

# Spectrum and Clinical Characteristics of Symptomatic and Asymptomatic Coronavirus Disease 2019 (COVID-19) With and Without Pneumonia

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## Research

**Keywords:** spectrum, characteristics, asymptomatic COVID-19, symptomatic COVID-19

**Posted Date:** December 10th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-122864/v1>

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# Abstract

## Background

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic. Based on symptoms, COVID-19 cases can be classified as symptomatic or asymptomatic. However, there is limited information about the differences between COVID-19 patients with and without pneumonia. Our study aimed to further discuss the spectrum and clinical characteristics of symptomatic and asymptomatic COVID-19 patients with and without pneumonia.

## Methods

In China, all COVID-19 cases are hospitalized in designated hospitals until two continuous negative oropharyngeal swabs obtained, which allows the professional monitoring of symptoms and clinical characteristics. We stratified all COVID-19 cases in our database, and evaluated clinical characteristics in different COVID-19 subgroups (symptomatic with pneumonia, symptomatic without pneumonia, asymptomatic with pneumonia and asymptomatic without pneumonia).

## Results

According to symptoms and laboratory and radiologic findings, COVID-19 cases were defined as symptomatic with pneumonia, symptomatic without pneumonia, asymptomatic with pneumonia or asymptomatic without pneumonia. There were differences in the clinical characteristics and prognosis among the four groups. Both noninvasive (18, 4.2%) and invasive mechanical ventilation (11, 2.6%) were applied in only the symptomatic with pneumonia group. Likewise, extracorporeal membrane oxygenation (ECMO) and continuous renal replacement therapy (CRRT) were applied in only the symptomatic with pneumonia group. There were no differences in the durations of viral shedding and hospitalization among the four groups.

## Conclusion

We have defined a comprehensive spectrum of COVID-19 with and without pneumonia. The symptomatic with pneumonia group consumed more medical resources than the other groups, and extra caution and monitoring should be applied in this group. The asymptomatic COVID-19 group had a similar viral shedding duration as the symptomatic COVID-19 group.

## Trial registration

Not available

## Introduction

Coronavirus disease 2019 (COVID-19) emerged since December 2019 in Wuhan, Hubei province, central-South China, and is an ongoing global pandemic(1). As of 2 November 2020, there were more than 45 million COVID-19 patients worldwide, and more than one million patients lost their lives(2). The causative pathogen has been identified as a novel enveloped RNA beta coronavirus with phylogenetic similarity to severe acute respiratory syndrome coronavirus (SARS-CoV)(3) and has been named SARS-CoV-2 by the World Health Organization (WHO). Antiviral drugs were effective for SARS-CoV-2 only in vitro, and a recent clinical trial of lopinavir–ritonavir, an antiviral therapy, was not associated with any benefits in COVID-19 patients(4). Because of pandemic transmission and ineffective therapeutics, early diagnosis and quarantine seem to be crucial to combat COVID-19. The spectrum of Covid-19 ranges from asymptomatic or mild, self-limiting respiratory tract illness to severe progressive pneumonia and acute respiratory distress syndrome (ARDS)(1, 5). Approximately 80% of COVID-19 patients have nonsevere illness, but the asymptomatic ratio varies widely in the literatures, which could be explained by different definitions of asymptomatic COVID-19 cases and the late onset of symptoms(5–7) during the disease course. Despite inconsistencies in the asymptomatic case proportions, it is well accepted that asymptomatic COVID-19 patients can serve as transmission sources(7–9).

SARS-CoV-2 relies on the ACE2 receptor for cellular entry, and the expression of ACE2 has been confirmed in nasal goblet cells and alveolar epithelial cells, indicating that SARS-CoV-2 can infect both the upper and lower airways(10). However, there is limited information about differences between upper airway and lower airway (pneumonia) infections in COVID-19 patients. To better understand and identify the spectrum of COVID-19, we conducted this retrospective study to discuss the clinical characteristics in different COVID-19 groups stratified by the presence or absence of symptoms and pneumonia.

## Methods

### Study design

This study was approved and supervised by the Medical Research Ethics Committee of the Second Xiangya Hospital, Central South University. This retrospective study was performed at the Public Health Treatment Center of Changsha, People's Hospital of Junshan District, Loudi Central Hospital, People's Hospital of Lucheng District, Xiangtan Central Hospital and People's Hospital of Yunyang District, which were designated COVID-19 hospitals in Hunan and Hubei provinces. COVID-19 patients were admitted to a designated hospital, once they were diagnosed with COVID-19. A total of 228 patients were hospitalized in Changsha, the closest neighboring capital city of Wuhan. COVID-19 was confirmed by real-time reverse transcription polymerase chain reaction (RT-PCR) detecting SARS-CoV-2 as described previously(3). To analyze the characteristics and outcomes of symptomatic and asymptomatic COVID-19 patients with or without pneumonia, we reviewed medical records and enrolled all COVID-19 patients (n=498) from the above designated hospitals who had been discharged or died before 30th March.

The following medical information was obtained: demographics, symptoms during the whole course of COVID-19 (fever, cough, expectoration, dyspnea, temperature and respiratory rate), laboratory findings

(arterial blood pH, arterial blood PaO<sub>2</sub>, white blood cell count, neutrophils, lymphocyte count, and serum lactate dehydrogenase), chest computed tomography (CT) findings, comorbidities and concomitant diseases, duration of hospitalization, use of antiviral treatments, and concomitant treatments during admission (corticosteroids and antibiotics).

## **Variables and definitions**

Temperature was examined at least three times a day, and fever was defined as an axillary temperature greater than 37.3°C. Chest CT was conducted every 3 to 5 days during hospitalization, and the classification of abnormal CT findings associated with COVID-19-related pneumonia followed those of previous research(11). Clinical improvement was defined as no fever for > 3 days, the resolution of symptoms and radiologic improvement(1). Patients were discharged after clinical improvement and the receipt of two negative continued SARS-CoV-2 RT-PCR tests with an interval of more than 24 hours.

Severe COVID-19 was defined as a respiratory rate  $\geq 30$  breaths/min, blood oxygen saturation (SaO<sub>2</sub>)  $\leq 93\%$ , a PaO<sub>2</sub>/ fraction of inspired oxygen (FiO<sub>2</sub>) ratio <300 mmHg, and/or lung infiltrates in >50% of the lung field within 24-48 hours(1). Patients with respiratory failure, septic shock, and/or multiple organ dysfunction/failure were defined as critical COVID-19 patients(1).

The duration of viral shedding for mild or moderate COVID-19 patients was defined as the time from the date of symptom onset to the date of the last negative result from two consecutive throat swab samples with an interval of more than 24 hours, without positive result in subsequent test. The duration of viral shedding for asymptomatic COVID-19 patients was defined as the time from the first-time positive SARS-CoV-2 RT-PCR test to the date of the second consecutive negative RT-PCR results, with 24-hours interval and without a positive subsequent test.

According to the presence symptoms, COVID-19 patients were divided into asymptomatic and symptomatic COVID-19 groups. Following the pneumonia guidelines from the American Thoracic Society(12), asymptomatic patients with normal chest CT findings during hospitalization were classified as the asymptomatic without pneumonia group. In contrast, asymptomatic patients with abnormal laboratory and radiologic findings during hospitalization were classified as the asymptomatic with pneumonia group. Likewise, symptomatic COVID-19 patients were classified into symptomatic with pneumonia groups and symptomatic without pneumonia groups. Symptoms, laboratory examination results, chest CT findings and outcomes were confirmed by two independent pulmonologists.

## **Statistical analysis**

Continuous variables are presented as medians (interquartile ranges [IQRs]), and categorical variables are presented as n (%). We used the Mann-Whitney U test,  $\chi^2$  test, or Fisher's exact test to compare differences between groups. A two-sided  $\alpha$  less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS software (version 23.0, SPSS Inc., Chicago, US).

## Results

In our study, 498 patients with confirmed COVID-19 were admitted to designated hospitals, and all of them were discharged or died before 30th March. A total of 461 (92.6%) patients had symptoms and were included in the symptomatic group, while the other 37 (7.4%) patients were included in the asymptomatic group. Of the 461 symptomatic patients, 430 (93.3%) had abnormal laboratory and chest CT findings and were included in the symptomatic with pneumonia group, while the other 31 (6.2%) were included in the symptomatic without pneumonia group. Of the 37 asymptomatic COVID-19 patients, 23 (62.2%) had abnormal laboratory and chest CT findings and were classified in the asymptomatic with pneumonia group, while the other 14 (37.8%) were classified in the asymptomatic without pneumonia group (Fig. 1). The greater frequency of pneumonia in the symptomatic group than in the asymptomatic group ( $P < 0.001$  by Chi-square test) supports the theory that symptomatic COVID-19 might be more likely to be associated with lower airway infection than with upper airway infection.

### Demographic characteristics and reported symptoms

The median age of the 430 symptomatic COVID-19 with pneumonia patients was 45.0 years (IQR 34.0–57.0), and 171 (39.8%) of the 430 patients were male (Table 1). The median ages of the 31 symptomatic COVID-19 without pneumonia patients, 23 asymptomatic COVID-19 with pneumonia patients and 14 asymptomatic COVID-19 without pneumonia patients were 35.0 years (17.0–50.0), 48.0 years (38.0–59.0) and 25.0 years (11.0–51.5), respectively (Table 1). Statistical analysis showed that COVID-19 patients without pneumonia were younger than COVID-19 patients with pneumonia ( $P = 0.001$ , Table 1). Of the 23 asymptomatic pneumonia patients, only 6 (26.1%) were male, presenting a significantly lower proportion of males than females (Table 1). There were no differences in comorbidities, except for a higher frequency of hypertension (39.1%) in the asymptomatic with pneumonia group, among the groups (Table 1).

Table 1

Epidemiological and clinical characteristics in symptomatic and asymptomatic COVID-19 cases

Items	Symptomatic COVID-19		Asymptomatic COVID-19		p-value
	with pneumonia (n = 430)	without pneumonia (n = 31)	with pneumonia (n = 23)	without pneumonia (n = 14)	
Age, years	45.0 (34.0–57.0)*	35.0 (17.0–50.0)*	48.0 (38.0–59.0)	25.0 (11.0–51.5)*	0.001
Sex, male	206 (47.9)	17 (54.8)	6 (26.1)*	7 (50.0)	0.175
Exposure to Wuhan	171 (39.8)	12 (38.7)	6 (26.1)	1 (7.1) *	0.055
Family clusters <sup>#</sup>	92 (47.9)*	13 (72.2)	8 (88.9)	5 (55.6)	0.018
Comorbidity	86 (20.0)	4 (12.9)	7 (30.4)	2 (14.3)	0.424
Influenza A or B <sup>#</sup>	0 (0)	0 (0)	0 (0)	0 (0)	NA
Cardiovascular disease	17 (4.0)	2 (6.5)	1 (4.3)	0 (0)	0.790
Diabetes mellitus	37 (8.6)	0 (0)	4 (17.4)	0 (0)	0.020
Hypertension	63 (14.7)	4 (12.9)	9 (39.1)*	1 (7.1)	0.032
COPD	12 (2.8)	1 (3.2)	0 (0)	0 (0)	0.374
Chronic liver disease	14 (3.3)	0 (0)	0 (0)	0 (0)	0.173
Chronic kidney disease	2 (0.5)	0 (0)	0 (0)	0 (0)	0.611
Malignancy	4 (0.9)	0 (0)	1 (4.3)	1 (7.1)	0.028
Cerebrovascular disease	9 (2.1)	0 (0)	0 (0)	0 (0)	0.278
Rheumatic disease	3 (0.7)	0 (0)	0 (0)	0 (0)	0.533
<b>Signs and symptoms at admission</b>					
Temperature at admission, °C	36.8 (36.5–37.3)*	36.7 (36.3–37.0)	36.6 (36.5–37.0)	36.6 (36.4–36.9)	0.021
Respiratory rate	20.0 (20.0–20.0)*	20.0 (20.0–20.0)	20.0 (20.0–20.0)	20.0 (18.0–20.0)	0.042
Fever	312 (72.6)	18 (58.1)	0 (0)	0 (0)	< 0.001
Cough	297 (69.1)**	14 (45.2)	0 (0)	0 (0)	< 0.001

	Symptomatic COVID-19		Asymptomatic COVID-19		
<b>Expectoration</b>	178 (41.4)**	7 (22.6)	0 (0)	0 (0)	< 0.001
<b>Dyspnea</b>	36 (8.4)	0 (0)	0 (0)	0 (0)	0.012
<b>Fatigue</b>	156 (36.3)	8 (25.8)	0 (0)	0 (0)	< 0.001
<b>Muscle soreness</b>	56 (13.0)	5 (16.1)	0 (0)	0 (0)	0.016
<b>Headache</b>	34 (7.9)	1 (3.2)	0 (0)	0 (0)	0.053

**Notes:** Values are presented as median (IQR) or number (percentage); \*  $p < 0.05$  compared with other groups combined, \*\*  $p < 0.05$  compared with symptomatic COVID-19 with pneumonia cases; <sup>□</sup> data were only analyzed using cases from Changsha (n=228);  $p$  values were compared by Chi-square test, Fisher's exact test or One-way ANOVA.

**Legends:** COPD-chronic obstructive pulmonary disease; NA- not available.

Moreover, we found that the proportion of patients reporting an exposure history to Wuhan was significantly lower in the asymptomatic without pneumonia (7.1%) than in the other groups (Table 1), implicating that asymptomatic patients without pneumonia were more likely to be secondary cases than index cases. We have only collected family cluster history in 228 COVID-19 patients from the Public Health Treatment Center of Changsha. The results showed that symptomatic COVID-19 patients with pneumonia were less likely to be family cluster cases (47.9%, Table 1) than their counterparts.

As expected, the symptomatic with pneumonia group had higher rate of symptoms, including a higher body temperature at admission ( $^{\circ}\text{C}$ ) (36.8 [IQR 36.5–37.3]) and respiratory rate at admission (rate per min) (20 [IQR 20–20]), cough (69.1%), and expectoration (41.4%) than the other groups (Table 1).

### Laboratory findings

Routine blood tests showed a higher white blood cell count ( $\times 10^9$  per L) (6.5 [IQR 4.7–7.5]) and lymphocyte count ( $\times 10^9$  per L) (2.4 [IQR 1.7-3.0]) in the asymptomatic without pneumonia group than in the other groups (Table 2). In contrast, the symptomatic with pneumonia group had a higher frequency of lymphocytopenia (37.7%) and lower platelet count ( $\times 10^9$  per L) (187.5 IQR [147.0-246.0]) than the other groups (Table 2). However, there were no differences in hemoglobin levels among groups.

Table 2  
Laboratory findings in symptomatic and asymptomatic COVID-19 cases

Items	Symptomatic COVID-19		Asymptomatic COVID-19		p-value
	with pneumonia (n = 430)	without pneumonia (n = 31)	with pneumonia (n = 23)	without pneumonia (n = 14)	
White blood cell count, *10 <sup>9</sup> /L	4.6 (3.6–5.8)*	5.7 (4.0-6.8)	5.7 (4.8–7.8)*	6.5 (4.7–7.5)*	0.001
< 4*10 <sup>9</sup> /L	148 (34.4)*	9 (29.0)	3 (13.0)*	3 (21.4)	0.095
> 10*10 <sup>9</sup> /L	10 (2.3)	1 (3.2)	1 (4.3)	2 (14.3)	0.021
Neutrophil count, *10 <sup>9</sup> /L	2.9 (2.2–3.8)	3.3 (2.2–3.8)	3.6 (3.0-4.5)*	3.4 (2.1–4.6)	0.167
Lymphocyte count, *10 <sup>9</sup> /L	1.2 (0.8–1.6)*	1.8 (1.3–2.7)*	1.5 (1.3-2.0)*	2.4 (1.7-3.0)*	< 0.001
Lymphocytopenia	162 (37.7)*	4 (12.9)*	3 (13.0)*	3 (21.4)	0.001
Hemoglobin, g/L #	130.0 (119.0-140.0)	129.0 (119.8-147.8)	133.0 (127.0-151.0)	125.0 (119.0-139.5)	0.431
Platelet, *10 <sup>9</sup> /L	187.5 (147.0-246.0)*	221.0 (163.5–246.0)	238.0 (217.0-305.0)*	232.5 (187.8–261.0)	0.002
Alanine aminotransferase, U/L	21.3 (15.0-30.4)*	17.7 (11.7–24.7)*	20.5 (16.3–23.4)	16.7 (15.1–45.1)	0.139
Aspartate aminotransferase, U/L	23.4 (18.8–31.0)	23.3 (18.7–28.0)	20.8 (17.8–24.9)*	24.1 (18.3–33.4)	0.249
Total bilirubin, mmol/L	11.0 (8.1–17.0)	9.6 (6.6–12.6)	10.7 (9.0-19.5)	11.2 (8.3–13.5)	0.296
Lactose dehydrogenase, U/L	177.1 (145.6–221.0)*	155.7 (138.5-173.5)*	146.2 (133.0-185.0)*	146.5 (128.0-198.3)	0.002
Creatinine, μmol/L	62.0 (49.0–76.0)	57.0 (38.8–75.6)	59.8 (49.9–73.0)	51.2 (29.1–66.1)	0.280
D-dimer, mg/L	0.31 (0.18–0.52)*	0.24 (0.12–0.37)	0.26 (0.17–0.37)	0.14 (0.09–0.24)*	0.009
Prothrombin time (PT), s	12.0 (11.1–12.7)8	11.8 (11.1–12.8)	11.1 (10.3–12.4)*	11.8 (10.8–12.2)	0.066

	Symptomatic COVID-19		Asymptomatic COVID-19		
<b>Activated partial thromboplastin time (APTT), s</b>	32.4 (29.2–35.6)	31.3 (30.3–33.7)	31.8 (29.6–36.8)	34.1 (32.0–36.1)	0.622
<b>Creatine kinase (CK), U/L</b>	66.9 (43.0–104.9)	78.0 (58.6–94.7)	67.1 (57.0–109.0)	76.2 (50.3–104.9)	0.736
<b>Erythrocyte sedimentation rate (ESR), mm/h #</b>	44.0 (22.0–67.3) *	18.0 (11.0–28.5) *	33.0 (9.5–65.5)	19.0 (7.0–22.8) *	0.001

**Notes:** Values are presented as median (IQR) or number (percentage); \*  $p < 0.05$  compared with other groups combined; † data were only analyzed using cases from Changsha ( $n=228$ );  $p$  values were compared by Chi-square test, Fisher's exact test or One-way ANOVA.

Elevated alanine aminotransferase levels (ALT, U per L) and lactose dehydrogenase (LDH, U per L) were observed in the symptomatic with pneumonia group compared with the symptomatic without pneumonia group (21.3 [IQR 15.0–30.4] vs. 17.7 [IQR 11.7–24.7] and 177.1 [IQR 145.6–221.0] vs. 155.7 [IQR 138.5–173.5], respectively) (Table 2). Compared with those in the other groups, the symptomatic with pneumonia group had a significant higher level of D-dimer (mg per L) (0.31 [IQR 0.18–0.52]) (Table 2). In contrast, a significantly lower level of D-dimer was observed in the asymptomatic without pneumonia group (mg per L) (0.14 [IQR 0.09–0.24]) than in the other groups (Table 2).

We also found a higher erythrocyte sedimentation rate (ESR) (mm per hour) (44.0 [IQR 22.0–67.3]) and C-reactive protein (CRP) (U per L) (8.6 [IQR 2.8–24.0]) in symptomatic with pneumonia group than in the other groups, whereas the asymptomatic without pneumonia group had a lower level of CRP (U per L) (1.7 [IQR 0.3–3.0]) than the other groups (Table 2). Accordingly, among the 228 COVID-19 patients from the Public Health Treatment Center of Changsha, symptomatic COVID-19 with pneumonia patients were more likely to have procalcitonin (PCT) levels  $> 0.05$  ng per mL (54, 28.1%) than the others (Table 2).

### Treatments and outcomes

Excluding 10 patients who were only treated with traditional Chinese medicine in the symptomatic with pneumonia group and 1 patient who was treated with traditional Chinese medicine in the asymptomatic without pneumonia group, 487 patients received antiviral treatment, including arbidol, lopinavir/ritonavir, interferon, ribavirin and chloroquine phosphate. In total, 254 patients (51.0%) received antibiotics, indicating the presence of secondary or concomitant bacterial infection. The symptomatic with pneumonia group had higher frequencies of antibiotic use (54.2%) and corticosteroid use (28.8) than the other groups (Table 3).

Table 3  
Treatments and outcomes in symptomatic and asymptomatic COVID-19 cases

Items	Symptomatic COVID-19		Asymptomatic COVID-19		p-value
	with pneumonia (n = 430)	without pneumonia (n = 31)	with pneumonia (n = 23)	without pneumonia (n = 14)	
<b>Treatments</b>					
<b>Antiviral therapy</b>	420 (97.7)	31 (100)	23 (100)	13 (92.9)	0.865
<b>Abidol</b>	200 (46.5)	16 (51.6)	14 (60.9)	6 (42.9)	0.543
<b>Lopinavir/Ritonavir</b>	310 (72.1)	24 (77.4)	10 (43.5) *	8 (57.1)	0.022
<b>Interferon</b>	259 (60.2)	24 (77.4)	14 (60.9)	8 (57.1)	0.295
<b>Ribavirin</b>	44 (10.2)	2 (6.5)	2 (8.7)	1 (7.1)	0.876
<b>Chloroquine phosphate</b>	53 (12.3)	2 (6.5)	4 (17.4)	2 (14.3)	0.635
<b>Antibiotic therapy</b>	233 (54.2)*	11 (35.5)	7 (30.4)*	3 (21.4)*	0.004
<b>Administration of corticosteroids</b>	124 (28.8)*	2 (6.5)*	0 (0)*	0 (0)*	< 0.001
<b>Noninvasive mechanical ventilation</b>	18 (4.2)	0 (0)	0 (0)	0 (0)	0.121
<b>Invasive mechanical ventilation</b>	11 (2.6)	0 (0)	0 (0)	0 (0)	0.229
<b>ECMO</b>	7 (1.6)	0 (0)	0 (0)	0 (0)	0.339
<b>CRRT</b>	9 (2.1)	0 (0)	0 (0)	0 (0)	0.278
<b>Clinical outcomes</b>					
<b>Severe cases</b>	61 (14.2)*	3 (9.7)	0 (0)	0 (0)	0.011
<b>Admission to ICU</b>	46 (10.7)*	1 (3.2)	0 (0)	0 (0)	0.019
<b>ARDS</b>	18 (4.2)	0 (0)	0 (0)	0 (0)	0.121
<b>Death</b>	3 (0.7)	0	0	0	0.533
<b>Duration of viral shedding, days</b>	14.0 (9.0–21.0)	15.0 (8.8–23.8)	13.0 (7.0–19.0)	13.0 (8.3–17.8)	0.524
<b>Duration of hospitalization, days</b>	16.0 (11.5–24.0)	16.0 (10.0–23.0)	16.0 (11.0–22.0)	12.0 (8.8–17.0)*	0.234

**Notes:** Values are presented as median (IQR) or number (percentage); \*  $p < 0.05$  compared with other groups combined;  $p$  values were compared by Chi-square test, Fisher's exact test or One-way ANOVA.

**Legends:** ECMO - Extracorporeal membrane oxygenation, CRRT - Continuous renal replacement therapy, ARDS - acute respiratory distress syndrome; ICU - intensive care unit.

Both noninvasive (18, 4.2%) and invasive mechanical ventilation (11, 2.6%) were used in only the symptomatic with pneumonia group (Table 3). Likewise, extracorporeal membrane oxygenation (ECMO) and continuous renal replacement therapy (CRRT) were employed in only the symptomatic with pneumonia group (Table 3). The above results indicated that patients in the symptomatic with pneumonia group suffered from more severe conditions and consumed more medical resources than those in the other groups.

All 64 severe cases occurred in symptomatic COVID-19 patients; 47 of them were admitted to the intensive care unit (ICU), of which 18 developed acute respiratory distress syndrome (ARDS) and 3 died. Of the 430 symptomatic with pneumonia patients, 61 (14.2%) were had severe COVID-19, and 46 (10.7%) were admitted to the ICU, implying that patients in the symptomatic with pneumonia group were more likely to develop severe COVID-19 and be admitted to the ICU than those in the other groups (Table 3). Interestingly, we did not find differences in the duration of viral shedding and hospitalization among the groups.

## Discussion

As in Middle East respiratory syndrome (MERS) patients(13, 14), mounting evidence supports that presymptomatic(15, 16) or asymptomatic COVID-19 patients are infectious(6, 17, 18). In contrast with the amount of research about asymptomatic and symptomatic COVID-19 patients, there is limited research on the differences between COVID-19 patients with and without pneumonia. It is well acknowledged that pneumonia should be confirmed by radiography findings(12). Therefore, this retrospective study describes the spectrum of COVID-19, including symptomatic COVID-19 with pneumonia, symptomatic COVID-19 without pneumonia, asymptomatic COVID-19 with pneumonia and asymptomatic COVID-19 without pneumonia, mainly according to symptoms and CT findings. This study observed and identified characteristics and differences among the four groups, suggesting that not only symptoms, but also the presence or absence of pneumonia should be considered when evaluating the spectrum of COVID-19. Unlike some other presymptomatic or incubational cohorts(6, 15, 16), the asymptomatic COVID-19 patients in our study were discharged and monitored or evaluated according to symptoms and laboratory findings by professional healthcare workers during hospitalization, to ensure the absence of symptoms and laboratory and radiologic abnormalities during the whole disease process.

Because senior patients are vulnerable to pneumonia(12), the higher prevalence of pneumonia in the symptomatic group could be explained by the older age of the symptomatic patients. Lower levels of lymphocyte and white blood cells were observed in the symptomatic groups and were associated with better outcomes than those in the asymptomatic groups, implying that lymphocyte and white blood cells

might play a protective role in COVID-19. The prevalence of hypertension was higher in the asymptomatic groups than in the symptomatic groups, suggesting that antihypertension treatment, especially angiotensin-converting enzyme inhibitors (ACEIs) might be effective for COVID-19.

A numbers of studies have demonstrated that SRAS-CoV-2 viral loads in the upper air way(17, 19), and that SARS-CoV-2 entry factors are highly expressed in upper air way cells(10). Moreover, Roman et al(7) isolated live SARS-CoV-2 from upper airway specimens, and found separate genotypes in upper and lower airways samples. All of the above findings demonstrate that SARS-CoV-2 can infect the upper airway. Therefore, we speculate that COVID-19 without pneumonia might be only the SARS-CoV-2 upper airway infection. As expected, lower prevalence rate of severe case and pneumonia were found in asymptomatic COVID-19 patients, and asymptomatic patients without pneumonia presented fewer abnormal laboratory findings and a lower risk of developing severe COVID-19 than symptomatic patients. The results suggested that SARS-CoV-2 infection in only the upper airway might be self-limiting, leading to a lack of symptoms and a favorable prognosis. Alba et al(20) found targeted T cell responses to SARS-CoV-2 in individuals not exposed to SARS-CoV-2, but possibly exposed to other coronaviruses. Therefore, we speculate that the asymptomatic COVID-19 patients without pneumonia might have been recently infected by other coronavirus, resulting in the production of T cells targeting SARS-CoV-2, limiting the infected region and attenuating the severity of COVID-19. To save and make effective use of medicine sources, asymptomatic COVID-19 patients without pneumonia should be quarantined in primary hospitals or even Fangcang shelter hospitals(21), rather than tertiary hospitals if possible.

COVID-19 originated in Wuhan in November 2019, and exposure to Wuhan was considered important in the medical history of patients in previous studies(5, 22). The lower frequency of exposure to Wuhan in the asymptomatic without pneumonia group indicated a lower percentage of index cases in this group than in the other groups. Coronaviruses have the potential to mutate, and SARS-CoV-2 has exhibited patients-derived mutations and varying pathogenicity according to subtype(23, 24). Therefore, it is possible that SARS-CoV-2 in secondary patients has mutated, leading to decreased pathogenicity and asymptomatic COVID-19. Because of airborne transmission, family clusters play a role in SARS-CoV-2 spread(25, 26). Awareness of social distancing and personal protection caused by obvious symptoms in family members could explain the lower percentage of family clusters in the symptomatic with pneumonia group than in the other groups.

Both the symptom and laboratory finding in results support that symptomatic COVID-19 patients suffer from more severe disease than asymptomatic COVID-19 patients. A higher rate of ECMO and a higher frequency of ICU admission in the symptomatic with pneumonia group indicated not only the greater consumption of medical resources but also the need of additional monitoring in this group. In contrast, we did not find differences in viral shedding and hospitalization durations between the symptomatic and asymptomatic groups, suggesting that asymptomatic COVID-19 might present similar process of viral shedding as symptomatic COVID-19.

Due to a lack of significant clinical symptoms, using symptoms to screen for asymptomatic COVID-19 is difficult(15, 27, 28). In China, The Center for Disease Control and Prevention conducted SARS-CoV-2 PCR testing for all close contacts of COVID-19 patients(1). Because of the strict and comprehensive screening strategy, the prevalence of asymptomatic cases seems to be higher in our study than in other studies(15). Since asymptomatic COVID-19 patients can be transmission sources(7–9), and our results showed that 7.4% of COVID-19 patients were asymptomatic, a more comprehensive screening strategy for COVID-19 is urgently needed.

There are some limitations in this study. Because almost all the patients accepted antiviral treatment, it was possible that some presymptomatic COVID-19 patients did not develop symptomatic disease and were thus classified in the asymptomatic group. However, effective antiviral drugs targeting COVID-19 have not been identified thus far(29). Therefore, we considered the confusion of presymptomatic and asymptomatic COVID-19 patients under professional monitor during hospitalization might be rare. Moreover, to assess the mutations and the infectivity of SARS-CoV-2, viral sequencing should be conducted in future studies.

## Conclusion

This spectrum of COVID-19 includes symptomatic COVID-19 with pneumonia, symptomatic COVID-19 without pneumonia, asymptomatic COVID-19 with pneumonia and asymptomatic COVID-19 without pneumonia. The symptomatic with pneumonia group consumed more medical resources than the other groups, and extra caution of monitoring should be applied in this group. Asymptomatic COVID-19 case presented a similar viral shedding duration as symptomatic COVID-19 case.

## Abbreviations

coronavirus disease 2019: COVID-19

severe acute respiratory syndrome coronavirus 2: SARS-CoV-2

extracorporeal membrane oxygenation: ECMO

continuous renal replacement therapy: CRRT

World Health Organization: WHO

acute respiratory distress syndrome: ARDS

real-time reverse transcription polymerase chain reaction: RT-PCR

computed tomography: CT

oxygen saturation: SaO<sub>2</sub>

fraction of inspired oxygen: FiO<sub>2</sub>

interquartile range: IQR

alanine aminotransferase: ALT

lactose dehydrogenase: LDH

erythrocyte sedimentation rate: ESR

C-reactive protein: CRP

Procalcitonin: PCT

intensive care unit: ICU

angiotensin-converting enzyme inhibitors: ACEIs

## **Declarations**

### **Ethics approval and consent to participate**

This study was approved and supervised by the Medical Research Ethics Committee of the Second Xiangya Hospital, Central South University (2020-010). The consent to participate was waived because of the retrospective design.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

The data that support the findings of this study are available from the corresponding author for reasonable requests.

### **Competing interests**

None reported.

### **Funding**

This study was supported by the National Key Clinical Specialist Construction Programs of China; the National Natural Science Foundation of China 81400032; the Natural Science Foundation of Hunan Province 2019JJ50877; and Emergency Project of Prevention and Control for COVID-19 of Central South University 160260009.

## Authors' Contributions

Every author contributed to reviewing the paper. Huihui Zeng performed and designed the work, and drafted the manuscript. Yiming Ma performed the statistical analyses. Zhiguo Zhou, Wenlong Liu, Peng Huang, Mingyan Jiang and Qimi Liu treated and monitored COVID-19 cases. Prof. Hong Luo and Prof. Ping Chen inspired the research questions and helped to draft the manuscript. Prof. Yan Chen is the principal investigator of the study and supervised the study and preparation of the manuscript.

## Acknowledgment

None.

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## Figures

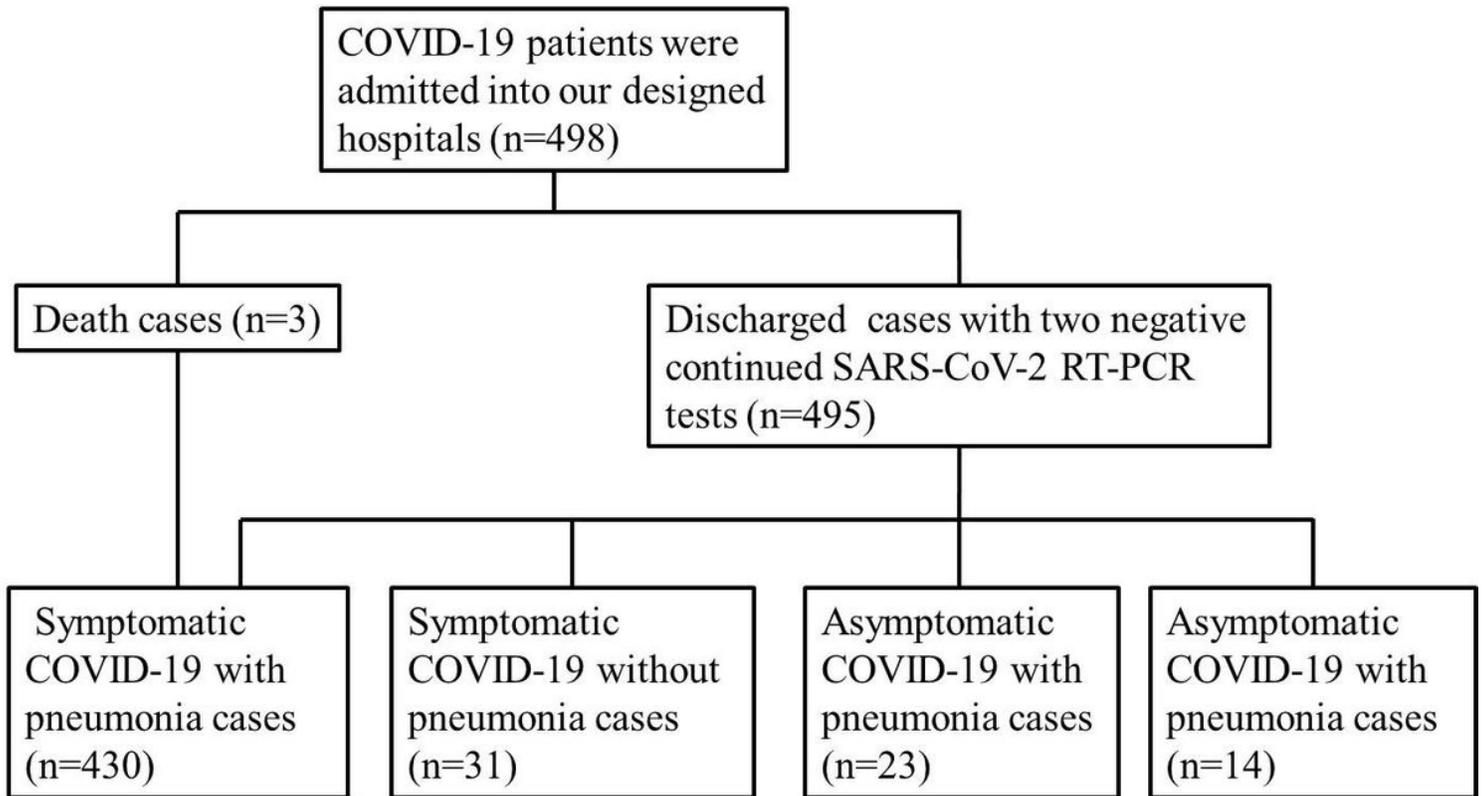


Figure 1

Flow chart of eligible patients.