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Original article

Characteristics of asymptomatic patients with SARS-CoV-2 infection in Jinan, China

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) is continuously and rapidly circulating at present. Asymptomatic patients have been proven to be contagious and thus pose a significant infection control challenge. Here we describe the characteristics of asymptomatic patients with SARS-CoV-2 infection in Jinan, Shandong province, China. A total of 47 patients with confirmed COVID-19 were recruited. Among them, 11 patients were categorized as asymptomatic cases. We found that the asymptomatic patients in Jinan were relatively young and were mainly clustered cases. The laboratory indicators and lung lesion on chest CT were mild. No special factors were found accounting for the presence or absence of symptoms. The presence of asymptomatic patients increased the difficulty of screening. It is necessary to strengthen the identification of such patients in the future.

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Since an outbreak of COVID-19 in Wuhan and related regions in Hubei province [1–5], an increasing number of exported cases have been confirmed in other provinces of China and multiple countries around the world [6–8]. As of March 10, 2020, more than 110 000 confirmed cases of COVID-19 have been reported in 110 countries [9]. The most common clinical manifestation of the disease is fever, fatigue, and dry cough and some patients may present with nasal congestion, runny nose, and diarrhea. In some cases, dyspnea usually occurs one week after the disease onset and some patients can rapidly progress to septic shock, acute respiratory distress syndrome (ARDS), refractory metabolic acidosis, and coagulation disorders [10,11]. As the situation progressed over time, more and more asymptomatic individuals were identified due to increased surveillance and contact screening [12]. Those asymptomatic cases may play a role in the transmission and thus pose a significant infection control challenge. To best of our knowledge, so far, there is no special paper describing the features of these patients. Here we report the characteristics of asymptomatic patients with confirmed SARS-CoV-2 infection admitted to Jinan infectious disease hospital, Shandong University. The hospital is the only one designated medical institution for the hospitalization of confirmed patients with COVID-19 in Jinan, capital of Shandong province, China. Furthermore, we compared the features between asymptomatic and symptomatic cases to determine whether there exist factors accounting for the presence or absence of symptoms.

1. Patients and method

1.1. Patients involvement

All the inpatients with COVID-19 confirmed by pharyngeal swab COVID-19 nucleic acid test from January 23 to March 10 in Jinan infectious disease hospital, Shandong University were included in this study. The patients were diagnosed and treated according to the “Diagnosis and Treatment Guideline for COVID-19” distributed by Chinese National Health Commission [10].

1.2. Data collection

The medical records of patients were analyzed by the research team. Demographic information, epidemiological history, clinical characteristics, laboratory findings, chest computed tomographic (CT) scan and outcome of each patient were obtained from the electronic medical record system of Jinan infectious disease hospital. Laboratory test results included a complete blood count,

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serum biochemistry, coagulation function, C-reactive protein(CRP), erythrocyte sedimentation rate(ESR), and myocardial enzyme spectrum. The data for some patients were missing due to the absence of tests or delayed results. Clinical outcomes were followed up until 24:00, March 10, 2020. The study was approved by the Ethics Committee of Jinan infectious disease hospital, Shandong University, with a waiver of written informed consent because of the retrospective nature of the study.

1.3. Statistical analysis

The continuous variables were expressed as medians with ranges and were compared with the Mann–Whitney U test. The categorical variables were presented as frequencies and percentages and were analyzed by the χ^2 test. All statistical analyses were done with SPSS software version 19.0, and a P value less than 0.05 was considered statistically significant.

2. Results

2.1. Baseline characteristics of asymptomatic patients in the study

A total of 47 patients were diagnosed as COVID-19 from January 23 to March 10, with 11(23.4%) patients categorized into asymptomatic group and 36(76.6%) patients categorized into symptomatic group. Among asymptomatic patients, 6(54.5%) patients were men and 5 patients (45.5%) were women. The median age for the patients was 23 years, ranging from 1 to 60 years old; of them, 5(45.5%) were children and 6 were adults. 3(27.3%) patients came from Wuhan, Hubei Province of China. 8 (72.7%) patients were residents of Jinan, 7 (63.6%) of which contacted with confirmed cases. Among 11 asymptomatic patients, 9(81.9%) were cluster cases, 8(72.7%) of which were family cluster cases and 1 (9.1%) were other cluster cases. Compared with symptomatic patients, asymptomatic patients were relatively younger (median age, 23 years vs 35.5 years), and were more likely cluster cases (81.8% vs 72.2%), but there was no statistical significance between the two groups. The detailed baseline characteristics of the study population are summarized in Table 1.

2.2. Clinical characteristics of asymptomatic patients in the study

For 11 asymptomatic patients, 5 were mild cases and 6 were common cases; the median time from admission to negative conversion of viral RNA was 10 days, ranging from 3 days to 34 days; and the median time of hospital stay was 14 days, ranging from 10 days to 30 days. Compared with symptomatic patients, the hospital stay of asymptomatic patients is significantly shorter (14 days vs 22.5 days, P = 0.004), while the diagnostic classification and time of negative viral RNA conversion did not differ between two groups. For the 36 symptomatic patients, the most common symptoms were fever (28, 77.8%), followed by dry cough (17, 47.2%), expectoration (4, 11.1%), fatigue (4, 11.1%), sore throat (4, 11.1%), myalgia (4, 11.1%), headache (2, 5.6%), and coryza (1, 2.8%). The detailed clinical characteristics were found in Tables 2 and 3.

Table 1
Baseline characteristics of patients infected with SARS-CoV-2.

Item	All cases	Asymptomatic	Symptomatic	P-value
No. (%)	47	11(23.4)	36(76.6)	–
Age, years(median, range)	34(1–72)	23(1–60)	35.5(3–72)	0.179
Age group (n, %)				0.069
<18	10(21.3)	5(45.5)	5(13.9)	
≥18	37(78.7)	6(54.5)	31(86.1)	
Gender (N, %)				0.568
Male	20(42.6)	6(54.5)	14(38.9)	
Female	27(57.4)	5(45.5)	22(61.1)	
Comorbidities	11(23.4)	2(18.2)	9(25.0)	0.952
Exposure history				0.683
Resident of Wuhan	9(19.1)	3(27.3)	6(16.7)	
Recent travel to Wuhan	4(8.5)	0(0.0)	4(11.1)	
Recent travel to other epidemic areas	7(14.9)	1(9.1)	6(16.7)	
Close contact with confirmed patients	27(57.4)	7(63.6)	20(55.6)	
Cluster cases(N,%)	35(74.4)	9(81.8)	26(72.2)	0.807
Family	28(59.6)	8(72.7)	20(55.6)	
Other	7(14.9)	1 (9.1)	6(16.7))	

2.3. Laboratory and radiologic findings of asymptomatic patients in the study

The blood cell test results showed that 27.3% (3/11) asymptomatic patients had decreased white blood cell and 36.4% (4/11) had increased lymphocyte count. Increased or decreased platelet counts were also found in these patients. Levels of lactate dehydrogenase and creatine kinase-MB increased in about half of the patients. Other laboratory findings in the asymptomatic patients included higher or lower levels of fibrinogen, higher levels of D-dimmer, C-reactive protein and ESR. Although there were many laboratory abnormalities in asymptomatic patients, compared with symptomatic patients, most of the indicators were not statistically significant.

Abnormalities on chest computed tomograms (CT) were detected in 7 asymptomatic patients (63.6%) (Table 4), of which 4 (36.4%) showed bilateral involvement and 3 (27.3%) showed unilateral involvement. Compared with symptomatic patients, asymptomatic patients had fewer lung CT lesions (63.6% vs 83.3%), and there was no statistical difference between the two groups. The typical chest CT findings of these patients were unilateral or bilateral multiple ground-glass opacities or consolidation. Fig. 1 showed representative lung images of an asymptomatic patient in which lesions developed in multiple lobes, most of which were subpleural ground-glass opacity co-existed with consolidation. Fig. 2 showed dynamic changes of the chest CT of an asymptomatic patient obtained on February 5(A), February 8(B), February 14(C) and February 19(D).

2.4. Treatment and clinical outcomes

All patients received antiviral treatment, including lopinavir/ritonavir tablets, arbidol, and inhalation of recombinant human interferon. The duration of antiviral treatment was 10–15 days. As of 24:00, March 10, 2020, 100%(36/36) symptomatic patients and 81.8% (9/11) asymptomatic patients have been discharged, and the remained 2 patients still have positive nucleic acid test results.

3. Discussion

The current coronavirus outbreak in China and other countries is the third epidemic caused by coronavirus in the 21st century, already surpassing SARS and MERS in the number of individuals infected [6]. The COVID-19 can present a variety of manifestations ranging from no symptoms or mild disease to severe pneumonia or multi-organ failure. It is expected that early in the development of an outbreak, severe cases are recognized first and then less severe (mild or asymptomatic) cases are detected with increasing surveillance. The occurrence of asymptomatic individuals increased the difficulty of screening, helped spread the disease, therefore, posed a significant public health issue.

In our study, a total of 47 patients were diagnosed as COVID-19 from January 23 to March 10, of which 11 (23.4%) patients had no

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Table 2
Clinical characteristics of patients infected with SARS-CoV-2.

Item	All cases	Asymptomatic	Symptomatic	P-value
No. (%)	47	11(23.4)	36(76.6)	–
Diagnostic classification(N, %)				0.077
Mild case	10(21.3)	5(45.5)	5(13.9)	
Common case	36(76.6)	6(54.5)	30(83.3)	
Severe case	1(2.1)	0(0.0)	1(2.8)	
Time from admission to negative conversion of viral RNA (days, median, range)	13.5(3–39)	10(3–34)	16(5–39)	0.182
Time of hospital stay (days, median, range)	22(10–44)	14(10–30)	22.5(12–44)	0.004
Outcome(N, %)				0.051
Discharge	45(95.7)	9(81.8)	36(100)	
Hospitalization	2(4.3)	2(18.2)	0(0.0)	

Table 3
Symptoms of patients infected with SARS-CoV-2.

Items	N	Percentage, %
No. of patients	36	100
Symptoms		
Fever	28	77.8
Dry cough	17	47.2
Expectoration	4	11.1
Fatigue	4	11.1
Sore throat	4	11.1
Myalgia	4	11.1
Headache	2	5.6
Coryza	1	2.8
Nausea and vomiting	0	0.0
Diarrhea	0	0.0

symptom. The asymptomatic proportion (23.4%) is higher than the data (17.9%) reported by Kenji Mizumoto [13]. Among 11 asymptomatic patients, 9(81.9%) were cluster cases, 8(72.7%) of which were family cluster cases and 1 (9.1%) were other cluster cases. The presence of cluster cases strongly suggested the need to isolate patients and quarantine for close contacts, especially those family close contacts. The median age of the asymptomatic patients was 23 years old, which is younger than the symptomatic patients(35.5 years), while there was no statistical significance between the two groups. For the 36 symptomatic patients, Fever (77.8%), dry cough (47.2%), expectoration (11.1%), fatigue (11.1%), sore throat (11.1%), myalgia (11.1%) were the most common symptoms, which was consistent with previous studies [3–5,14].

Laboratory findings of the asymptomatic patients showed that some patients might have abnormalities in indicators such as blood cell count, fibrinogen, D-dimmer, C-reactive protein, ESR and myocardial enzymes. Compared with symptomatic patients, most of the laboratory test results were not statistically significant. It is worth noting that creatine kinase-MB was significantly higher in the asymptomatic group than in the symptomatic group($P = 0.020$). Future research is needed to expand the sample to clarify that this indicator does indeed differ between the two groups. Although some asymptomatic patients' laboratory indicators were abnormal, the damage was minor and soon returned

Table 4
Laboratory and radiological findings of patients infected with SARS-CoV-2.

Items	All cases(n)	Asymptomatic (n, %)	Symptomatic (n, %)	P-value
No. of patients	47	11(23.4)	36(76.6)	–
White blood cell count ($\times 10^9$/L, normal range 4–10)	47			1.000
Decreased		3(27.3)	11(30.6)	
Neutrophil count ($\times 10^9$/L, normal range 2–7)	47			0.166
Decreased		1(9.1)	9(25.0)	
Increased		1(9.1)	0(0.0)	
Lymphocyte count ($\times 10^9$/L, normal range 0.8–4)	47			0.011
Decreased		0(0.0)	4(11.1)	
Increased		4(36.4)	1(2.8)	
Platelet count (× 109/L, normal range 100–300)	47			0.151
Decreased		1(9.1)	1(2.8)	
Increased		2(18.2)	2(5.6)	
Fibrinogen (g/L, normal range 2–4)	43			0.122
Decreased		2(22.2)	1(2.9)	
Increased		1(11.1)	11(32.4)	
D-dimmer (μg/ml, normal range 0–0.5)	43			1.000
Increased		1(11.1)	4(11.8)	
C-reactive protein (mg/L, normal range 0.068–8.2)	47			0.137
Increased		1(9.1)	14(38.9)	
Erythrocyte sedimentation rate (mm/H, normal range 0–15)	47			0.722
Increased		3(27.3)	14(38.9)	
Lactate dehydrogenase (U/L, normal range 109–245)	46			0.285
Increased		5(45.5)	8(22.9)	
Creatine kinase-MB (U/L, normal range 7–25)	46			0.020
Increased		6(54.5)	5(14.3)	
Abnormalities on CT	37	7(63.6)	30(83.3)	0.659
Bilateral distribution of patchy shadows or ground glass opacity		4(36.4)	21(58.3)	
Unilateral distribution of patchy shadows or ground glass opacity		3(27.3)	9(25.0)	

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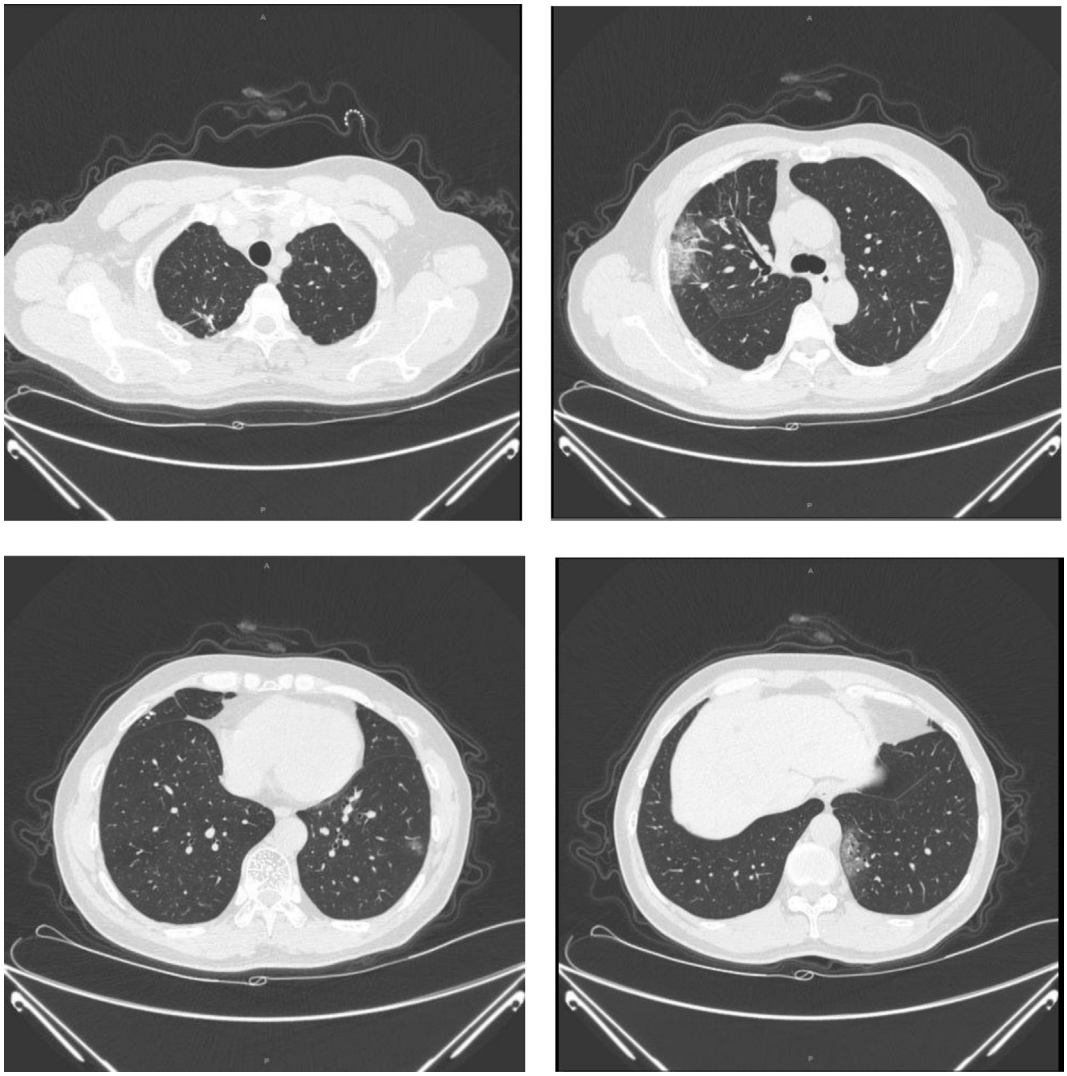

Fig. 1. Representative lung images of an asymptomatic patient in which lesions developed in multiple lobes, most of which were subpleural ground-glass opacity co-existed with consolidation.

to normal. 7 asymptomatic patients (63.6%) were detected lung abnormalities on chest CT. Compared with symptomatic patients, asymptomatic patients had fewer lung CT lesions (63.6% vs 83.3%), and there was also no statistical difference between the two groups. All of the laboratory test results and radiologic findings showed the patients experienced relatively mild illness, which was further evidenced by the short hospital stay of asymptomatic patients($P = 0.004$). All the patients' treatment regimen were produced according to the diagnostic and treatment guidelines for COVID-19 issued by the National Health Commission of the People's Republic of China. As of 24:00, March 10, 2020, 100%(36/36) symptomatic patients and 81.8% (9/11) asymptomatic patients have been discharged. 2 asymptomatic patients still hospitalized for nucleic acid positive.

Asymptomatic patients have been proven to be contagious and thus pose a significant infection control challenge [15–17]. Initially, we hoped to find whether there existed factors accounting for the presence or absence of symptoms which could help us to screen the asymptomatic individuals, and further help to control the disease. In our study, we compared the characteristics of asymptomatic and symptomatic cases and have not found effective indicators to meet our requirements. Therefore, the symptomatic patients should be given timely isolation and treatment, and relevant contacts should be tracked and quarantined as soon as possible. The timely diagnosis, isolation and treatment of these asymptomatic patients will help control the further spread of SARS-CoV-2. Future studies should investigate viral loads and viral dynamics of asymptomatic patients, and examine whether they are different from symptomatic patients. Such researches will enhance the understanding of the pathogenesis of the new emerging virus and would help to control the disease early.

Our study has some limitations. First, our research samples are relatively small and it was difficult to get a full picture of the spectrum of the disease. Second, our asymptomatic patients may truly have no symptoms, or they may not feel it because the symptoms are not obvious. Third, some indicators related to patient's viral loads or immunity, such as $CD4^+$ and $CD8^+$ cells, are not involved in this study. All of those can lead to a biased understanding of the disease.

In conclusion, our study showed the clinical characteristics of asymptomatic patients with COVID-19 in Jinan, China. The patients were relatively young and were mainly clustered cases. The laboratory indicators and lung lesion on chest CT were mild. No special factors were found accounting for the presence or absence of

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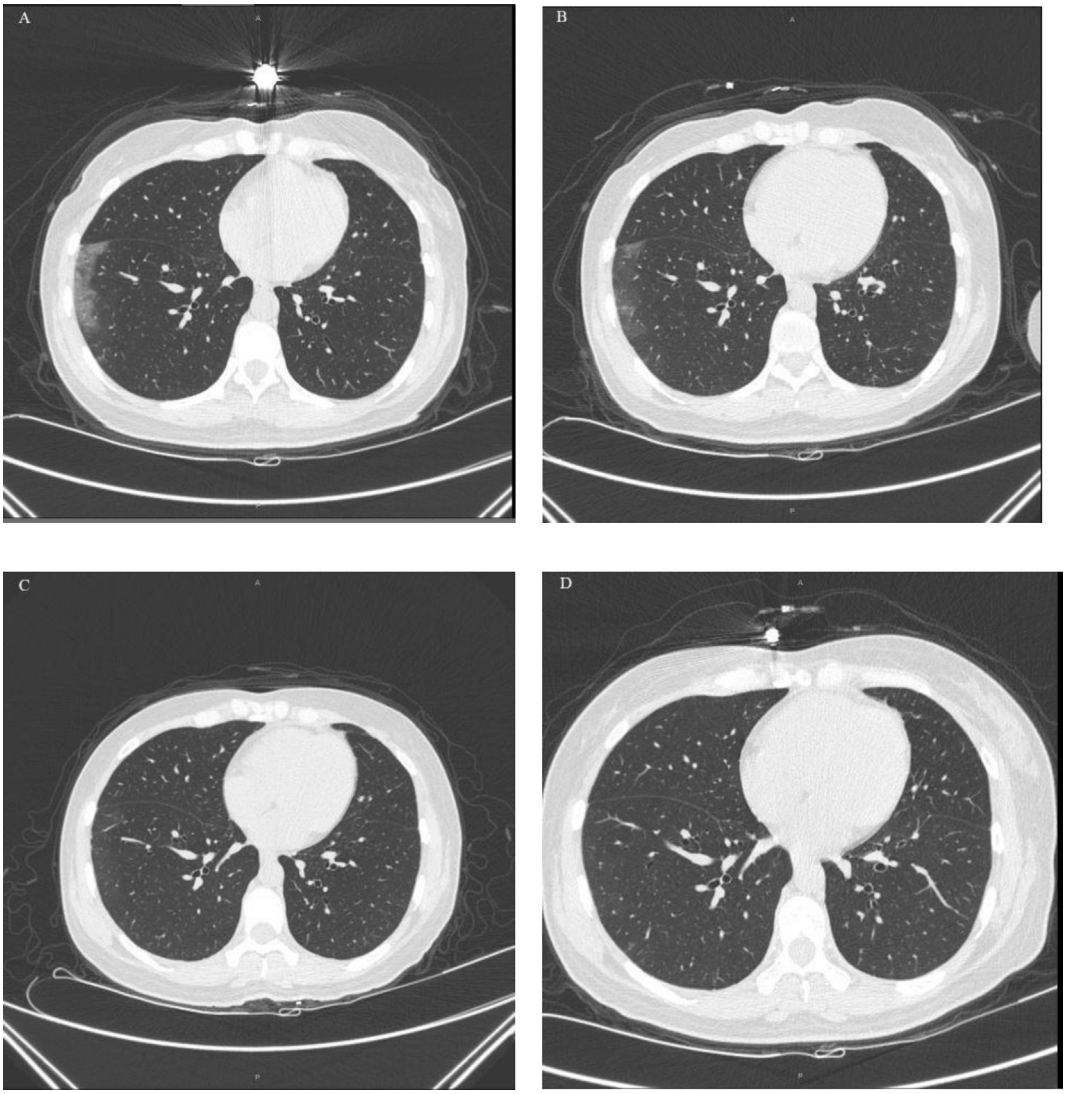

Fig. 2. Dynamic changes of the chest CT of an asymptomatic patient obtained on February 5(A), February 8(B), February 14(C) and February 19(D).

symptoms. The presence of asymptomatic patients increased the difficulty of screening. It is necessary to strengthen the identification of such patients in the future.

Declaration of Competing Interest

None of the authors have any conflict of interest to declare.

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