

## REVIEW ARTICLE

# UNDERSTANDING EPIDEMIOLOGY AND HEALTH BURDEN FROM COVID-19 PANDEMIC: A REVIEW OF GLOBAL CASE REPORTS IN THE EARLY PANDEMIC PERIOD

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## ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic has affected people globally. In many countries, the situation is getting worse with rapid transmission of COVID-19. The daily incidence is drastically increasing. In this review, we aim to summarize epidemiological information and adverse health outcomes of severe acute respiratory syndrome coronavirus 2 infection. The major outcomes are described based on information from the literature and hospital reports. COVID-19 has affected individuals both physiologically and psychologically. The physiological effect on human health includes respiratory distress, pneumonia, cardiac injury, kidney failure, nervous system symptoms, and gastrointestinal symptoms. The psychological effect was observed in patients, health care workers, and general population in the community. This review could be a source of clinical information on COVID-19 for physicians, researchers, and general population for further studies to deal with this pandemic.

**Keywords:** COVID-19, Corona virus, pandemic, epidemiology, adverse health outcomes

## INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection or coronavirus disease 2019 (COVID-19) is an emerging infectious disease, which was first reported in Wuhan City, Hubei Province of China, in December 2019. Fresh-meat and animal markets were suspected to be the source of the disease after confirmation regarding an association between the fresh-meat market and the disease<sup>1-4</sup>. According to the genomic profile, 79% and approximately 50% nucleotides of this virus are identical to those of severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome (MERS-CoV) coronavirus (MERS), respectively. The phylogenetic network analysis suggested that 96.2% of this virus is similar to the coronavirus found in bats<sup>4,5</sup>.

SARS-CoV-2 spreads from patients to the general people through respiratory tract secretions (e.g., coughing, sneezing, or talking) or close contact. Close proximity (within 2-m distance) and poorly ventilated areas have the highest risk of airborne transmission of infection through droplets or aerosols from respiratory secretions<sup>1,2,6-8</sup>. Case report analyses have indicated that periods from exposure to virus until hospitalization and symptom onset are on average 5–6 days and < 11.5 days, respectively. Thus, 14 days of active monitoring is suggested for a patient with

suspected infection<sup>9</sup>. In this review, we provide the summary of epidemiology and health burden related to SARS-CoV-2 infection during the early stage of pandemic. The information was retrieved from literatures published in various scientific journal databases (i.e. PubMed, Scopus, and Web of Science), reports, and media with the aim to understand how disease were spread and caused the adverse health outcomes in population worldwide.

## Disease Epidemiology Case Fatality

Among coronavirus infections, the fatality rates of severe acute respiratory syndrome (SARS) and MERS were 9.6% and 35%–40%, respectively, whereas the initial estimated fatality rate of COVID-19 was 1%<sup>10</sup>. COVID-19 has widely spread to all regions worldwide. On March 11, 2020, the World Health Organization (WHO) characterized COVID-19 as a pandemic. No country is unaffected by COVID-19. As of July 27, 2020, the worldwide counts of confirmed COVID-19 and death from COVID-19 were 16,301,736 and 650,069, respectively, and the case fatality rate is approximately 4%. Recently, the highest number of confirmed cases was noted in the United States, followed by Brazil and India<sup>6</sup>. Compared with SARS and MERS, the fatality rate of COVID-19 infection is relatively low, but it is highly contagious and has a wide range of symptoms.

The case fatality rate differed among regions. A study from Japan suggested that the case fatality may be associated with the population genetic variation and bacilli Calmette-Guérin vaccination. Their analysis revealed that East and Southeast Asian countries had a lower fatality than did western countries. However, the analysis did not consider potential confounders such as patient age group, pandemic stage, and pandemic management<sup>11</sup>.

### **Morbidity and Infectivity**

COVID-19 is highly contagious, spreading rapidly from one city to the entire country within a month and spreading to > 200 countries and regions around the world in almost 2 months. The WHO regular press conference on March 23, 2020, indicated that since the virus outbreak, the number of patients with COVID-19 grew from 1 to 100,000 within 67 days, whereas the next 100,000 patients were reported in 11 days and the third 100,000 in only 4 days, which proves the fact that COVID-19 is accelerating globally<sup>12</sup>.

An early case report of a clustered outbreak in a Chinese family showed that COVID-19 is particularly contagious. In two cases in Wuhan, the virus was transmitted to close family members. Only one of the six close contacts developed the disease later than the transmitting patient did, and five contacts had onsets earlier than or on the same day as did the transmitting patient. Therefore, people with COVID-19 infection are inferred to promptly transfer the disease during the incubation period of the virus<sup>13</sup>. The COVID-19 outbreak on the Diamond Princess cruise ship departing from Yokohama, Japan, in early February 2020 provided a strong evidence of asymptomatic transmission. Approximately 18% of the infected people on the cruise were asymptomatic. However, this number could be an understatement because testing was initially provided only to those who developed symptoms<sup>14</sup>. Disease transmission from asymptomatic cases has been consistent in various studies<sup>15,16</sup>.

Patients with different blood types showed different infectivity rates. A study in China showed that people with blood type A had a higher risk of COVID-19 infection, whereas people with blood type O had a lower risk<sup>17</sup>. Although this study has many limitations and needs further confirmation, some of the findings are comparable with those of a study conducted in Massachusetts, United States, which indicated that blood type O has a lower infection risk than blood types B, AB, and Rh+. However, the blood type did not affect the disease severity of each individual<sup>18</sup>.

### **Health burden of disease**

#### **Physiological health impacts**

The virus causing COVID-19 belongs to the Coronavirus family, a large group of zoonotic viruses, with health impacts ranging from common cold to serious symptoms such as pneumonia. According to early case reports of hospital admission, most patients had a cluster of respiratory illnesses, but the disease severity varied among patients. Common symptoms include fever (83%–100%), dry cough (59%–82%), shortness of breath (31%), myalgia (11%–41%), headache (7%–8%), and diarrhea (2%–10%)<sup>19-24</sup>. Although fever is the most common symptom in most cases, it cannot be used as an indicator of illness severity according to a study conducted in Seattle, United States. Only 50% of the patients had fever at the time of admission. Thus, including fever in the diagnosis algorithm may delay the diagnosis and treatment<sup>25</sup>. The following are the common severe adverse outcomes of COVID-19.

#### **Acute Respiratory Distress Syndrome**

Similar to SARS and MERS, COVID-19 can cause acute respiratory distress syndrome (ARDS). The proportion of SARS- and MERS-infected patients with ARDS who succumbed to the disease is high. Reports from hospitals in Wuhan, China, have indicated that approximately 17% – 29% of COVID-19 patients developed ARDS<sup>19,22</sup>. A retrospective cohort study of COVID-19 patients at Wuhan Jinyintan Hospital showed that many patients developed ARDS. Approximately 42% of the patients developed ARDS, of whom 52.4% died. Patient with ARDS were found to be old and to have a high rate of dyspnea during initial symptom occurrence, as well as a high proportion of them had comorbidities such as hypertension and diabetes<sup>26</sup>. Compared with the case series of 24 patients in Seattle, United States, a higher number of patients with ARDS was reported. The report suggested that 75% of the patients received mechanical ventilation and had consistent moderate to severe ARDS. Moreover, a high fatality rate (50%) was observed in these case series, especially in patients aged > 65 years<sup>25</sup>.

The results of the pooled data analysis revealed that 7.2% of 234 patients with ARDS received extracorporeal membrane oxygenation (ECMO). The fatality rate of patients with ECMO was high (94.1%). However, in this study, the results of ECMO and conventional therapy were not significantly different, which means that ECMO neither benefits nor harms to patients with ARDS.<sup>27</sup> Studies have suggested that methylprednisolone use to prevent ARDS can reduce death risk<sup>26,28,29</sup>.

#### **Pneumonia**

The last three coronavirus outbreaks have been linked to severely rapid pneumonia development

in patients<sup>3,10,30</sup>. Chest computed tomography has shown bilateral lung and peripheral ground-glass opacity (GGO) and comorbid pulmonary turbidity<sup>31,32</sup>. Most patient with COVID-19 had bilateral lung involvement, and changes in the lungs throughout the disease course can be divided into four stages. In the first stage, unilateral or bilateral GGO was detected under the pleura; in the second stage, GGO expanded to more lobes; in the third stage, lung involvement peaked at approximately 10 days after the initial symptoms appeared, and then the proportion of patient with GGO began to decline; and in the fourth stage, GGO showed consolidated absorption<sup>33,34</sup>.

### **Cardiac injury**

Studies analyzing death and discharge of patients with COVID-19 have revealed that patients with COVID-19 had a risk of death from cardiovascular disease<sup>19,23</sup>. Although most deaths resulted from respiratory problems, an analysis of these cases confirmed that some patients died due to explosive myocarditis. A study showed that among all causes of deaths, approximately 7% of patients died because of circulatory failure due to myocardial injury. Thus, physicians must pay attention to cardiac injury as well<sup>35</sup>. Furthermore, acute myocarditis was observed along with hypotension in critically ill pediatric patients admitted to a pediatric intensive care unit (ICU). Moreover, these children presented with one feature of Kawasaki diseases, such as fever, rash, and conjunctivitis<sup>36,37</sup>.

Some patients with COVID-19 have initial symptoms of palpitations and chest tightness rather than respiratory symptoms. People with COVID-19 have obvious cardiovascular symptoms due to inflammation and immune system disorders and have to be admitted to an ICU. Among these, some patients showed a significantly high level of the myocardial damage biomarker (creatinine kinase). Therefore, closely monitoring patients with underlying cardiovascular diseases is necessary<sup>38</sup>.

### **Kidney failure**

A study of 85 COVID-19-infected people in Wuhan, China showed that COVID-19-infected people had an increased likelihood of developing acute renal failure, especially patients aged > 60 years with comorbidities, such as hypertension and heart failure. The autopsy results of six deceased patients showed varying degrees of tubular necrosis, glomerular sclerosis, or glomerular telangiectasia. A study found that COVID-19 directly affected renal tubule<sup>39</sup>.

The prevalence of acute kidney injury (AKI) varied among medical centers depending on the sample size and illness severity of patients being hospitalized. The prevalence ranged from 0.5% to 8.3%. The results suggested that patient AKI increased higher in-hospital mortality<sup>23,40,41</sup>.

Moreover, kidney injury was observed in pediatric patients. A cohort study of 52 patients in the United Kingdom suggested that nearly half of them had kidney dysfunction and 25% had kidney injury as indicated by a high level of serum creatinine. The symptoms were likely to be observed in ICU patients. Moreover, this study observed that patients with kidney dysfunction had an increased likelihood of diarrhea and vomiting<sup>42</sup>.

### **Nervous System**

Neurological symptoms such as dizziness, headache, nausea, and vomiting, have also been observed in COVID-19 patients, although at a lower proportion than do respiratory outcomes.<sup>19,23,43</sup> An observational case series from China found that 36% of the patients had neurological symptoms, and patients with a severe condition were more likely to have neurological symptoms than those with less severe ones. The patients mainly presented the central nervous system symptoms of acute cerebrovascular disease and unconsciousness and skeletal muscle injury<sup>44</sup>.

In the study of, SARS-CoV particles were found to be almost completely located in the neurons. Although the mechanism by which SARS and MERS enter the central nervous system is unclear, the high degree of similarity among COVID-19, SARS, and MERS suggested that COVID-19 also has the potential for neural invasion<sup>45</sup>. Furthermore, recent reports have revealed that virus can be detected in the cerebrospinal fluid, which means the virus can directly invade and damage the nervous system, increasing illness severity<sup>43,46</sup>.

### **Gastrointestinal symptoms**

The prevalence of gastrointestinal symptoms (GI) was varied among studies. A hospital report in Wuhan during the first wave reported about 2 to 10%<sup>19,23</sup>. The common GI symptoms observed in the patient on the admission were diarrhea, nausea, and vomiting. A meta-analysis study from Hongkong found that the prevalence of GI related symptoms 17.6%. The result also suggested that viral RNA was detected nearly 40% in the stool sample of the patient who had diarrhea<sup>47</sup>. GI symptoms were treated according to common practice such as using electrolyte fluid and antibiotics. However, the antibiotics or other medication may also cause GI symptom during the hospitalize as well. Although these symptoms were not a main cause of fatality in the patient, but it associated with the illness severity as suggested by a study from India which found that nearly 20% of GI present patients need oxygen and ventilator and may lead to death<sup>48</sup>.

### **Other physiological effect**

In addition to the aforementioned adverse health outcomes, some minor symptoms were reported,

the ocular symptom being one of them. The prevalence of the ocular symptom varied among studies from 2% to 32% and was related to disease severity<sup>49</sup>. A report from special shelter hospitals in China suggested that approximately 4.68% of the infected patients developed conjunctival hemorrhage. The three major ocular symptoms were dry eyes, blurred vision, and foreign body sensation. The incidence of these three major symptoms was > 10%, particularly dry eyes, which was approximately 20%<sup>50</sup>. Furthermore, one study observed the presence of SARS-CoV-2 in conjunctival specimens. Although this sample size was small, this result could be an important indication for physicians to take measures to avoid disease transmission through eye secretion<sup>51</sup>.

Another observable symptom is olfactory disturbances. Studies have reported that some patients also experienced olfactory and gustatory dysfunction<sup>52,53</sup>. Although these minor symptoms are less likely to lead to death, monitoring the patient and providing appropriate treatment are crucial.

### **Psychological health impacts**

#### **Patients and caregivers**

Psychological effect is another important adverse outcome that affects patients as well as caregivers. Particularly in caregivers, COVID-19 can cause serious mental problem. In the early days of COVID-19 pandemic, China quickly responded by blocking the outbreak in Wuhan, and the quarantined area continued to expand to other provinces in China. Almost all the people in China isolated themselves at home. Therefore, the majority of people have a sense of isolation, uncertainty, lack of resources, especially personal protective equipment, and the loss of income caused by the inability to return to work after the Chinese New Year<sup>54</sup>.

#### **Health care workers**

Health care use among international workers during the pandemic appears to be one of the factors affecting the psychological health of this population. It is relatively difficult for international workers to access medical services and personal protective equipment in the host country. The mental burden of international workers may worsen due to loss of income and isolation due to self-quarantine<sup>55-57</sup>.

Health care workers were directly affected psychologically during this epidemic. A study in China indicated that the prevalence of mental health symptoms among medical workers is generally high, especially in the epidemic outbreak areas in Wuhan and among frontline medical workers<sup>58</sup>. The psychological research center in Hunan, China quickly formulated a detailed psychological intervention plan for medical workers, but the implementation process was not smooth. The main reason is that

health workers' first concern is not the infection because they are prepared from the moment they join the health work. Second, they do not want their families to worry about them, and third, they were unable to deal with patients' lack of cooperation during the treatment. Medical workers believe that they do not need to psychological treatment but patients do for emotional well-being. However, undoubtedly, medical workers were affected, and some nurses showed signs of excitement and irritability<sup>59</sup>.

#### **General population**

Although the general population faces mental problem, most people have a safe place to live and protect themselves from the disease. However, the situation is different for homeless people. This vulnerable group usually lives in an environment that is conducive to viral transmission, such as shelter, halfway house, abandoned building, or even on the street. Some of these people have chronic psychological conditions. During the pandemic, they faced increased psychological problems because many cities and countries announced curfew and lockdown. This restricted their movement outdoors. The homeless could not go out and do their job. Some of them may have lost their residence<sup>60</sup>.

A report based on an online self-assessment Depression, Anxiety, and Stress Scale by the general population, which assessed participants from 194 cities in China showed that more than half of the people indicated that they had moderate or even severe psychological health problems. A separate analysis of depression, anxiety, and stress scales found that the proportion of people in the normal range was > 60% followed by 17%, 29%, and 8% of the people with moderate depression, anxiety, and stress, respectively. In this population, women, student status, and physical condition were related to serious mental health<sup>61</sup>. The psychological effect of the pandemic was not only observed in adults but also children and adolescents. The common stressors for this population group were the lack of contact with friends, classmates, and teachers, the lack of personal space at home, fear of infection, boredom, and the burden of online teaching<sup>62,63</sup>.

### **CONCLUSION**

COVID-19 cause various severe adverse outcomes in patients. Furthermore, it can psychologically affect the general population. The pandemic is getting worse with many countries having a high number of daily infected cases. Only a few countries are controlling the situation well. However, many resources and effort must be invested in order to deal with this situation. Many ongoing studies are attempting to and solve the problem. Vaccine development appears to be the only hope of mankind to end this pandemic.

### Conflict of interest

The authors declare no potential conflict of interest.

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