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Title: **Understanding of COVID-19 based on current evidence**

Running head: Current understanding of COVID-19

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Abstract: Since December 2019, a series of unexplained pneumonia cases has been reported in Wuhan, China. On January 12, 2020, the World Health Organization (WHO) temporarily named this new virus as the 2019 novel coronavirus (2019-nCoV). On February 11, 2020, the WHO officially named the disease caused by the 2019-nCoV as Corona Virus Disease (COVID-19). The COVID-19 epidemic is spreading all over the world, especially in China. Based on the published evidence, we systematically discuss the characteristics of COVID-19 in the hope of providing a reference for future studies and help for the prevention and control of the COVID-19 epidemic.

Keywords: COVID-19, SARS-CoV-2, 2019-nCoV, pneumonia, epidemiology, coronavirus

Introduction

Since December 2019, there has been a series of unexplained cases of pneumonia reported in Wuhan, China. The Chinese government and researchers took rapid measures to control the epidemic and carried out etiological research. On January 12, 2020, the World Health Organization (WHO) tentatively named this new virus as the 2019 novel coronavirus (2019-nCoV). On January 30, 2020, WHO

announced the 2019-nCoV epidemic a public health emergency of international concern (PHEIC). On February 11, 2020, the WHO formally named the disease triggered by 2019-nCoV as Corona Virus Disease 2019 (COVID-19). On the same day, the Coronavirus Study Group (CSG) of the International Committee on Taxonomy of Viruses named 2019-nCoV as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). On February 23, 2020, there were 77041 confirmed cases of SARS-CoV-2 infection in China. The number of infections has exceeded that of the Severe Acute Respiratory Syndrome (SARS) outbreak in China in 2002 [1,2]. In order to help healthcare workers around the world to better deal with the SARS-CoV-2, we review the relevant published papers on COVID-19 to provide a reference for future COVID-19 research.

Sources of SARS-CoV-2

SARS-CoV-2 is a coronavirus and belongs to the β-coronavirus cluster. COVID-19 is the third known zoonotic coronavirus disease after SARS and Middle East Respiratory Syndrome (MERS). SARS-CoV and MERS-CoV also belong to the β-coronavirus cluster[3]. Zhu *et al.*[4] confirmed that SARS-CoV-2 was a new β-coronavirus belonging to the subgenus botulinum of Coronaviridae. According to the current data[5], the early COVID-19 cases were related to the Huanan Seafood Market, and the possibility of human-to-human transmissions could not be ruled out. The WHO report claimed that the SARS-CoV-2 could be

detected in the environmental samples collected from the seafood market, but it has not yet been determined if a specific animal species carries the SARS-CoV-2. A study by Ji *et al.*[6] showed that the SARS-CoV-2 was a chimeric virus between a bat coronavirus and a coronavirus of unknown origin. By comparing with other animals, they found that snakes are the most likely wildlife repository for the SARS-CoV-2[6]. The research by Benvenuto *et al.*[7] showed that the SARS-CoV-2 was only closely related to the coronavirus isolated from Chinese chrysanthemum-headed bats in 2015. Their research supported the theory that the transmission chain started from bats to humans.

Chan *et al.* [8] and Hui *et al.* [9] confirmed that SARS-CoV-2 was a new coronavirus closely related to the bat SARS coronavirus (SARS-CoV). Recently, Zhou *et al.* [10] and Wu *et al.* [11] found that the sequence homology between SARS-CoV-2 and SARS-CoV was 79.5%. They also found that the SARS-CoV-2 had high homology with bat coronaviruses. Therefore, the current evidence strongly supports that the SARS-CoV-2 was derived from bats, although the intermediate hosts of SARS-CoV-2 remain to be determined.

Epidemiological characteristics of COVID-19

A study by Wang *et al.*[12] showed that from January 10 to 24, 2020, the number of people diagnosed with the SARS-CoV-2 infection in China increased by 31.4 times. On February 23, 2020, the number of people diagnosed with COVID-19 in

China was 1879 times of that on January 10, 2020. They estimated the case fatality rate of COVID-19 to be 2.84% based on their patient pool. The authors also found that the ratio of male to female deaths was 3.25:1, the median age of death was 75 years, the median time from the first symptom to death was 14 days, and the median time from early symptoms to death in people aged 70 or older (11.5 days) was shorter than that in people under 70 years old (20 days). These findings suggest the disease may progress faster in the elderly than in the young.

A study by Li *et al.* [5] showed the median age of 425 patients infected with SARS-CoV-2 was 59 years, of which 56% were males, the average incubation period was 5.2 days, and almost half of the adult patients were 60 years old or older. In the early stages, the number of infected patients doubled every 7.4 days. The transmission rate of individual infected patients was 2.2. Although 55% of the earliest SARS-CoV-2-infected patients related to the Huanan Seafood Market, the number of unrelated cases has increased exponentially since late December 2019.

Huang *et al.* [13] showed among the 41 patients with SARS-CoV-2 infections in their study, 73% of the patients were male, and 32% of the patients had underlying diseases, including diabetes (8 patients), hypertension (6 patients), and cardiovascular disease (6 patients). The median age was 49 years. Out of the 41 patients, 27 patients were associated with the Huanan Seafood Market. The case fatality rate among the SARS-CoV-2-infected patients in this study was 15%. A

study by Wu *et al.* [14] estimated the transmission rate of individual infected patients to be 0.3. The case fatality rate among the SARS-CoV-2-infected patients in this study was 14%.

Mechanism, symptoms, and diagnosis of COVID-19

Zhao *et al.* [15] found that angiotensin-converting enzyme 2 (ACE2) was the receptor for SARS-CoV-2. In the normal human lung, ACE2 is expressed on type Ⅰ and Ⅱ alveolar epithelial cells. Among them, 83% of the type II alveolar cells have ACE2 expression. Men had a higher ACE2 level in their alveolar cells than women. Asians have a higher level of ACE2 expression in their alveolar cells than the white and African American populations. The binding of SARS-CoV-2 on ACE2 causes an elevated expression of ACE2, which can lead to damages on alveolar cells. Damages to alveolar cells can, in turn, trigger a series of systemic reactions and even death. They also confirmed that Asian males are more susceptible to SARS-CoV-2 infection. Wrapp *et al.* [16] found that the receptor-binding ability of SARS-CoV-2 is 10-20 times stronger than that of SARS-CoV.

Huang *et al.* [13] found that 98% of the patients in their study had fevers, of which 78% had a temperature higher than 38°C. They reported that 76% of the patients had coughs, 44% of patients experienced fatigue and muscle pain, and 55% of patients had dyspnea. A small number of patients also developed expectoration

(28%), headaches (8%), hemoptysis (5%), and diarrhea (3%). Laboratory tests found that 25% of infected patients had leukopenia and 63% had lymphocytopenia. The level of aspartate aminotransferase was elevated in 37% of the patients. Myocarditis was diagnosed in 12% of the patients, and the level of hypersensitive troponin I (hs-cTnI) was significantly increased in these patients. Abnormalities in chest computed tomography (CT) images were found in 100% of the patients. Grinding glass-like and consolidation areas were found in 98% of the infected patients' bilateral lungs.

Zhu *et al.* [4] reported 3 cases of COVID-19. Patient 1 was a 49-year-old female with a fever (body temperature 37 to 38 °C) and had coughs accompanied by chest discomfort. Four days after the onset of the disease, her coughs and chest discomfort aggravated, but her fever subsided. Patient 2, a 61-year-old male, also developed fevers and coughs at the initial stage of the disease. Respiratory distress appeared seven days after the onset of symptoms and worsened within the next two days. He was treated with mechanical ventilation. Patient 3 was a 32-year-old male whose symptoms were not described in the article. Patients 1 and 3 recovered and were discharged from hospital after treatment, but patient 2 died after 20 days of treatment.

Guan *et al.* [17] reported 1099 cases of 2019-nCoV infection. They found that fevers (87.9%) and coughs (67.7%) were the most common symptoms. Diarrhea

(3.7%) and vomiting (5.0%) were rare. Abnormalities in chest CT images were found in 96% of the SARS-CoV-2-infected patients, and lymphopenia was observed in 82.1% of them.

Prevention and treatment of COVID-19

As of February 23, 2020, no COVID-19 vaccine has been successfully developed. At present, the treatments of patients with SARS-CoV-2 infection are mainly symptomatic treatments. The study by Huang *et al.* [13] reported that the most common complications in patients with 2019-nCoV infection were acute respiratory distress syndrome (ARDS), followed by anemia, acute heart injuries, and secondary infections. Therefore, empirical antibiotics, antiviral therapy (oseltamivir), and systemic corticosteroids were often used for treatments. Patients with intractable hypoxemia were given invasive mechanical ventilation. Holshue *et al.* [18] used remdesivir in the treatment of patients with SARS-CoV-2 infection and achieved good results. Lu [19] postulated that, in addition to antiviral interferers and antibiotics, neuraminidase inhibitors, RNA synthesis inhibitors, and Chinese traditional medicine could also be used in the treatment of COVID-19. Nevertheless, the efficacy of these drugs still needs to be verified by clinical trials.

In the absence of effective treatments, the best way to deal with the SARS-CoV-2 epidemic is to control the sources of infection. Strategies include early diagnoses,

reporting, isolation, and supportive treatments; timely release of epidemic information; and maintenance of social orders. For individuals, protective measures, including improving personal hygiene, wearing medical masks, adequate rest, and keeping rooms well ventilated, can effectively prevent SARS-CoV-2 infection [17].

Discussion

Regarding the case fatality and transmission rates among patients with SARS-CoV-2 infection, the findings from various studies were different. The studies of Wang *et al.* [12] showed that the case fatality rate was 2.84%. According to Huang *et al.* [13], the number was 15%. The study by Wu *et al.* [14] estimated that the case fatality rate was 14%. In the study by Zhu *et al.* [4], the number was 33%. Guan *et al.* [17] reported that the case fatality rate was 1.36%. According to the official data released by China, the case fatality of COVID-19 patients was 3.17% [2]. In terms of the transmission rate, Li *et al.* [5] showed that the transmission rate was 2.2 per patient. Wu *et al.* [14] estimated that the transmission rate was 0.3 per patient. Yang *et al.* [20] reported that the transmission rate was 3.77. We think that the transmission rate of 2.2 per patient seems to be more in line with the current situation [2]. Different sample sizes and possible viral variations may have contributed to the differences between the studies. Studies with a larger sample size may give a better estimation of the case fatality rate and transmission rate of

the COVID-19. We know that the other two major zoonotic coronavirus diseases, SARS and MERS which caused widespread transmission, have case fatality rates of 9.6% and 35%, respectively [9]. According to the official Chinese data, the case fatality rate among the SARS-CoV-2-infected patients was much lower than that of SARS and MERS [2].

In response to the COVID-19 epidemic, we believe that the focus of future studies will still be on the development of COVID-19 vaccines and effective drugs to treat COVID-19. These studies will help further reduce the case fatality and transmission rates among SARS-CoV-2-infected patients. Moreover, super-spreaders were reported during the SARS and MERS epidemics [21]. Although the transmission rate for SARS-CoV-2 patents is about 2.2 at present, the number of cases inside and outside Wuhan is increasing rapidly. With the progress of diagnostic technology, potential super-spreaders may be discovered in the future. In the prevention of the spread of SARS-CoV-2, asymptomatic spreaders also need to be focused [22].

In addition, Sheng *et al.* [23] found that viral infections can increase the risk of pulmonary fibrosis. Therefore, pulmonary fibrosis may be one of the severe complications after patients recover from 2019-nCoV infections. The prevention of pulmonary fibrosis in patients recovered from 2019-nCoV infections is an issue that urgently needs to be addressed.

Contributors: Bo Pan and Pengfei Sun had the idea for and designed the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Pengfei Sun and Xiaosheng Lu contributed to writing of the report. Bo Pan contributed to critical revision of the report. Chao Xu and Wenjuan Sun contributed to the statistical analysis. All authors contributed to data acquisition, data analysis, or data interpretation, and reviewed and approved the final version.

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