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## Letter to the Editor

### Clinical Features and Outcomes of Asymptomatic Cases of SARS-CoV-2 Infection



Dear Sir,

We read with great interest the paper of Wenjie Yang *et al.*<sup>1</sup> on “Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multi-center study in Wenzhou city, Zhejiang, China” that allow us to share our experiences and observations during the past several months. COVID-19 is a new emerging infectious disease globally. Current understanding on its pathogen termed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is limited. The virus is thought to mainly transmit from person to person by air droplets and close contact. Essential steps of controlling this disease focus on early detection and isolation of the confirmed cases, followed by tracing and screening their contacts, which is fundamental for minimizing the risk of spread, specifically the isolation and management of the asymptomatic cases<sup>2</sup>. Previous report has demonstrated the existence of incomplete clinical presentations of SARS<sup>3</sup>, 80% genetically similarity with SARS-CoV-2. We found 15 asymptomatic cases who were tested positive by RT-PCR assay during the contact-screening of the confirmed COVID-19 patients in Fengjie county, northeastern Chongqing, where is adjacent to Hubei, the center of COVID-19 outbreak in China. Fifteen people in the absence of complaints were tested positive by twice real time reverse transcription-polymerase chain reaction (RT-PCR) method through nasopharyngeal or rectal swabs. All of these cases were either family members or close contacts with certain confirmed cases either symptomatic or asymptomatic, consisting of five males and ten females. The age ranged from 5 to 76 years old. We did not see any significant alternation of WBC, lymphocytes, PLT, CRP and PCT as previous described in the symptomatic patients<sup>4,5</sup>. Nonetheless, there are three notable changes of the laboratory examinations, which is likely to offer some clues for the identification, management and prevention of asymptomatic cases. Firstly, the initial laboratory examinations showed that erythrocyte sedimentation ratio (ESR) increased in 10/15 cases. Considering of the less specificity and reproducibility, of course, it is true that ESR cannot be the sole clue to disease in asymptomatic state, which must combined with epidemiological link and other evidence<sup>6</sup>; secondly, eight of the fif-

teen cases had decreased albumin; thirdly, twelve cases presented with abnormal electrolytes such as hypokalemia and hypomagnesium. The abnormality of the albumin and electrolytes may indicate the insufficient nutrition weaken the immune system. A diet supplementation especially on these elements should be considered for the asymptomatic cases. Fig 1

We agree with Wenjie Yang *et al.* that a normal chest CT scan cannot exclude the diagnosis of COVID-19. In their paper, 17 out of 149 (11.4%) symptomatic patients had normal chest CT findings on admission. And 12 out of the 17 patients kept being negative 10 days later. In our observation, chest CT scan was taken twice or three times for each case. Eleven cases did not show any significant lesions on all initial and imaging follow-ups. Therefore, the initial establishment of confirmatory diagnosis for COVID-19 must be a combination of exposure history and/or laboratory detection whether cases have symptoms, signs, imaging manifestations or not. Notably, the remaining four cases in our investigations showed ground glass opacity or small patchy infiltrates and recovered around 14 days, suggesting that people do not necessarily show any discomfort even with the typical imaging lesions.

Twelve cases were confirmed by nasopharyngeal specimen initially while two cases proven by rectum swabs. And one case positive by nasopharyngeal, rectum and feces detection whose final twice RT-PCR negative time was 26 days whereas the time from the first positivity to the twice negativity for the remaining 14 cases ranged from 8 to 16 days with the average negative time 11.93 days. All the urine specimen were negative. Most recently, Wang *et al* did the detection of this virus in different types of clinical specimens from the symptomatic patients and found that none of the urine specimens tested positive, in line with the results of our asymptomatic cases<sup>7</sup>. The cycling threshold (Ct) of RT-PCR assay is negatively related to the viral load. Four cases presented with low Ct values less than 27. The results here suggested that in asymptomatic cases the initial viral loading can be high which has been linked to the ability of airborne transmission rather than the appearance of symptoms. The studies on SARS virus found the higher viral load in nasopharyngeal the higher incidence of major impact on the airborne transmission, which played a major role during the outbreak in Hong Kong<sup>8</sup>. The relationship between the Ct value and the transmissibility of SARS-CoV-2 virus in asymptomatic patients warrants further investigation.



Fig. 1. Chest CT scans of four cases presenting with ground glass opacity or small patches of infiltrates.

According to the Guideline<sup>9</sup>, the broad spectrum antiviral of 1000mg ribavirin infusion was given to each case combined with airway spray of interferon- $\alpha$ 1b 60 $\mu$ g bid. Either Kaletra (Lopinavir/Ritonavir tablets) 2 tablets, bid (8 cases), or Arbidol 200mg tid (7 cases) was administered simultaneously. In Kaletra group, five patients presented with epigastric discomfort or pain, anorexia, nausea, vomit or diarrhea after 1–4 days of administration. Three cases showed slightly elevated aminotransferase or bilirubin. And the symptoms and liver function were alleviated once suspension of Kaletra and ribavirin. We need to differentiate the symptoms caused by the drugs or due to the virus itself based on the response of stopping suspicious medicines. Here, the abnormalities on those cases were alleviated therefore probably due to the reverse response caused by antivirals. Clinically, considering the undefined high toxicity of SARS-Cov-2 virus, combination of antivirals were often administered for each case which is likely to result in confusing clinical situations.

Our investigation showed that the asymptomatic cases of SARS-CoV-2 infection are not carriers or colonizers of the virus, thus this presentation may serve as a clinical spectrum of COVID-19. Its role deserves for further exploration and the potential as a source of infection needs to be carefully assessed in larger population.

#### Declaration of Competing Interest

None.

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Jianguo Wu, Jun Liang  
Department of Infectious Diseases, People's Hospital of Fengjie  
County, Chongqing, China. 404600

Hongji Zhou, Fengying Peng, Bin Wang, Wei Jiang, Bei Jia\*,  
Tao Luo\*\*

The Key Laboratory of Infectious and Parasitic Diseases in  
Chongqing, Department of Infectious Diseases, the First Affiliated  
Hospital of Chongqing Medical University, Chongqing, China. 400016

\*Corresponding author: Bei Jia, Female, M.D., Professor.  
Tel:13883052216, Fax: +86 23 8901 2430, Department of  
Infectious Diseases, the First Affiliated Hospital of Chongqing  
Medical University, Chongqing, China 400016

\*\*Co-Corresponding author: Tao Luo, Geriatrics Department, the  
first affiliated hospital of Chongqing medical university,  
Chongqing, China 400016  
E-mail addresses: [jiabei@hospital.cqmu.edu.cn](mailto:jiabei@hospital.cqmu.edu.cn) (B. Jia),  
[loto1314@yeah.net](mailto:loto1314@yeah.net) (T. Luo)