1.4 | 0.01 | 8 | 12.5 | 32.1 | 0.11 |
| P31 | 7.3 | 1.5 | 0.9 | 0.01 | 13 | 10 | 15.0 | 0.33 |
| P32 | 6.6 | 2.5 | 0.1 | 0.03 | 10 | 11.6 | 27.8 | 0.55 |
| P33 | 4.1 | 1.3 | 0.1 | 0.01 | 5 | 29 | 22.6 | 0.61 |
| P34 | 7.7 | 2.8 | 1.7 | 0.01 | 16 | 21 | 13.1 | 0.27 |
| P35 | 8.2 | 2.0 | 0.3 | 0.01 | 13 | 18 | 14.6 | 0.15 |
| P36 | 5 | 1.4 | 1.1 | 0.56 | 7 | 23.5 | 28.9 | 0.15 |
| P37 | 4.3 | 0.9 | 0.1 | 0.01 | 32 | 21 | 17.7 | 1.08 |
| P38 | 5.5 | 1.8 | 3.4 | 0.01 | 4 | 16 | 22.1 | 0.88 |
| M (QL, QU) | 5.7 (0.3, 15.3) | 19.2 (12.5, 23.2) | 18.5 (14.9, 25.0) | 0.2 (0.1, 0.4) |

ALT = alanine transaminase, 0–35 U/L; AST = aspartate aminotransferase, normal value is 8–40 U/L; CRP = C-reactive protein, normal value is 0–4 mg/L; D-dimer = plasma D-dimer quantification, 0–1 mg/L; ESR = erythrocyte sedimentation rate, normal value is 0–20 mm/h; LYM = absolute value of lymphocytes, normal value is 0.8–4 × 10^9/L; PCT = procalcitonin, normal value is 0–0.04 ng/mL; WBC = white blood cells, normal value is 4–10 × 10^9/L.
patients received the test at an interval of 6 days since the first test (all turned negative at the second test), 2 patients with an interval of 8 days (both turned negative at the second test), and 7 patients with an interval of 9 days (6 turned negative at the second test). The viral shedding time was 6 (2, 10) days, with a median of 6 days, a minimum of 2 days, and a maximum of 17 days, while 89.5% (34/38) patients exhibited the same as <10 days, and 63.2% (24/38) patients showed <7 days (Table 3 and Fig. 1).

4. Discussion
This study defined and reviewed the clinical and nucleic acid testing of asymptomatic SARS-CoV-2 infection. All the cases included in this study had a history of close contact with confirmed cases or occupational exposure. Six worked in the quarantine places and were in contact with the patients in the latency period or asymptomatic infected patients. This also suggests that patients in the latency period of COVID-19 and asymptomatic infected patients are infectious. Nevertheless, the sample size in this paper is small for a firm conclusion. To study the infectivity of asymptomatic COVID-19, a large number of samples and detailed epidemiological investigations or prospective studies are needed.

The primary challenge of asymptomatic infected persons for epidemic prevention and control lies in their concealed transmission. The patients have no symptoms or suspicion of
being infected and will not actively report or go to relevant medical institutions to seek medical treatment, and hence, it is difficult to identify such patients by the infectious disease surveillance network, which could lead to widespread pre-outbreak spread. As of April 2, 00:00 a.m., 1075 asymptomatic patients with COVID-19 (226 imported) were under medical observation, according to the Chinese reports. The findings of such infection were mainly attributed to the active screening of close contacts of confirmed patients, clustering epidemics, exposed populations, and personnel in the areas where epidemics persisted both nationally and internationally. The current screening of asymptomatic infection focuses on infected persons, which is downstream in the transmission chain of COVID-19. Since asymptomatic individuals spread the virus to others, which are later confirmed as patients and are difficult to be detected, the National Health and Epidemic Prevention authorities might find it difficult to substantially control the spread of COVID-19.

Among the asymptomatic patients included in this study, we found that the viral shedding time was 6 (2, 10) days, with a median time of 6 days, a minimum of only 2 days, and a maximum of 17 days. The shedding time of 89.5% (34/38) and 63.2% (24/38) of the patients did not exceed 10 days or 1 week, respectively. Furthermore, since 55.3% (21/38) of the patients failed to have nucleic acid testing every alternate day, some turned negative at the first nucleic acid re-test, and we could not identify an accurate nucleic acid turning-negative time point in some patients. This suggests that the actual shedding time might be shorter than that estimated in this study. We defined the viral shedding time as the interval between the first nucleic acid positive and persistent nucleic acid turning negative, which was used to replace the results of the virus culture. The viral shedding time of asymptomatic infection is significantly shorter than that of symptomatic confirmed cases, suggesting that the infectivity of asymptomatic individuals should not be stronger than that of symptomatic patients. The median viral shedding time was also shorter than 9.5 days, as reported in another study of asymptomatic infection. Herein, we reconfirmed that during the 14-day period of medical observation, the virus nucleic acid RT-PCR test was negative for 2 consecutive times (tested at an interval of >24 hours). Any obvious or observable symptoms and signs or abnormalities were not detected by relevant laboratory testing and imaging.

Currently, there are no criteria for estimating the viral shedding time in asymptomatic infection because it is difficult to assess when the infection actually starts and when the virus begins to shear. In this study, we tentatively defined the time interval from the first nucleic acid positive to the consecutive nucleic acid test negative. Typically, the viral infection begins viral shedding before and after the onset of the disease. For asymptomatic infection, we cannot know the onset time, which might require indirect speculation. Thus, we hypothesize that asymptomatic COVID-19 has an incubation period similar to that of symptomatic COVID-19. A study with a large sample size showed that COVID-19 has an average incubation period of 5 days. Another study suggested that COVID-19 has a viral shedding of 2 days before symptom onset. Therefore, rigorous viral shedding should be initiated 3 days after the last exposure/exposure (average incubation period minus 2 days). The correction is more consistent with the characteristics of the virus than the onset of the identified disease before the start of the shedding.

Is asymptomatic infection infectious? The answer is yes. In this study, there were 6 cases of staff in quarantine places who were in contact with patients still in the incubation period or asymptomatic infected individuals, implying that COVID-19 might be infectious during the incubation period or in asymptomatic infected people. Small clusters of outbreaks caused by the asymptomatic infection have been reported. A study has even accurately analyzed the characteristics of the population transmission kinetics, revealing that asymptomatic infection contributes 5% of the basic reproduction number. If we consider the transmission caused by those patients was still in the incubation period, the proportion will increase by 50%, which is an astonishing number. This was in agreement with the results of a previous study, wherein the premorbid transmission accounts for 44% of all transmissions.

Interestingly, the mechanism underlying the spread of the infection by asymptomatic patients with no obvious respiratory symptoms, such as coughing and sneezing, is yet to be elucidated. It could be speculated that the transmission mode of these patients is different from the respiratory droplets (the patients are not coughing and do not produce droplets). Some studies have suggested that the virus samples in the air of the patients’ room and in the exhaust fan of the negative pressure ward are positive. Thus, we suspected that the transmission mode might be
being close to aerosols or an air vent. Kim et al[16] verified the possibility of this conjecture through a well-designed preliminary experiment.

This study has some limitations. The sample size is small, and the patients were only one hospital. The exact start of the infection is unknown in most cases. Many patients were not tested every other day, and the exact shedding time is uncertain. This was a retrospective study. The laboratory tests that could be analyzed are those routinely performed in the clinical setting. Of note, the SARS-CoV-2 antibodies were not tested routinely. In addition, we only have the final official test results reported by the CDC, which is reported as negative/positive. The qRT-PCR results are not reported by the CDC, precluding the analysis of the viral load. Future studies will have to look to the raw qRT-PCR data as some Institutes now recommend patient discharge when they reach a pre-specified threshold.[17] Finally, there is no comparator group, and the shedding time of asymptomatic patients compared with mild cases is unknown. In conclusion, according to these conjectures and results, a serious reality of prevention and control is as follows: massive emergence of presymptomatic transmission reveals the lag of our existing isolation policy and contact tracking, and even if we detect and effectively isolate the patients immediately after onset, we may block only 50% to 56% of the possible transmission. Therefore, patients in the incubation period or with asymptomatic infections need to be identified in advance. How can this be achieved? It is possible to simulate the life trajectory of the incubation period or asymptomatic infected individuals and the contact process with the surrounding people. Based on data modeling after propagation, clustering analysis can be conducted, which is a promising direction.

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