

The clinical feature of silent infections of novel coronavirus infection (COVID-19) in Wenzhou

Dear Editor,

A typical symptomatic case of the novel coronavirus disease (COVID-19) includes fever, muscle soreness, and cough.¹ However, there is another pattern of cases that do not exhibit typical clinical symptoms, referred to as asymptomatic. At least one case of COVID-19 has been reported without presentation of clinical symptoms.² It has also been shown that during the incubation period of patients with COVID-19 can spread the virus, which is different from many other infectious diseases. Hence, it is particularly important to address asymptomatic cases because if left untreated, damage can occur to the respiratory system and others can be infected.

The asymptomatic cases play an important role in the prevention and transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, little is known to date about the clinical manifestations of COVID-19. As a result, we collected and analyzed the clinical features of 12 patients with confirmed SARS-CoV-2 infection who did not have typical clinical symptoms.

The data was derived from 137 confirmed cases hospitalized in the Wenzhou Sixth People's Hospital, Wenzhou Central Hospital Medical Group China, as well as from 69 confirmed cases hospitalized in the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University. All of the cases were diagnosed by using a real-time polymerase chain reaction assay, according to the criteria established by the Chinese Center for Disease Control and Prevention for detection of SARS-CoV-2.³ All of the patient's throat swab samples and blood samples were collected. The chest radiography or computed tomography was performed as a standard process when they were admitted to the hospital. The potential epidemiological exposure of the COVID-19 were also collected by a questionnaire. All of the data were analyzed in SAS statistical software (9.4). The ethics commissions of Wenzhou Central Hospital Medical Group hospital. An informed consent was obtained from each participant.

Of the 12 patients (median age was 31 years with a range from 10 to 54 years, 50% were female), three had a trip to Wuhan recently. Due to the silent nature of the infection, the patients did not manifest any clinical symptoms and did not report any health complaints. Table 1 shows the basic demographic characteristics, history of chronic diseases before hospitalization, and blood test results. Compared with other patients, these cases are more likely to be young and healthy. Except for one patient with lymphocytopenia, the white blood cells and lymphocytes of the other patients were normal, and the nucleic acid continued to be positive in 12 patients.

All patients had no chronic underlying diseases except for one with rheumatoid arthritis. Two of the patients had the virus for more than a month and pulmonary lesions in the asymptomatic infected patients were mild and resulted in no pneumonia.

In the present study, the 12 asymptomatic cases (5.8%, 95% confidence interval [CI]: 3.4%-9.9%) were found among 206 confirmed cases. The asymptomatic infections are more likely to occur in young adults patients, except for one child found positive in these cases (median age of 31, range of 10-54 years). Only three cases reported that they had a trip to Wuhan before admission to the hospital. All those 12 cases were identified through the screening process of close contacts of confirmed positive cases. All of the 12 patients admitted to the hospital were given alpha-interferon aerosol inhalation, or lopinavir/ritonavir, or arbidol hydrochloride and made a full recovery.

Our study demonstrates that the prevalence of the silent infection of COVID-19 is 5.8% (95% CI: 3.4%-9.9%), which is much higher than the 1.2% which has been reported from the Chinese CDC.⁴ Whereas, the estimated asymptomatic proportion is 17.9% (95% CI: 15.5%-20.2%) among COVID-19 cases aboard the Diamond Princess cruise ship in Japan.⁵ Our results could be partly explained by the fact that all of the silent infectious cases from this current study were found from the screening of the close contacts of confirm positive cases. The silent infection patients were also more likely to be young adults without chronic disease.

Asymptomatic cases could be infected with COVID-19 during the incubation period. However, if this was true, the symptoms should present after 14 days (the assumed longest incubation period). Of note, COVID-19 can be transmitted during the incubation period, which is different from many other infectious diseases. This is why it can be referred to as a silent infection as they these cases are lacking significant clinical signs of disease. Asymptomatic patients could belong to a subtype of the silent infection such as subclinical infection or latent infection. During the early stages of the incubation period, or silent infection for SARS-CoV-2, cases can spread the virus.

Our study data cannot draw conclusions on the national prevalence of asymptomatic cases due to the selection bias inherent in the patients admitted to the hospital not generalizable to the entire population. The prevalence derived from the hospital tends to underestimate the prevalence of asymptomatic carries at a national level. Lacking the available testing tool, the virus load of those asymptomatic patients was not measured. In the current study, we did not find any confirmed case infected by those asymptomatic patients. However, a study from Ningbo indicated less than 5% of

TABLE 1 Clinical characteristics of asymptomatic patient with COVID-19 (N = 12)

	Median (IQR) OR no. (%)
Age, y	31 (24-51)
Female	6 (50)
Return from Wuhan	3 (25)
BMI	22.4 (20.5-23.1)
Smoking history	
Never smoker	0
Ever smoker	1 (8.3)
Smoker	0
Comorbidities	
Hypertension	0
Diabetes	0
Rheumatoid arthritis	1 (8.3)
Blood routine	
White blood cell count (×10 ⁹ /L)	6.1 (4.6-6.9)
Neutrophil count (×10 ⁹ /L)	3.4 (2.6-5.0)
Lymphocyte count (×10 ⁹ /L)	1.9 (1.5-2.1)
Hemoglobin, g/L	136 (121-144)
Platelet count (×10 ⁹ /L)	272 (210-311)
Blood biochemistry	
Alanine aminotransferase, U/L	18 (11-25)
Total bilirubin, mmol/L	9.2 (6.3-15.2)
Albumin, g/L	42.7 (38.3-46.0)
Blood urea nitrogen, mmol/L	3.9 (3.5-4.2)
Creatinine, μmol/L	56.0 (46.1-76.8)
Lactate dehydrogenase, U/L	154 (134-182)
Creatine kinase, U/L	65.1 (36.0-73.9)
Creatine kinase Isoenzyme, U/L	10.9 (7.7-12.3)
Infection-related biomarkers	
Erythrocyte sedimentation rate, mm/h	14 (10-15)
C-reactive protein, mg/L	0.80 (0.46-1.10)
Procalcitonin, μg/mL	0.014 (0.010-0.025)
Chest x-ray and CT findings	
Bilateral involvement	4 (33.3)
patchy shadows or ground-glass opacity	5 (41.7)
Oxygen support	0
Antiviral therapy	
Alpha-interferon aerosol inhalation	6 (50)
Lopinavir/ritonavir	6 (50)
Arbidol hydrochloride	12 (100)

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease; CT, computed tomography; IQR, interquartile range; OR, odds ratio.

confirmed cases could be attributed to the transmission from asymptomatic patients.⁶ Future studies are warranted that examine the level of the viral load among asymptomatic patients.

Our study has an important implication not only in the clinical setting, but also for public health. It provides firsthand information on the importance of addressing those with silent infection of

SARS-CoV-2. All of the cases in the presented study were only found because they were traced as close contact of confirmed positive cases. Hence, screening close contacts of confirmed case is necessary to identify those with silent infection and prevent subsequent spread. Our study underscores the importance of tracing close contracts of confirmed cases, having long time self-quarantine, and that screening is necessary to prevent secondary cases in the community.

CONFLICT OF INTERESTS

The authors declares that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

GH conceptualized and designed the study, collected data, and reviewed and revised the manuscript. WS conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. PF and JH collected data, and reviewed and revised the manuscript. MG critically reviewed the manuscript for important intellectual content, and reviewed and revised the manuscript. JW and JC carried out the analyses, critically reviewed the manuscript for important intellectual content, and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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