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BRIEF REPORT

Clinical Outcomes in 55 Patients With Severe Acute Respiratory Syndrome Coronavirus 2 Who Were Asymptomatic at Hospital Admission in Shenzhen, China

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An epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has spread unexpectedly in Wuhan, Hubei Province, China, since December 2019. There are few reports about asymptomatic contacts of infected patients identified as positive for SARS-CoV-2 through screening. We studied the epidemiological and clinical outcomes in 55 asymptomatic carriers who were laboratory confirmed to be positive for SARS-CoV-2 through nucleic acid testing of pharyngeal swab samples. The asymptomatic carriers seldom occurred among young people (aged 18–29 years) who had close contact with infected family members. In the majority of patients, the outcome was mild or ordinary 2019 novel coronavirus disease during hospitalization.

Keywords. SARS coronavirus 2; asymptomatic infection; outcome.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the focus of global attention which began with an outbreak of a febrile respiratory illness in December 2019 in Wuhan, Hubei Province [1]. It was reported that the virus was transmitted between humans [2, 3], especially among family members [4]. Prompt public health measures were taken in China, including intensive surveillance and epidemiological investigations. According to the latest recommendations [5], 2019 novel coronavirus disease (COVID-19) is classified into 4 types: mild, ordinary, severe, and critical. Mild and ordinary cases have good prognoses, but severe cases, and especially critical cases, always present with systematic organ dysfunction and involve prolonged hospitalization [6]. To date, no obvious breakthroughs in the treatment of severe coronavirus infection have been identified. Previous reports have indicated that the onset of symptoms may help physicians identify patients with poor prognosis and that meticulous supportive care can be effective [7].

Shenzhen City is located in the southern part of Guangdong, China, and approximately 70% of the population is migrant people. After the traditional Chinese New Year holidays, massive human movement occurred. Since the first clinical case of COVID-19 was reported on 11 January 2020, Shenzhen has become one of the main epidemic areas for this disease. Close contacts are isolated and monitored at home or at designated hotels, and more and more asymptomatic cases were found. We reviewed findings in asymptomatic cases that were laboratory confirmed to be positive for SARS-CoV-2 through nucleic acid testing of pharyngeal swab samples. We retrospectively analyzed clinical outcomes in 55 asymptomatic patients who were infected with SARS-CoV-2 and admitted to the Third People's Hospital of Shenzhen, China.

METHODS

Ethical Considerations

This study was approved by the Ethics Committee of the Third People's Hospital of Shenzhen, China, on 23 February 2020. Informed consent was obtained from all of the patients or their guardians.

Clinical Classification

Cases were classified as follows: (1) mild, mild clinical symptoms without pneumonia seen at chest computed tomography; (2) ordinary, fever and other respiratory symptoms with pneumonia seen at imaging; (3) severe, respiratory distress, hypoxia (oxygen saturation, ≤93%), or abnormal results of blood gas analysis (PaO_2 < 0 mm Hg or $PaCO_2$ >50 mm Hg); and (4) critical, respiratory failure requiring mechanical ventilation, shock, or other organ failure requiring intensive care unit monitoring and treatment.

Data Collection

We obtained data from medical records, including all symptoms at onset, physical examination findings (all study subjects were asymptomatic at admission; symptoms that developed during hospitalization were recorded), laboratory and imaging data, and personal history. We included in the study asymptomatic patients who had laboratory-confirmed positive results for SARS-CoV-2 (based on nucleic acid testing of pharyngeal swab samples [8]) after the diagnosis of COVID-19 in a family member and who were admitted to the Third People's Hospital of Shenzhen from

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11 January 2020 to 29 February 2020. The exclusion criteria were suspected COVID-19 with symptoms such as fever, cough, fatigue, poor appetite, diarrhea, and headache at admission.

Laboratory data include complete blood cell count, C-reactive protein (CRP) level, erythrocyte sedimentation rate, liver and renal function, electrolyte levels, coagulation test results, and levels of procalcitonin, interleukin 6, lactate dehydrogenase (LDH), and creatine kinase. Pharyngeal swab samples were collected for the SARS-CoV-2 test on the day of admission.

The collected samples, stored at 2°C–8°C, were sent on ice to the Center for Disease Control and Prevention of Shenzhen. Viral RNA was extracted from pharyngeal swab samples using the QIAamp RNA Viral Kit (Qiagen), and quantitative reverse-transcription polymerase chain reaction was performed using the primers and probes targeting the *ORF1ab* and *N* genes of SARS-CoV-2, as recommended by the Chinese Center for Disease Control and Prevention [9]. Virus clearance was defined as 2 consecutive negative nucleic acid test results (at a sampling interval of ≥1 day).

All acquired data were cross-checked by 2 investigators to ensure that there was no duplicated information. Investigators were trained to use a standardized questionnaire to collect epidemiological information immediately after patients were admitted, with face-to-face interviews with the patients or their guardians and relevant medical staff.

Statistical Analysis

Basic descriptive analyses were performed in all patients. IBM SPSS 18.0 statistical software was used for statistical analyses.

RESULTS

General Characteristics of Asymptomatic Patients With Confirmed SARS-CoV-2 Infection

A total of 55 asymptomatic case patients were identified with SARS-CoV-2 infection after the onset of illness in an infected family member. These included 22 male and 33 female patients, aged from 2 to 69 years; their median age was 49 years, and 30.9% were 30–49 years old (Table 1). More than half of the patients belonged to the native population of Hubei Province. Ordinary COVID-19 was the outcome in 70.9% of the asymptomatic case patients.

Clinical Characteristics

Of the 55 patients, only 7 had mild cough and 7 had low fever (<38.0°C) 3–5 days later (including 2 with both). A 2-year-old boy had ordinary COVID-19 diagnosed after being testing 3 times within 2 weeks. Despite being asymptomatic, the 55 patients were admitted immediately and medically isolated. The interval between hospitalization and illness onset was 1–7 days. On admission, all 55 patients underwent chest computed tomography (CT), which showed pneumonia in 37. Chest CT findings were initially normal in 18 patients (32.7%); 16 experienced no symptoms during hospitalization. Two women >60 years old were admitted promptly after their infected family members and had normal chest CT findings on day 1. During the course of hospitalization, they both had mild cough and low fever 5 days later, along with hypoxia (oxygen saturation, 90%) and restlessness. Repeated CT showed pneumonia (Figure 1).

Table 1. General Characteristics of Asymptomatic Patients With Confirmed Infection

	Patients by Infection Classification, No. (%)[a]			
Data	Total (N = 55)	Mild (n = 14 [25.5%])	Ordinary (n = 39 [70.9%])	Severe (n = 2 [3.6%])
Age, median (range), y	49 (2–69)	25 (3–63)	49 (3–69)	62 (62–64)
Age groups, y				
<18	15 (27.3)	5 (9.1)	10 (18.2)	0 (0.0)
18–29	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)
30–49	17 (30.9)	8 (14.5)	9 (16.4)	0 (0.0)
50–59	6 (10.9)	0 (0.0)	6 (10.9)	0 (0.0)
>60	16 (29.1)	1 (1.8)	13 (23.6)	2 (3.6)
Sex				
Male	22 (40.0)	4 (7.3)	18 (32.7)	0 (0.0)
Female	33 (60.0)	10 (18.2)	21 (38.2)	2 (3.6)
Native to Hubei Province				
Yes	31 (56.4)	7 (12.7)	22 (40.0)	2 (3.6)
No	24 (43.6)	7 (12.7)	17 (30.9)	0 (0.0)
Underlying diseases				
Hypertension	8 (14.5)	0 (0.0)	6 (10.1)	2 (3.6)
Hypothyroidism	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)
Chronic pharyngitis	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)
Hepatitis B	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)
Asthma	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)
Cholecystitis	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)

[a]Data represent no. (%) of patients unless otherwise specified. Percentages in column headings are row percentages.

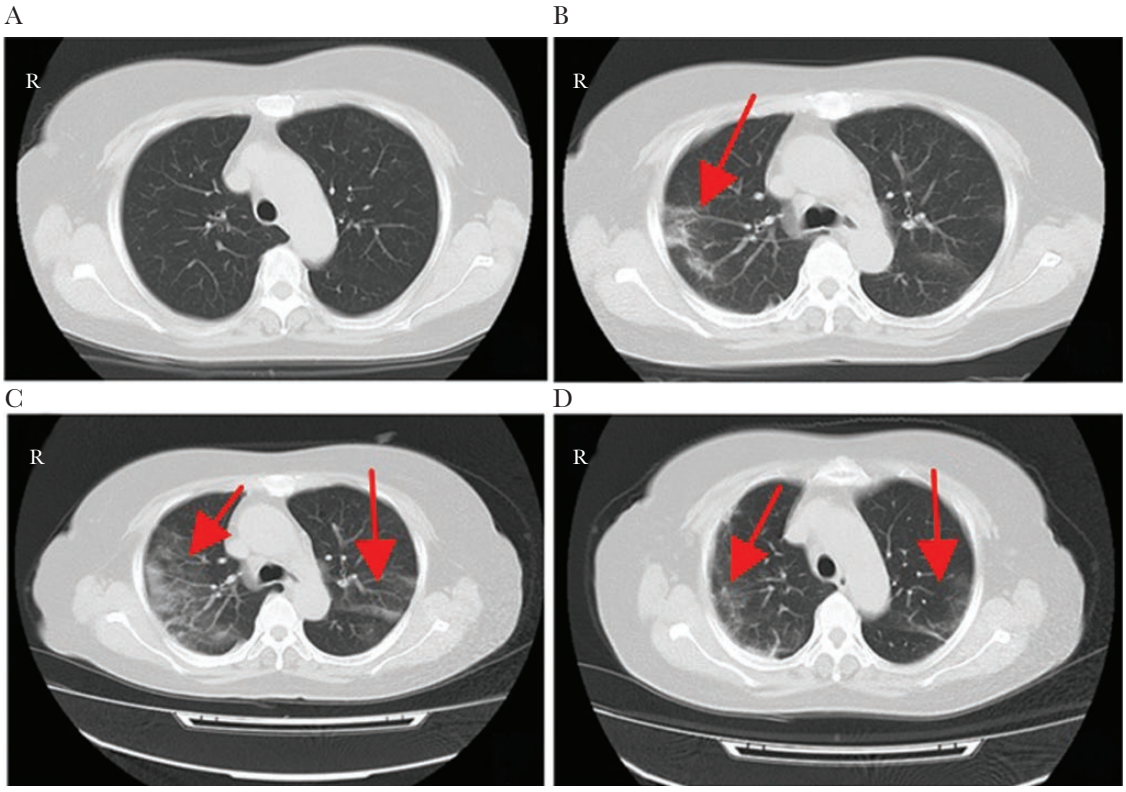

Figure 1. Representative thoracic computed tomographic scans of a patient with severe illness, showing normal findings on admission day 1 (*A*), diffuse patchy shadowing (*arrow*) on day 5 (*B*), more diffuse patchy shadowing (*arrows*) on day 8 (*C*), and recovery stage on day 15 (*D*). R indicated the right lung.

After informed consent was obtained, lopinavir-ritonavir therapy was initiated in all 55 patients and continued for 7 days. The 2 patients with hypoxia were also treated with intravenous immunoglobulin (10 g/d) and methylprednisolone (1–2 mg/kg/d) therapy for 3 days and with a heated humidified high-flow nasal cannula for 5 days. Eventually, they both recovered without complications. None of the patients were admitted to the intensive care unit.

All the patients recovered and were discharged to home. In all patients, results of 2 consecutive nucleic acid tests of nasopharyngeal swab samples (sampling interval, ≥1 day) were negative for SARS-CoV-2 after 4–21 days. Three sputum samples from patients with ordinary COVID-19 were negative 3–5 days after nasopharyngeal swab testing. A history of hypertension was present in 8 patients, and a history of cholecystitis. hypothyroidism, chronic pharyngitis, hepatitis B, and asthma in 1 patient each. Epstein-Barr virus was diagnosed serologically in 1 patient, and *Mycoplasma pneumoniae* in 3. Neutropenia and lymphocyte counts below normal occurred in 11 patients each. Initial biochemical results showed elevated CRP levels, erythrocyte sedimentation rate, and LDH levels in 10, 20, and 13 patients, respectively (Table 2).

DISCUSSION

Overall, of the 55 patients admitted with asymptomatic SARS-CoV-2 infection in this study group, 14 had mild, 39 had ordinary, and 2 had severe COVID-19 during hospitalization. Age was significantly associated with asymptomatic occurrence. Asymptomatic cases occurred seldom among young people (18–29 years old). This was a novel discovery but one

Table 2. Laboratory and General Results in Asymptomatic Patients With Confirmed Infection

Results	Patients, No. (N = 55)[a]
Elevated WBC count (>1.5 × 10^9/L)	1
Decreased WBC count (<4.0 × 10^9/L)	11
Decreased lymphocyte count (<1.5 × 10^9/L)	11
Elevated CRP level (>8 mg/L)	10
Elevated ESR (>20 mm/h)	20
Elevated LDH level (>250 U/L)	13
Complicated infection	
Epstein-Barr virus[b]	1
Mycoplasma pneumoniae[b]	3
Time interval, median (time), d	
From hospitalization to illness onset[c]	5 (1–7)
From positive to negative nucleic acid test result	10 (4–21)

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; WBC, white blood cell.

[a]Data represent no. of patients unless otherwise specified.

[b]Epstein-Barr virus and M. pneumoniae infections were diagnosed serologically.

[c]Illness onset was defined as the appearance of symptoms or abnormal computed tomographic findings.

we should interpret with caution owing to the small number of patients.

In the current study, we found that 3.6% of asymptomatic patients with SARS-CoV-2 infection might take a turn for the worse. Only 2 patients had typical symptoms (both cough and fever) [10], 3–5 days after hospital admission. Family members with fatigue and dry cough, and particularly those with fever, were easily noticed, but asymptomatic members were initially ignored. Many asymptomatic persons were actually a source of SARS-CoV-2 infection but were considered healthy before they underwent screening. The risk of viral spread from asymptomatic patients with infection suggest that prompt screening of family members of infected persons is important.

It is evident that family cluster transmission of SARS-CoV-2 was one main mode of transmission [11]. A previous study in Nanjing found that people (<15 years old) were prone to be asymptomatic [12]. We found that asymptomatic cases of infection occurred seldom in young people (18–29 years old) in Shenzhen. Nucleic acid testing would therefore be crucial to screen for asymptomatic infections in this population.

A previous study indicated that CRP and LDH levels may be predictors of disease severity [13]. CRP levels, LDH levels, and white blood cell counts were elevated occurred in 10, 13 and 1 patient, respectively. Eleven patients (including the 2 with severe infection) had leukopenia. Here we found no relationship between clinical type and laboratory results; this should be further investigated.

In 3 patients, sputum samples became negative 3–5 days later than nasopharyngeal swab samples. To et al [14] reported that serial monitoring of saliva viral load generally showed a declining trend. We therefore recommend that monitoring viral loads in sputum samples is crucial in late-stage COVID-19, as previously recommended [15].

However, the current study has several limitations. First, the data are retrospectively analyzed, so the possibility of recall bias cannot be ruled out. Second, we collected most but not all laboratory data. However, Shenzhen is an international city with adequate public health interventions and medications. The enrolled patients were identified through systematic screening of the family members of patients with COVID-19. All asymptomatic patients were admitted to the Third People's Hospital of Shenzhen, the only designated hospital in Shenzhen, so the study population is representative of the whole city.

In conclusion, we present here the epidemiological and clinical characteristics of patients with asymptomatic SARS-CoV-2 infection in Shenzhen. In our study, asymptomatic infection was seldom seen in young people; the proportion with severe COVID-19 was low, and the proportion with ordinary COVID-19 was high. To better minimize the risk of SARS-CoV-2 infection, preventive measures focusing on high-risk populations are recommended. A negative sputum swab test was recommended to the isolation of the infection source.

Notes

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Author contributions. Y. W. and Y. L. searched the literature and conceived the study; L. Liu designed the study; N. L. and L. Li collected the data; and X. W. interpreted the results and drafted the report.

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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