

# Review of potential risk groups for coronavirus disease 2019 (COVID-19)

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## Abstract

The current pandemic of coronavirus disease 19 (COVID-19) is a global issue caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Studies have revealed that this virus results in poorer consequences and a higher rate of mortality in older adults and those with comorbidities such as cardiovascular disease, hypertension, diabetes and prolonged respiratory illness. In this review, we discuss in detail the potential groups at risk of COVID-19 and outline future recommendations to mitigate community transmission of COVID-19. The rate of COVID-19 was high in healthcare workers, smokers, older adults, travellers and pregnant women. Furthermore, patients with severe medical complications such as heart disease, hypertension, respiratory illness, diabetes mellitus and cancer are at higher risk of disease severity and mortality. Therefore, special effort and devotion are needed to diminish the threat of SARS-CoV-2 infection. Proper vaccination, use of sanitizers for handwashing and complete lockdown are recommended to mitigate the chain of COVID-19 transmission.

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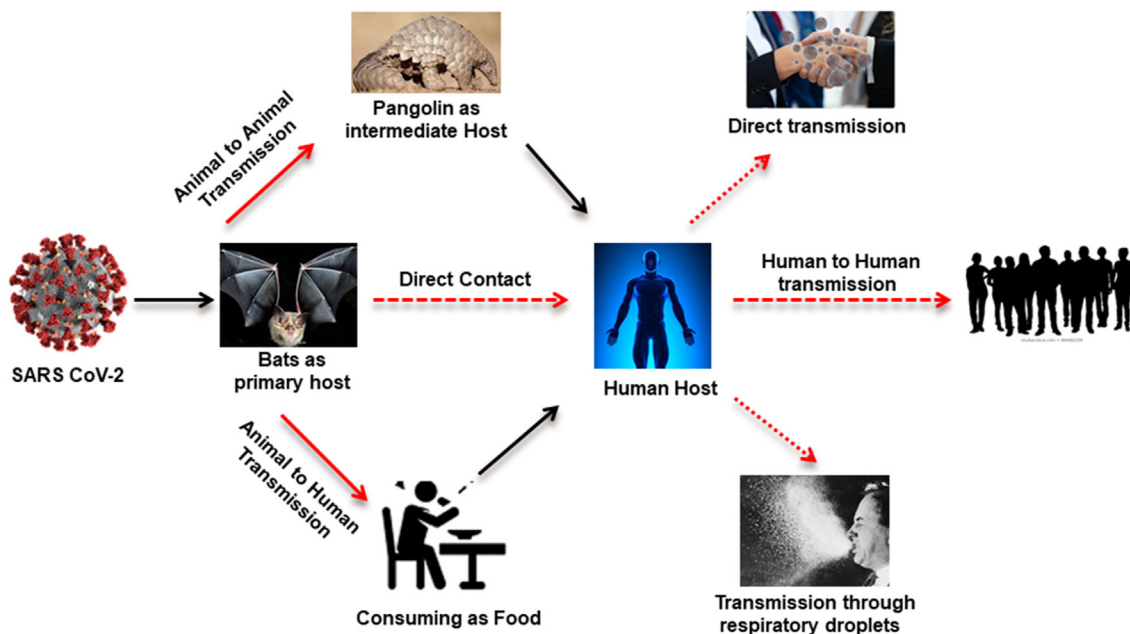
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## Introduction

Coronavirus disease 2019 (COVID-19) is a persistent pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The epidemic began in the city of Wuhan, the capital of Hubei province, China, in late 2019 and was declared a public health emergency of international concern on 30 January 2020 [1]. More than 48 136 225 COVID-19 cases have been identified globally, resulting in more than 1 225 913 deaths; over 31 919 360 patients have recovered [2]. This pandemic has caused socioeconomic mayhem worldwide, with

rescheduling and cancellation of outings and sporting events as well as political, religious and traditional events [3]. In more than 193 countries, schools and universities have been closed at a local or national level – about 99.4% of the worldwide student population [3].

COVID-19 is a highly transmittable and pathogenic viral infection caused by SARS-CoV-2. Genomic analysis has revealed that SARS-CoV-2 is phylogenetically related to severe acute respiratory syndrome (SARS)-like bat viruses, with approximately 96% genome sequence similarity [4]. Therefore, bats could be the possible primary reservoir for human coronavirus (CoV) [5,6]. A growing body of research has identified bats as the evolutionary sources of SARS and Middle East respiratory syndrome (MERS) CoVs [7,8] and as the source of progenitors of human CoV [9]. The emergence of SARS-CoV-2 further underscores the importance of bat-origin CoVs to global health, and understanding their origin and cross-species transmission is a high priority for pandemic preparedness [10,11]. Scientists have also proposed pangolins as a potential



**FIG. 1.** Coronavirus disease 2019 (COVID-19) transmission cycle.

intermediate species for SARS-CoV-2 emergence, suggesting that they are a potential reservoir species [12,13]. A metagenomic study identified pangolin-associated CoVs that belong to two sublineages of SARS-CoV-2-related CoVs, including one that exhibits strong similarity in the receptor-binding domain to SARS-CoV-2. The discovery of multiple lineages of pangolin CoV and their similarity to SARS-CoV-2 suggests that pangolins should be considered as possible hosts in the emergence of new CoVs [14]. It was concluded from the above-mentioned theories that CoV may be transmitted directly from bats to humans, or it may transmit into pangolins as an intermediate host (Fig. 1). Among humans, it is mainly spread through coughing, sneezing, respiratory droplets and contact routes (Fig. 1) [1,15]. Droplet transmission occurs via the infected person (respiratory illness) to an adjacent person as a result of the high risk of exposure when infectious droplets are inhaled through mucosa or conjunctiva. Transmission may also occur through fomites in the atmosphere near the infected person [16]. Subsequently, the transmission of the COVID-19 virus can occur through direct contact with a person with disease and through indirect contact with surfaces in the nearby atmosphere or with items used by an infected person, like stethoscopes or thermometers [17].

Patients with COVID-19 generally experience nausea, dry or painful cough, sore throat, tiredness or myalgia, headache, shortness of breath and general weakness [18,19]. Although most COVID-19 patients are thought to have a good prognosis, older patients and those with chronic illness may

experience poorer outcomes [20]. Patients with chronic underlying conditions can experience viral pneumonia, hypoxaemia and dyspnoea within 1 week of disease onset, which may lead to respiratory or end-organ failure and even death [21]. Patient-reported loss of smell and taste has been related to COVID-19 infection, although no clinical olfactory tests have been conducted on a cohort of COVID-19 patients. It has been reported that quantitative odor testing shows that decreased odor activity is a significant marker for SARS-CoV-2 infection and suggests the possibility that odor testing may help in recognizing COVID-19 patients in need of early treatment [22].

COVID-19 is often more serious in people over the age of 60 or those who have health problems such as lung or heart disease, cancer, diabetes or immune-affecting disorders [23]. The basic rates of mortality vary, ranging from 5.6% to 15.2% throughout the world [24], with a greater risk of dying for the elderly and those with comorbid conditions like diabetes mellitus (DM) and hypertension [25]. A global study of 46 248 cases showed that the most prevalent comorbidities are obesity, cardiovascular disease, DM and respiratory morbidity [26]. In COVID-19, smoking appears to increase the probability of adverse outcomes [16]. It can increase angiotensin-converting enzyme expression 2 (ACE2) in current Asian smokers and make them vulnerable to COVID-19 [27]. Likewise, air pollution also increases the risk of extreme COVID-19 [28]. Air pollution such as particulate matter acts as a vector to carry the virus and increases its transmission. These

particulate matters may damage the lung cells, resulting in severe inflammation [29].

Here we summarize the potential groups at risk of COVID-19 and propose future recommendations to control the transmission of COVID-19 among the community and health-care workers (HCWs).

## COVID-19 risk groups

According to the World Health Organization, most virus-infected people will develop mild or uncomplicated COVID-19, which comprises 80% of cases; the remaining 20% may develop its extreme version, requiring hospitalization (14%) or care in an intensive care unit (ICU) (6%) [30]. Well-described risk factors for severe disease among patients with COVID-19 in China include HCWs [31], older age [32,33] and serious medical conditions such as diabetes [32,34], cardiovascular disease [32,35], hypertension [32,35], cancer [32,36], chronic respiratory disease [32] and cerebrovascular disease [33,35]. The United States and Europe recently confirmed these risk features and suggested new ones, such as obesity, chronic kidney disease, smoking and asthma [37].

## Healthcare workers

The well-being of healthcare professionals is the backbone of every health system that works well. As a result of the pandemic, healthcare providers are under immense strain from a heavy workload coupled with increased overall health expenses. The excessive burden of COVID-19 may lead to stress in HCWs. The main causes of psychologic distress in Health care workers (HCWs) include long hours of work, sleep disturbances and exhaustion as well as the possibility of becoming infected and placing their families at risk of a life-threatening condition [38].

According to the China National Health Commission, by late February, more than 3000 HCWs were reportedly infected in China, and many have died [39]. Additionally, in Iran, about 40 HCWs died of COVID-19, and several have been placed under observation after showing signs and symptoms of COVID-19 [38]. However, according to official online records, it was reported that 10% of HCWs in Italy were infected – a total of 7763 patients. HCWs are at greater risk of infection according to the Italian National Federation of Medicine Surgery and Odontology; anesthetists and surgeons are highly susceptible to exposure. It has been proposed that a community-centred or home care programme for COVID-19 could minimize disease transmission and physician exposure, rather than a hospital-

focused system [31]. Dental HCWs are typically at a higher risk of transmitting this infectious disease, and oral HCWs may spread disease [40]. It has also been demonstrated that patients may visit dental settings for daily or emergency treatments, with dental HCWs serving as reservoirs for microbes that lead to a variety of diseases, including COVID-19 [41]. Dentists are exposed to oral secretions for prolonged periods, and their high-speed handpieces and ultrasonic devices aerosolize body fluids. It has been reported that dentists comprise about 5% of the total deaths [42].

Public health administrators worldwide [43,44], including the Ministry of Health in Saudi Arabia, are working diligently to prevent the transmission of COVID-19 by disseminating timely educational videos, instructional brochures and social networking notifications to HCWs [45]. All healthcare specialists from psychiatry to urology have died of work-related infection with COVID-19. Doctors whose specialties include the airway, such as anesthesiologists, dentists and otorhinolaryngologists, are susceptible to COVID-19; this group accounted for 12% of all doctor deaths. During the course of their work, ophthalmologists are also around oronasal secretions for long periods. Dr Li Wenliang, the Chinese ophthalmologist who first notified the globe of COVID-19, died at the age of 33 from this disease [46]. Two more ophthalmologists at Li's workstation died of COVID-19, possibly because of prolonged exposure to the airways of infected patients during ophthalmoscopy or nasolacrimal manipulation or from virus transmission via tears [47]. Countries like Singapore, South Korea and Taiwan, which have taken decisive measures to prevent travel from affected areas, strictly implemented quarantines and engaged in widespread testing, managed to control the epidemic; there are very few reports of physician deaths in these countries in social media [48].

In South Korea, until 10 weeks after the disease outbreak, there was no death of a physician or nurse reported from COVID-19 [49]. Because the onset of the disease in the United Kingdom and North America lagged behind Asia and Europe, there may be an increase in COVID-19-related physician deaths in these areas in the coming weeks. At least 12 COVID-19-related physician deaths occurred in North America on 5 April 2020. A rising number of North American doctors have contracted COVID-19 and are receiving critical care [50]. Senior doctors and those with comorbidities should preferably not be allocated to frontline duties with COVID-19 patients but rather should be given roles such as video or phone reviews, consultation or public liaison [51]. Finally, international communities should learn early how to protect their HCWs, especially in low- and middle-income countries with potential COVID-19 outbreaks. The increase in knowledge of personal safety, adequate personal protective equipment (PPE) and

proper preparedness and response will play an essential role in decreasing the risk of infection for medical professionals.

## Patients with medical complications

According to the World Health Organization, COVID-19 infects people of all ages. However, it has been suggested that people with severe medical complications such as cardiovascular disease, chronic respiratory disease, diabetes and cancer are at higher risk of disease morbidity and mortality [52].

### Heart disease

COVID-19 interacts with the circulatory system at multiple levels, increasing morbidity and causing myocardial injury and dysfunction in patients with underlying cardiovascular disorders [53]. SARS-CoV-2 infection is caused by binding the surface spike protein of the virus to the human ACE2 receptor after the spike protein activates by the transmembrane protease serine 2 [54]. ACE2 is found in the lung (mainly alveolar type II cells) and tends to be the dominant portal of entry [55]. ACE2 is also highly expressed in the heart, countering the angiotensin II effects with extreme activation of the renin–angiotensin system, such as hypertension, atherosclerosis and congestive heart failure [56]. In addition to heart and lung, ACE2 is also found in intestinal epithelium, kidney and vascular endothelium, providing a basis for the multiorgan dysfunction observed with SARS-CoV-2 infection [55,56].

There is cumulative evidence that COVID-19 is linked with increased severity of and mortality from cardiovascular disease. Comorbidities including the cardiovascular system are common in patients with COVID-19, and these patients are at higher risk of disease severity and mortality. However, it is unknown whether cardiovascular comorbid conditions alone influence the risk of COVID-19 or whether some other factors are involved, such as age [53]. According to the US Centers for Disease Control and Prevention (CDC), 44 000 cases of laboratory-confirmed COVID-19 were reported. It was shown that cardiovascular disease, older age, diabetes, cancer, chronic respiratory disease and hypertension were all associated with an increased risk of morbidity and mortality [32]. Similar factors were also associated with 191 severe COVID-19 cases in China, with 54 deaths recorded while 137 patients were discharged [57]. It was observed that the risk of mortality was strongly associated with coronary heart disease, hypertension, DM and multiple organ failure.

### Respiratory illness

The presence of a respiratory illness such as asthma and tuberculosis (TB) has been listed as a potential risk factor

indicating COVID-19 severity and mortality, as described by the CDC [58]. Asthma is widely recognized as an important risk factor for serious respiratory disease in patients with COVID-19, especially in the United States. There is some evidence that patients with asthma who have COVID-19 are overrepresented among adult patients who have been admitted to hospital [59]. This overrepresentation may occur because SARS-CoV-2 causes exacerbations of asthma, as do other viruses, which is why asthma is identified as a risk factor for COVID-19 comorbidity [59]. Another study revealed that a 37-year-old man with asthma had postmortem lung findings which met the clinical criteria for severe acute respiratory distress syndrome; he died of COVID-19 less than 2 weeks after seeking care at the hospital. His lungs displayed plugging of mucus and other asthma-related histologic changes as well as early diffuse alveolar damage and fibrinous pneumonia. Diffuse alveolar damage is common in patients diagnosed with influenza virus, including influenza A/H1N1, and is often followed by a combination of haemorrhage, acute bronchopneumonia in which neutrophils predominate, peripheral pulmonary macroscopic thrombosis and haemophagocytosis [60]. The most frequent symptoms associated with COVID-19 – fever, dry cough and shortness of breath – are also normal during acute asthma exacerbation. A study showed a 14% prevalence of asthma in COVID-19 patients [58]. The use of appropriate PPE should be recommended to asthma patients to reduce the risk of disease.

Similarly, TB is also a severe bacterial disease which mainly affects the lungs of infected patients [2]. There is evidence that patients with latent TB infection and TB disease are at increased risk of infection with SARS-CoV-2 and are predisposed to severe COVID-19 pneumonia [61]. Because the portal of entry for both TB and COVID-19 is the upper respiratory tract, the relationship between serious influenza coinfection and pulmonary TB disease has remained unclear [62,63]. Similarly, a case report noted that the disease course of older TB patients easily progressed to the severe type of COVID-19, and patients had a long recovery process. These case reports notify us of the risk of COVID-19 patients with poor recovery being coinfecting with TB; they also show the importance of the effective use of steroids for case management [64]. The importance of primary prevention measures should be emphasized, especially in TB patients. Hospitals and TB care centres need to be prepared for early detection and management of serious COVID-19.

### Diabetes mellitus

Diabetes is an important cause of mortality and morbidity globally. The condition is related to a few macrovascular and microvascular complexities, which eventually affect patient survival [65]. A relationship between diabetes and infection, especially influenza A (H1N1) [66], SARS-CoV [67], MERS-CoV

[68] and pneumonia is normal relation but it could effect the older people with DM (T2DM) [62,69,70]. According to current information, patients with T2DM do not seem to be at a higher risk of contracting SARS-CoV-2 than the overall population. However, the features of patients with diabetes at high risk for developing severe and serious forms of COVID-19, as well as the prognostic effect of diabetes on the course of COVID-19, are currently under examination [70]. However, it was reported from China and Italy that elderly people with chronic diseases (e.g. diabetes) were shown to have a high risk of dying from COVID-19 [32,71,72].

SARS-CoV-2 infection in patients with diabetes probably stimulates higher stress via the release of hyperglycemic hormones – for example catecholamines and glucocorticoids – leading to an increase in blood glucose levels as well as glucose inconsistency [34]. Furthermore, a retrospective study from Wuhan noted that about 10% of the patients with T2DM and COVID-19 experienced at least one bout of hypoglycaemia (<3.9 mmol/L) [10]. As the pandemic progresses to other continents, data from Europe and the Americas have shown a perturbing relationship between DM and COVID-19 prognosis. A study of 1099 COVID-19 patients was conducted in China, with results indicating that 16.2% of the patients had DM, 23.7% hypertension, 2.3% cerebrovascular disease and 5.8% coronary heart disease [71]. Similarly, another study including 140 patients showed a similar rate of hypertension (30%) and DM (12%) [73]. In Belgium, more than half a million individuals were identified with T2DM, and 20% of them were older than 65 [74,75]. Similarly, a French study indicated that diabetes affects more than 3 million individuals, mostly as T2DM, with 25% of them older than 75 years [2,76]. In Hong Kong, the first three deaths related to COVID-19 were reported in people with diabetes. A study of 1099 laboratory-confirmed COVID-19 cases found that 173 patients (16%) had severe disease with diabetes, while the remaining 926 patients (5.7%) had mild disease with diabetes. Similarly, 24% of those with severe disease had hypertension compared to 13% among those with mild disease, thus highlighting the increased risk of infection among those with chronic diseases like diabetes [71]. DM has been related to death and disease severity in patients with COVID-19.

### Cancer

The outbreak of COVID-19 has infected thousands of people in at least 186 countries, with the cancer care delivery system affected in addition to affecting the overall health system. Cancer patients are more vulnerable to COVID-19 than cancer-free people because of their suppressed immune systems, the result of malignancy or cancer therapy [77]. Furthermore, cancer patients are frequently older (60 years of age) with one or

more significant comorbidities, placing them at greater risk of COVID-19–related morbidity and mortality [78]. In addition, as a result of frequent physician visits for anticancer treatment, cancer screening and preventive and supportive care, they also have high rates of interaction with the healthcare system. Therefore, the concern is that the potential coexistence of a cancer diagnosis and an infection with COVID-19 may produce a synergistic negative prognostic effect.

The rates of COVID-19 mortality and morbidity were significantly higher among individuals with a cancer history (39%) than those without such a history (8%) ( $p$  0.0003) [36]. Similarly, a 57-year-old Chinese male patient with lung cancer was reported to be COVID-19 positive, with disease manifesting symptoms such as fever, shortness of breath, cough, diarrhoea and myalgia [73]. A recent retrospective study of 28 cancer patients with confirmed COVID-19 was conducted in Wuhan to measure the risk factors associated with COVID-19 severity and mortality. It was reported that cancer patients at high risk of COVID-19 developed severe complications such as acute respiratory distress syndrome (28.6%), acute myocardial infarction (3.6%) and septic shock (3.6%) [79]. However, cancer patients require ongoing treatment, so it is not a privilege to undergo medical testing or clinical treatments; their future exposure to COVID-19 may be risky or even fatal. Remarkable strides are being made to identify the unique characteristics of patients with cancer who contract the novel CoV to address diagnostic and therapeutic obstacles and to develop guidelines to protect this vulnerable population from both virus exposure and disease progression resulting from testing and treatment delays.

### Smoking

Smoking is considered a possible risk factor associated with negative disease prognosis. Extensive evidence has demonstrated the adverse effect of tobacco use on the lungs and its fundamental association with a plethora of respiratory illnesses [80]. Smoking is also harmful to the immune system and increases its sensitivity to infection, making smokers more susceptible to infectious diseases [81]. Previous studies have demonstrated that smokers are 2-fold more likely to contract influenza than nonsmokers and have more severe symptoms, while smokers were also more likely to have higher severity and mortality to the previous outbreak of MERS-CoV [82,83].

According to recent literature reported by the World Health Organization, smoking is associated with increased severity of disease and mortality of hospitalized COVID-19 patients [84]. Similar results have been described, mostly from China, suggesting that smoking is a potential risk factor associated with progression and adverse consequences of COVID-19 [71]. An epidemiologic study of 191

COVID-19–infected individuals reported 54 deaths while the remaining 137 patients survived. Among those who died, 9% were recent smokers compared to 4% among those who lived. There was no statistically significant difference between the smoking rates of survivors and nonsurvivors ( $p$  0.21) to mortality from COVID-19 [81]. Similarly, a meta-analysis was conducted describing 11 590 COVID-19 patients showing that the risk of disease progression was almost double in smokers compared to nonsmokers. However, the rate of COVID-19 mortality among smokers was 25.8% [35]. Smoking involves the close contact of fingers and polluted cigarettes tubes with the lips, which increases the risk of COVID-19 transmission from hand to mouth [85]. Therefore, smoking is a possible mode of virus transmission for both direct and indirect smokers. Smokers with COVID-19 have a 3.25 times higher chance of getting serious forms of the disease compared to nonsmokers [71]. A study of 78 COVID-19 patients was conducted which showed adverse outcomes in patients with a history of smoking (27.3%) compared to nonsmokers (3.0%). The results were statistically significant ( $p$  0.018), indicating that a history of smoking is considered a potential risk factor in disease progression [15].

#### Older adults

COVID-19 appears to follow a pattern like that of influenza and previous SARS-CoV outbreaks: the frequency and mortality of the disease are higher among the elderly age group [25]. In most countries, older people are at a significantly higher risk of developing serious disease as a result of physiologic changes occurring during ageing and possibly underlying health conditions [86]. A study of 44 672 COVID-19–positive cases conducted in China showed that the mortality rate was 2.3%, which differed according to age and disease severity. Death occurred in 14.8% of patients over 80 years of age, 8.0% between 70 and 79 years of age and 49.0% of serious cases. For those who died who had chronic diseases, 10.5% had cardiovascular disease, 6.3% had a chronic respiratory disease, 7.3% had DM, 5.6% had cancer and 6.0% had hypertension [32]. A similar analysis of 72 314 cases showed an overall case fatality rate (CFR) of 2.3%, while an 8% CFR was observed in patients aged 70 to 79 years and was 14.5% in patients older than 80 [32]. A study of 355 COVID-19–positive patients showed a high mortality rate in patients whose average age was 79.5 years [87]. Another multi–age group study of 4226 cases was reported in the United States, showing a less than 1% CFR in patients younger than age 54, while an older group aged 65 to 84 showed 3% to 11% CFR, with 10% to 27% CFR shown in patients older than 85 [78]. The COVID-19 pandemic has resulted in a much higher rate of mortality in older adults, especially older adults with comorbidities.

#### Travellers

The current outbreak of the novel CoV has resulted in important concerns. Continuously and rapidly rising numbers of COVID-19 infections threaten the globe. Every old or new disease or infection has certain risk factors, including COVID-19, which has many risk factors, with one important one being travel. There has been a noticeable increase in travel over the last decade [88], with tourism and international travel at a peak [89]. This trend of tourism and travel will lead to a greatly increased risk of illness and infections [88]. Research has repeatedly shown that people are creatures of habit and custom; tourism and travel also depend on habits and routines [90]. Despite its high risk factor, travel is considered to be an important part of religious life, as with Catholic pilgrims and Holy Week travellers in Latin America [91] as well as the Umrah and Hajj pilgrims [5]; people also travel for business [92]. People have travelled around the world not only for religious and business activities but also for educational purposes; indeed, China is the biggest source of international students [93]. During the first 2 months after the epidemic began in Wuhan, the disease quickly travelled out of China to other countries through domestic and international travel [94]. By late February, many countries had developed large-scale epidemics, raising international concern [95]. As a result of such concern, the Australian government announced travel restrictions and denied entry to anyone who had been in China within 14 days of arrival [93]. In Australia, where there are more than 100 000 Chinese students [93], the travel ban prevented almost all students from continuing their studies [81].

One study revealed that most COVID-19 cases were related to a travel history to China [96]. The results of this study indicated that a lower proportion of COVID-19 infection was noted in nontravellers compared to travellers. Another study reported that on 19 January 2020, a man sought care at a clinic in Snohomish County, Washington State, with a history of coughing and fever. He was evaluated by doctors, and he disclosed that he had returned from Wuhan a few days before. Further investigation by real-time reverse transcriptase PCR revealed that the man was infected with COVID-19 [97]. Similarly, a 32-year-old student returned from the Wuhan University of Technology to Nepal with a heavy cough, sneezing and elevated temperature with mild breathing difficulties after some time [98]. The same scenario occurred in Pakistan when students returned there from China during the winter break. One case of COVID-19 infection discovered on 24 January 2020 occurred in a person with a travel history from China [99]. It is therefore concluded that travel is a main risk factor for transmission of COVID-19 infection. Many studies concluded that there should be a ban on travel, and a hard

lockdown should be applied to prevent the current outbreak from escalating [96]. This conclusion is supported by another study which reported that there was a ban on travel to and from Wuhan during the epidemic, and this travel ban led to a COVID-19-free environment in Wuhan within 50 days [100]. The above studies mainly focused on the fact that travel is a risk factor for COVID-19; some studies further suggested that lockdowns and travel bans are better tactics to tackle the COVID-19 infection. However, we suggest that there are consequences of lockdowns and travel bans which must be carefully analysed.

### Pregnant women

COVID-19 affects people of any age, with the elderly most affected, but cases have also been identified in newborns and young children, although these groups of patients tend to develop a milder disease course [32]. Pregnant women may be more vulnerable to COVID-19 because they are more susceptible to viral infections as a result of the physiologic immunosuppression that characterizes pregnancy; they also have a higher risk of developing a more serious type of disease [21]. The previous MERS-CoV and SARS-CoV outbreaks indicated that pregnant women are specifically susceptible to adverse outcomes, including ICU admission, renal failure and death and need for endotracheal intubation [101,102]. Pregnancy is characterized by some changes involving both the immune system and pulmonary physiology, thus exposing the pregnant woman to a greater susceptibility to viral infections and more serious complications [103]. Evaluation of COVID-19 during pregnancy is in progress. Research groups want to learn about the influence of COVID-19 on pregnant and nonpregnant women to see whether or not it is different. The limited data available indicate that there is no significantly higher influence of COVID-19 on pregnant women compared to the everyday person [38,104]. For the maintenance of foetal semiallografts, pregnant women have special immunologic adaptations. The immune system is temporarily suppressed because of the suppression of T-cell activity, and consequently pregnant women are predisposed to viral infections [105,106]. Moreover, the clinical outcomes of viral infections might be worse in pregnant women as a result of the physiologic and hormonal changes that occur in the circulatory and respiratory systems [104].

With pregnancy, many physiologic changes occur compared to nonpregnant women. In cases of infection of the lower respiratory tract, pregnant women have worse outcomes and need to be treated in the ICU. Most women were affected in the third trimester and had the same clinical findings as nonpregnant women. Preterm deliveries and foetal distress were observed in some cases [104,107]. The history of other CoVs indicates that pregnant women are at more risk than

nonpregnant women. Due to diabetes in pregnant women, their bodies respond in the form of suppression of TH1 and high expression of ACE2 receptors, which are responsible for the attachment of SARS-CoV and SARS-CoV-2, so they are more susceptible to the viral infection [55,108].

The common symptoms of pregnant women were cough, fever shortness of breath, myalgia and fatigue. From 0 to 14% of the woman were reported have severe pneumonia and needed to be admitted to the ICU [109]. To date, studies have shown that pregnant women are not at a higher risk than the general population, but they may be considered a high-risk group because of the results of studies of other viral infections demonstrating their detrimental impact on pregnant women. Approximate data indicate that 85% of pregnant women had mild disease; severe disease was reported in 10% and critical disease in 5% [110,111]. A comparison of pregnant and nonpregnant women with SARS-CoV-2 revealed a lower lymphocyte count in pregnant women. Other diagnostic parameters, like white blood cell count, haemoglobin level and platelet and liver enzyme counts, were reported to be in the normal range [112]. It has been reported that pregnant women with COVID-19 are not susceptible to its complications, and the outcomes of pregnancy are not significantly affected [113]. Pregnancy outcomes between symptomatic and asymptomatic patients show that the former group has a high rate of severe disease and preterm birth than the latter. Our results indicate that asymptomatic pregnant patients may not be at high risk of severe illness, at least relative to symptomatic pregnant women. The small sample size was the major limitation of the above study, so we cannot generalize any findings based on this study [114]. In seven confirmed cases from New York City, five patients were symptomatic, with symptoms like cough, myalgia, fever, chest pain and headache. This is not much different from their nonpregnant counterparts [110]. Comparing clinical courses and outcomes of pregnant and nonpregnant women found no association between pregnancy and severity of diseases, virus clearance time or length of hospital stay [115]. A survey of these studies reveals that pregnant women are not significantly more susceptible to COVID-19 than nonpregnant women. Scientific research and exploration of COVID-19 is currently in its infancy; more research needs to be done to gain insight into the risk posed to infected pregnant women.

It is well known that some virus species can cause congenital infections and affect the health status of the foetus – for instance, rubella virus infection [116]. The effects and consequences of COVID-19 transmission from mother to foetus remain poorly understood [117]. Testing for the presence of SARS-CoV-2 by reverse transcriptase PCR has repeatedly failed to identify the presence of the virus's genome in maternal and neonatal specimens including placenta, umbilical cord blood,

amniotic fluid or amniotic swab, maternal blood, vaginal secretions or breast milk [21,118]. The detection of SARS-CoV-2 RNA in placental or membrane samples supports the possibility of vertical transmission [119]. One detected virus RNA in three of 11 samples from COVID-19–positive women, all of whom had moderate to severe disease at the time of delivery. However, none of the infants tested positive for SARS-CoV-2 from postnatal days 1 through 5, and none showed symptoms of COVID-19 infection [117]. More recently, a case report has been published regarding placental transmission of COVID-19 [120]. A case occurred in a woman in her third trimester of pregnancy who had critical COVID-19; amniotic fluid, umbilical cord blood, placenta and neonatal gastric fluid were retained during Cesarean section. The COVID-19 nucleic acid test results of the specimens revealed no COVID-19 infection. There is no evidence of intrauterine vertical transmission during delivery in the third trimester, but the data are limited and need to be further explored.

### Hypertension

Hypertension has been reported to greatly increase the incidence and morbidity of patients with the novel CoV. Nevertheless, early COVID-19 studies reported mixed findings regarding hypertension [121]. Hypertension was found to be associated with an ~2.5-fold increased risk of both increased incidence and mortality and generally occurs in people over age 60 [121]. Likewise, the incidence of hypertension is high in patients affected by COVID-19 and tends to be associated with an increased risk of mortality and morbidity [122]. Early evidence from the United States and China shows that hypertension tends to be the most prevalent comorbidity in at least 30% to 49% of COVID-19–admitted patients [123,124]. Patients with hypertension whose COVID-19 improves are more likely to be admitted to hospital than normotensive persons [125]. Guan *et al.* [71] collected data from 1099 confirmed COVID-19 patients, with 15% reporting hypertension as the single highest risk factor of infection. Similarly, Zhang *et al.* [73] identified 140 patients with COVID-19 and found that 30% of all patients and 37.9% of those with severe illness had hypertension. Hypertension was found in 23.7% to 30% of patients admitted with COVID-19 associated with a more serious infection. Similarly, research from Italy that looked at patients admitted to the ICU found that 49% had hypertension.

Similar to influenza and SARS-CoV outbreaks, the incidence and mortality of COVID-19 is higher in the elderly. Nevertheless, because hypertension is strongly associated with age, an alternative definition is end-organ damage in patients with hypertension. As a result of hypertension, a number of

pathophysiologic changes occur in the cardiovascular system, such as fibrosis and left ventricular hypertrophy, which make the hypertensive heart susceptible to SARS-CoV-2 [25]. The scientific and epidemiologic characteristics of COVID-19 have been repeatedly published, which show specific comorbidities associated with COVID-19 severity and mortality. It has been reported that the most common comorbidities are hypertension (30%), coronary heart disease (8%) and diabetes (19%) [57]. Another study reported that the most common comorbidities in COVID-19 patients with established acute respiratory distress syndrome were hypertension (27%), cardiovascular disease (6%) and diabetes (19%) [20]. In Italy, of 1591 ICU patients treated between February and March 2020, 49% had systemic hypertension [37]. Hypertension in older patients should be considered a clinical indicator of COVID-19 severity and mortality.

### Future recommendations

The current COVID-19 pandemic caused by SARS-CoV-2 is of global concern. Environmental factors such as contaminated air and smoking as well as comorbid conditions (e.g. DM, hypertension and fundamental cardiorespiratory illness) may likely increase the mortality rate of COVID-19. Therefore, special attention and effort are required to mitigate the risk of SARS-CoV-2 infection. Some recommendations follow that indicate how to fight COVID-19 and how to reduce the risk of this disease at both national and international levels.

- The novel CoV spreads among the community through respiratory droplets, contacts and fomites [19,126]. Therefore, it is important to implement restrictive measures at the social level to reduce virus spread. Proper handwashing on a regular basis, sneeze and cough sanitization and the use of PPE for HCWs who treat COVID-19 patients are probably helping to mitigate the spread of this contagious infection [127,128].
- Similarly, complete lockdowns and strict limitations on travel and social interactions may help control the COVID-19 transmission chain. This approach is often effective for the elderly and those with prolonged comorbid conditions [129].
- It is important to develop a policy for mitigating local transmission of the virus and for providing mass-scale separation and treatment. It is also crucial to develop well-thought-out approaches for distributed care, including home-based diagnosis and quarantine, arrangements with



medical technology companies and the strong leadership of local authorities in encouraging social distancing throughout the pandemic.

- Frontline HCWs represent are at high risk of COVID-19 infection, so it is important to support HCWs during outbreaks. It is essential to take immediate measures to train HCWs to safely manage the burden of treating this disease. This must include guidance and training on screening, infection prevention protocols and case management.
- It is important to pursue extra manufacturing capability and strengthen the existing PPE supply chain and other critical medical supplies. It is also crucial to evaluate the availability of essential PPE and its supply chain for national and international use during a COVID-19 respiratory outbreak.
- Important guidelines from the CDC and the US National Institutes of Health must be issued; experts use these venues to communicate to the public regularly and to diminish the fear, panic and spread of misinformation among the community, as well as to provide updates to the public on planning for COVID-19's spread worldwide.
- As COVID-19 becomes an international matter, it is important to share policies internationally and to improve coordination for mitigating its transmission.

## Conclusions

COVID-19 is an emerging disease that was first diagnosed in Wuhan, China, and has consequently spread throughout the world. HCWs are at a potential risk for COVID-19 mortality because they serve as the backbone of every healthcare system. Hypertension may be associated with an up to 2.5-fold higher risk of severe and lethal COVID-19, particularly among older people. Moreover, smokers, travellers, pregnant women and patients with severe health complications (heart disease, respiratory illness, diabetes and cancer) are also at a greater risk of COVID-19 morbidity and mortality. Proper handwashing, sneeze and cough sanitization, the use of PPE and complete lockdowns are probably helpful in mitigating the spread of this contagious infection. Future research is urgently needed to provide a better understanding of the basic pathophysiologic mechanisms of the association between COVID-19 and comorbidities.

## Conflict of interest

None declared.

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