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## Review Paper:

## Review about COVID-19

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### Abstract

*Coronavirus Disease 2019 (COVID-19) is a respiratory disease caused by the SARS-CoV-2 virus. It has spread from China to many other countries around the world approximately all world. The aim of this review was to exhibit the information about the disease, the ways of treatment and prevention in this early stage of this outbreak.*

**Keywords:** COVID-19, pandemic, outbreak, Epidemiology.

### Introduction

Coronaviruses are a group of related viruses that cause diseases in mammals and birds, CoV belong to the genus Coronavirus in the Coronaviridae. All CoVs are pleomorphic RNA viruses characteristically containing crown-shape peplomers with 80-160 nM in size and 27-32 kb positive polarity<sup>31</sup>.

The outbreak was first identified in Wuhan, Hubei, China in December 2019 and was recognized as a pandemic by the World Health Organization (WHO) on 11 March 2020<sup>32</sup>. As of 21 March, the number of new cases per week has remained constant at 2 million for September 2020 with a cumulative total of over 34.8 million cases. Over 1 million deaths have now been reported worldwide, of which the majority were reported in the area of the Americas (55 %), followed by Europe (23 %). In the last week of September 2020, the regions of the Americas, South-East Asia and Europe account for 91 % of new cases.

Five countries (namely India, the United States of America, Brazil, Argentina and France) recorded 60 % of new global cases in the last week of September 2020, while Israel registered the highest incidence (3717 new cases per 1 million population) (3717 new cases per 1 million population). Globally, the largest number of cases have been reported in the 25-39 age group with approximately 50 % of cases in the 25-64 age group.

However, the number of deaths rises with age and nearly 75 % of deaths are among those aged 65 years and over<sup>33</sup>. There were some 65.6 million COVID-19 cases worldwide as of 4 December 2020. More than 45 million people have recovered, while around 1.5 million deaths have occurred. The United States, Brazil and India were among the pandemic's most critically affected nations<sup>11</sup>. Primarily, an unknown pneumonia case was detected on December 12, 2019 and possible influenza and other coronaviruses were

ruled out by laboratory testing. Chinese authorities announced on January 7, 2020 that a new type of Coronavirus (novel Coronavirus, nCoV) was isolated<sup>18</sup>.

This virus was named as 2019-nCoV by WHO on January 12 and COVID-19 on 11 February 2020. As of February 12, 2020, a total of 43,103 confirmed cases and 1,018 deaths have been announced<sup>14</sup>. Reports showed that the 2019-nCoV infection caused clusters onset similar to severe acute respiratory syndrome coronavirus (SARS)<sup>16,41</sup>. Previous study has shown that coronaviruses can cause respiratory and intestinal infections in animals and humans<sup>25</sup>. Generally, coronaviruses were not considered to be highly pathogenic to humans until the outbreak of severe acute respiratory syndrome (SARS) in 2002 and 2003 in Guangdong, China<sup>10,13</sup>.

Another highly pathogenic coronavirus, Middle East respiratory syndrome (MERS) coronavirus emerged in Middle Eastern countries in 2012<sup>23,40</sup>. 2019-nCoV is one more highly pathogenic coronavirus to human in history.

### Geographic Distribution of COVID-19

Since the first reports of cases from Wuhan, a city in the Hubei Province of China, at the end of 2019 and 27 viral pneumonia cases with seven being severe, were officially announced on December 31, 2019<sup>30</sup>. Etiologic investigations have been performed in patients who applied to the hospital due to similar viral medical histories of these patients has strengthened the likelihood of an infection transmitted from animals to humans<sup>12</sup>. A joint World Health Organization (WHO) China Fact finding mission estimated that the epidemic in China peaked between late January and early February 2020<sup>34</sup>. The majority of reports have been from Hubei and surrounding provinces, but numerous cases have been reported in other provinces and municipalities throughout China, many other countries have recorded outbreaks, among them Japan, Korea, Italy and the USA.<sup>27</sup>

These cases initially occurred mainly among travelers from China and those who have had contact with travelers from China, However, ongoing local transmission has driven smaller outbreaks in some locations outside of China including South Korea, Italy, Iran and Japan and infections elsewhere have been identified in travelers from those countries<sup>3</sup>.

### COVID-19 Transmission

Understanding of the transmission risk is incomplete. Epidemiologic investigation in Wuhan at the beginning of

the outbreak identified an initial association with a seafood market that sold live animals. However, as the outbreak progressed, person to person spread became the main mode of transmission<sup>9</sup>.

SARS-CoV-2, like other emerging high-threat pathogens, has infected health-care workers in China<sup>36</sup> and several other countries. To date, however, in China, where infection prevention and control were taken seriously, nosocomial transmission has not been a major amplifier of transmission in this epidemic. Epidemiological records in China suggest that up to 85% of human-to-human transmission have occurred in family clusters<sup>4</sup> and that 2055 health-care workers have become infected, with an absence of major nosocomial outbreaks and some supporting evidence that some health-care workers acquired infection in their families<sup>36</sup>.

Confirmed recent reports from many infected healthcare workers in Wuhan show that human-to-human transmission can occur. As in SARS and MERS epidemics in the past, human-to human transmission has accelerated the spread of the outbreak and case reports have also started from other states of China. The first non-Chinese case of the infection, which spread to the Chinese provinces and then to the Asian continent, was reported from Thailand on January 13, 2020. The case reported being a Chinese tourist who has traveled to Thailand and had no epidemiologic connection with the marketplace<sup>17</sup>. Other cases from overseas countries such as the USA and France have continued to be reported<sup>15</sup>.

The reported rates of transmission from an individual with symptomatic infection vary by location and infection control interventions. In households, SARS-CoV-2 is more widespread than SRAS-CoV and Middle East coronavirus respiratory syndrome. Older people (aged up to 60 years) are the most vulnerable to SARS-CoV-2 domestic transmission<sup>20</sup>. In the United States, the symptomatic secondary attack rate was 0.45 percent among 445 close contacts of 10 confirmed patients<sup>2</sup>.

Often, the human-to-human transmission occurs with close contact. The transmission primarily occurs when an infected person sneezes and through the respiratory droplets produced just as the spread of influenza and other respiratory pathogens. These droplets can settle in the mouth or nasal mucosa and lungs of people with inhaled air. Currently, it remains unclear whether a person can be infected by COVID-19 by touching an infected surface or object and then touching their mouth, nose, or possibly eyes<sup>35</sup>.

### Clinical Features Of COVID-19

The incubation period for COVID19 is thought to be within 14 days following exposure, with most cases occurring approximately four to five days after exposure<sup>7</sup>. Using data from 181 publicly reported, confirmed cases in China with identifiable exposure, one modeling study estimated that symptoms would develop in 2.5 percent of infected

individuals within 2.2 days and in 97.5 percent of infected individuals within 11.5 days<sup>24</sup>. The median incubation period in this study was 5.1 days. According to a joint World Health Organization (WHO) China fact finding mission, the case fatality rate ranged from 5.8 percent in Wuhan to 0.7 percent in the rest of China<sup>27</sup>.

Most of the fatal cases have occurred in patients with advanced age or underlying medical comorbidities (including cardiovascular disease, diabetes mellitus, chronic lung disease, hypertension and cancer)<sup>28</sup>. The proportion of severe or fatal infections may vary by location. As an example, in Italy, 12 percent of all detected COVID19 cases and 16 percent of all hospitalized patients were admitted to the intensive care unit; the estimated case fatality rate was 5.8 percent in mid-March. In contrast, the estimated case fatality rate in mid-March in South Korea was 0.9 percent<sup>21</sup>.

### COVID19 Diagnosis

Initial management should focus on early recognition of suspect cases, immediate isolation and institution of infection control measures. At present, the possibility of COVID19 should be considered primarily in patients with fever and/or respiratory tract symptoms (e.g. cough, dyspnea) who have had any of the following in the prior 14 days Although diarrhea was present in about 20-25% of patients with MERS-CoV or SARS-CoV infection, intestinal symptoms were rarely reported in patients with COVID-19.

In another study of 99 patients, chest pain, confusion and nausea-vomiting were noted in addition to previous findings<sup>8</sup>. On X-rays or thorax CT imaging of the examined patients, unilateral or bilateral involvement compatible with viral pneumonia was found and bilateral multiple lobular and sub segmental consolidation areas were observed in patients hospitalized in the intensive care unit<sup>38</sup>.

Similarly, to the previous data, X-rays or thorax CT images of the patients revealed unilateral or bilateral lung involvement, compatible with viral pneumonia. Bilateral multiple lobular and subsegmental consolidation areas were present in patients in the intensive care unit<sup>38</sup>. The patients with underlying comorbidity exhibited a more severe clinical course, as expected by the experience gained from the previous epidemics<sup>37</sup>.

As in SARS and MERS, the diagnosis of 2019 n-CoV infection is based on a history of detailed contact and travel and precise laboratory testing. The diagnostic tools are molecular methods, serology and viral culture. The most common diagnostic methods are molecular methods as RT-PCR (reverse transcription) or real-time PCR, which are made using RNA from respiratory samples such as oropharyngeal swabs, sputum, nasopharyngeal aspirate, deep tracheal aspirate, or bronchoalveolar lavage. In particular, lower respiratory tract samples can offer significantly higher viral load and genome fraction than upper respiratory tract samples<sup>42</sup>.

## Treatment of COVID-19

According to the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA), there are currently no medications or vaccines proven to be effective for the treatment or prevention of the 2019 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)<sup>4</sup>.

The China International Exchange and Promotive Association for Medical and Health Care (CPAM) issued a novel 2019 coronavirus disease (COVID-19) guideline in February 2020 with recommendations on methodology, epidemiological characteristics, disease screening and prevention, diagnosis, treatment and control, nosocomial infection prevention and control and disease nursing. For direct antiviral treatment of SARS-CoV-2, CPAM recommends use of lopinavir; ritonavir capsule (dose undefined) by mouth twice daily in combination with nebulized alfa-interferon (5 million units in Sterile Water for Injection inhaled twice daily). CPAM has based this recommendation on weak evidence from retrospective cohort, historically controlled studies, case reports and case series that suggest clinical benefit of lopinavir; ritonavir in the treatment of other coronavirus infection i.e. 2002 SARS-CoV and 2012 Middle East respiratory syndrome coronavirus (MERS-CoV)<sup>39</sup>.

Studies evaluating the antiviral activity of types I and II interferons have reported interferon-beta (IFN $\beta$ ) as the most potent interferon, reducing *in-vitro* MERS-CoV replication.<sup>15</sup> According to a human MERSCoV case report from South Korea, the use of the combination of Lopinavir/Ritonavir (LPV/RTV) (Anti-HIV drugs), pegylated interferon and ribavirin provided a successful viral clearance<sup>26</sup>. For this purpose, a randomized control trial (MIRACLE Trial), that aimed to determine whether LPV/RTV-IFN $\beta$  improved clinical results in MERS-CoV patients, was initiated in 2016 and 76 patients were enrolled. Although another antiviral drug, remdesivir was used in the first case reported from the United States of America, seemed successful, controlled studies with more cases needed<sup>29</sup>.

*In-vitro* studies have shown that viral RNA transcription was terminated with remdesivir in early stage<sup>36,38</sup>. There are publications demonstrating that remdesivir has a strong antiviral activity in epithelial cell cultures against SARS-CoV, MERS-CoV and related zoonotic bat CoVs<sup>1</sup>.

A group of Korean physicians with experience in treating SARS-CoV-2 infected patients have developed recommendations for the treatment of COVID-19. According to these physicians, antiviral medications are not recommended for use in young, healthy patients with mild symptoms and no underlying comorbid conditions. However, treatment with lopinavir 400 mg; ritonavir 100 mg (2 tablets by mouth twice daily) or chloroquine (500 mg by mouth twice daily) should be considered for use in older

patients or patients with underlying conditions and serious symptoms. If chloroquine is unavailable, they recommend considering use of hydroxychloroquine (400 mg by mouth once daily). Use of ribavirin and interferon was not recommended as first-line treatment because of the risk for side effects; however, use of these medications may be considered if treatment with lopinavir; ritonavir, chloroquine, or hydroxychloroquine is ineffective<sup>22</sup>.

Finally, expert opinion: remdesivir, teicoplanin, hydroxychloroquine (not in combination with azithromycin) and ivermectin might be effective as antiviral agents and are deemed promising candidates for the treatment of COVID-19<sup>19</sup>.

## Prevention of COVID19

For most employers, protecting workers will depend on emphasizing basic infection prevention measures. As appropriate, all employers should implement good hygiene and infection control practices, screening patients for clinical manifestations consistent with COVID19 (e.g. fever, cough, dyspnea) prior to entry into a health care facility can help identify those who may warrant additional infection control precautions. This can be done over the phone before the patient actually presents to a facility. Any individual with these manifestations should be advised to wear a facemask. Separate waiting areas for patients with respiratory symptoms should be designated, if possible, at least six feet away from the regular waiting areas. In some settings, such as long-term care facilities, the United States Centers for Disease Control and Prevention (CDC) recommends that standard, contact and droplet precautions in addition to eye protection be used for any patient with an undiagnosed respiratory infection who is not under consideration for COVID19<sup>5</sup>.

## Conclusion

CDC reminds basic measures such as hand washing, using disinfectant solutions, avoiding contact with patients in order to prevent the spread of viruses by droplets. Precautionary actions including the provision of medicines supply chains, personal protective equipment and hospital supplies should be made in a short time for the protection of the Chinese people and global health, especially in the places with close travel ports to major Chinese ports<sup>6</sup>.

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