# Emerging coronaviruses: first SARS, second MERS and third SARS-CoV-2. Epidemiological updates of COVID-19

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### **SUMMARY**

Since December 2019, the emergence of the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) infection has been reported unexpectedly in Wuhan, China, with staggering infection speed across China and around the world. To date, seven known strains of HCoVs belonging to four genera (i.e.,  $\alpha$ -,  $\beta$ –,  $\gamma$ , and  $\delta$ -CoV) have been recognized; the latest one has been identified as the SARS-CoV-2. Although the common transmission routes of SARS-CoV-2 is the respiratory tract, it seems that other routes such as the gastrointestinal tract may be effective for the entry of the virus in the body. Although there are no biological markers to predict the susceptibility of humans to COVID-19, several risk factors have been identified to predict the susceptibility of patients to COVID-19. Initial data revealed that males, pregnant women, elderly, and underlying conditions predispose patients

to higher morbidity or mortality and also might be at risk for a severe infection of COVID-19. There is a greater need to better understand the mechanisms and risk factors of transmission routes. To date, despite the whole world effort to review various aspects of SARS-CoV-2, including epidemiology, clinical manifestations, diagnosis, and treatment options, there are still gaps in the knowledge of this disease and many issues remain unclear. Therefore, there is an urgent need for update data on SARS-CoV-2. Here, this study provide the current epidemiological status (transmission routes and risk of transmission, possible origins and source, mortality and morbidity risk, and geographical distribution) of the SARS-CoV-2 in the world in 2020.

*Keywords:* Coronaviruses, COVID-19, SARS-CoV-2, pandemic.

### INTRODUCTION

Coronaviruses (CoVs) are a large family of single-stranded RNA (+ssRNA) viruses that were first discovered in the 1960s [1]. Some CoVs co-infect both humans and vertebrate animals such as camels, cattle, cats, and bats. Human coro-

naviruses (HCoVs) usually are associated with the common cold and more severe diseases such as pneumonia and bronchiolitis. In immunocompromised, elderly, and child patients, HCoVs can cause life-threatening pneumonia and bronchiolitis that in turn may also cause enteric and neurological diseases [2].

To date, seven known strains of HCoVs belonging to four genera (i.e.,  $\alpha$ –,  $\beta$ –,  $\gamma$ –, and  $\delta$ –CoV) have been recognized:

- 1) HCoV-NL63;
- 2) HCoV-229E (belonging to  $\alpha$ -CoVs);

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- 3) HCoV-OC43;
- 4) HCoV-HKU1 (belonging to β-CoVs);
- 5) Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV);
- 6) Middle East Respiratory Syndrome Coronavirus (MERS-CoV);
- 7) the latest one, which has been identified as the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [3, 4].

Among Betacoronavirus, MERS, SARS, and the new SARS-CoV-2 are considered as emerging zoonotic transmissions that have caused epidemics in humans. SARS-CoV was first reported from China in 2002-2003. MERS first emerged in September 2012 from a male Saudi Arabian patient in Saudi Arabia. In December 2019, the emergence of the SARS-CoV-2 infection was reported unexpectedly in Wuhan (China) with staggering speed across China and around the World. The World Health Organization (WHO) called the current infection outbreak caused by SARS-CoV-2: coronavirus disease 2019 (COVID-19) [5, 6].

So far, SARS-CoV-2 has affected more than 4,618,821 patients in 210 countries/area and has become a public health emergency of international concern. On March 11th, 2020, WHO declared COVID-19 as a pandemic. This is the first known pandemic caused by the emergence of a new coronavirus. Early studies indicated that most cases of infection were related to the seafood and wild animal markets and the majority of the earliest cases have been infected through zoonotic or environmental contacts and showing possible animal-to-human transmission. In recent weeks, it is now clear that human-to-human transmission of SARS-CoV-2 has been rising dramatically and has been confirmed through droplets or direct contact 17, 81.

After 5 months from the onset of the COVID-19 outbreak, this infection is still known as a public health concern with no vaccine or definite treatment and also with some unidentified epidemiological aspects related to it. Strategies to prevent COVID-19 depend on providing epidemiological information about this infection.

To date, despite the whole world's effort to review various aspects of SARS-CoV-2, including epidemiology, clinical manifestations, mortality and morbidity and diagnosis, there are still gaps in the knowledge of this disease and many issues remain unclear. Therefore, monitoring and period-

ical investigation of this emerging infection in an epidemiological study seems to be essential. The present study provide the current epidemiological status (i.e., possible origins and source, transmission routes and risk of transmission, mortality risk, potential risk factors, and geographical distribution) of the SARS-CoV-2 in the world in 2020.

### **■ TRANSMISSION ROUTES**

The unexpected pneumonia infection caused by SARS-CoV-2 has probably evolved from Wuhan to other provinces and countries. WHO declared a global health emergency over this global pneumonia outbreak on January 30th, 2020.

The contact with animals and the consumption of wild animals were suspected as the routes of disease origin. Therefore, the possible role of animals in COVID-19 infection most not be ignored [9]. Also, since the main symptoms of COVID-19 patients are fever and respiratory disorders, the spread of SARS-CoV-2 through food is improbable [10].

According to previous reports, the predominant transmission route of SARS-CoV-2 is a human-to-human transmission that includes contact transmission through contact with oral, nasal, and eye mucous membranes and direct or indirect transmission via cough, sneeze, and respiratory droplets [11]. Although the common transmission route of SARS-CoV-2 is the respiratory tract transmission, it seems that other routes such as unprotected eyes may be the effective route for the entry of the virus in the body.

Lu et al. suggested that exposure of unprotected eyes to SARS-CoV-2 could cause acute respiratory infection [11]. In this regard, Xia et al. reported that tears and conjunctival secretions of a patient were positive for SARS-CoV-2. Also, the sputum of a sample was detected positive for SARS-CoV-2 [12].

In another study, Wang *et al.* reported that saliva contains live viruses that may allow a person-to-person transmission, as a direct or indirect route of spread [13]. Interestingly, Rothe et al. also described that even contact with asymptomatic patients may transmit COVID-19 infection [14]. According to the Public Health Agency of Canada, the airborne transmission may occur under environments related to critical care and anesthesia clinicians. In experiences associated with

SARS outbreaks, there was the possibility of airborne transmission under certain circumstances. Wang et al. investigated the concern about the person-to-person transmission routes in dental clinics and hospitals [15]. Previous study in dental fields showed that many dental procedures produce droplets and aerosols, which are contaminated with the virus [5]. The transmission of SARS-CoV through droplet and aerosol are critical concerns in dental offices. Commonly, during dental practice, the patient's saliva, aerosol and droplet, and even blood are possible routes to virus transmission. Also, in close contact, the materials of patient, and the contaminated dental instruments or environmental surfaces may be considered as a possible route to the spread of SARS-CoV-2.

According to recent reports, SARS-CoV-2 RNA was identified in a feces specimen [7, 15]. These reports indicated that fecal-oral transmission may be considered as the route of spread [16]. One of the most important reasons for this phenomenon is that angiotensin-converting enzyme 2 (ACE2) protein, as a cell receptor for SARS-CoV-2, is highly expressed in the glandular cells of gastric, duodenal, and rectal epithelia. In this regard, Xiao et al. detected 39 (53.42%) stool samples positive for SARS-CoV-2 RNA. In another study on the SARS-CoV-2 shedding, 66.67% of patients were positive for SARS-CoV-2 RNA in stool specimens [16].

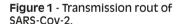
These findings suggested that fecal-oral transmission could be an additional route for transmission of SARS-CoV-2.

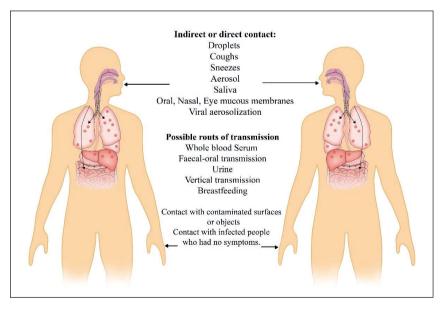
In a large study on 651 COVID-19 patients, 11.4% of them had gastrointestinal (GI) symptoms such as nausea, vomiting, and diarrhea. Taken together, the patients with COVID-19 without respiratory signs and fever presented a great tendency to show GI symptoms. Therefore, this point should be taken into account to control the further spread of the virus [18].

So far, SARS-CoV-2 nucleic acid has been detected in milk, blood, and urine. However, there has been no document on the transmission of the virus to humans through these routes [19, 20]. Moreover, some studies reported that none of the urine and serum samples were tested positive for SARS-CoV-2 RNA [21].

In an animal model study for SARS-CoV-2 virus transmission, SARS-CoV-2-infected animal shed virus in feces, saliva, nasal washes and urine up to 8 days post-infection [22]. Yuen et al. propounded the undeniable possibility of transmission of SARS-CoV-2 through sewage, waste, contaminated water, air condition system, and aerosols [23]. However, additional examinations are needed to investigate the role of these transmission routes in these cases [23].

To date, there has been no evidence on the occurrence of a human-to-animal transmission [24].





Moreover, there are no documents that pet animals can be the origin of SARS-CoV-2 for humans or other animals [24]. Different patterns of transmission route of SARS-CoV-2 human-to-human transmission are presented in Figure 1.

#### RISK FACTORS FOR TRANSMISSION

Since the transmission modes of SARS-CoV-2 is not yet entirely known, we investigated several new and important findings around the world. Commonly, several factors such as physical features, virological aspects (viral loading, location of virus receptor, etc.), environmental factors, and behavioral patterns can affect the transmission of viruses. In this regard, Cai et al. showed that asymptomatic infected people may spread SARS-CoV-2 through virus aerosolization and contact with contaminated objects and thus are considered as a carrier [25]. In a shopping mall survey in Wenzhou, COVID-19 cases probably were contaminant via asymptomatic. This significant finding is associated with the increased risk of disease transmission. In this regard, Rothe et al. showed the risk of transmission during the incubation period of asymptomatic patients [14].

Therefore, early detection and isolation of SARS-CoV-2 can be effective and even essential in reducing virus transmission. Accordingly, close and continuous monitoring in crowded places is critical, especially in asymptomatic or very mild symptomatic cases of COVID-19. Bi et al. surveyed 391 SARS-CoV-2 cases and 1286 cases with close contacts. According to their results, household members' contacts and those traveling with a coronavirus case are at higher risk of infection than other close contacts [26].

Moreover, Wang et al. indicated that saliva specimens of COVID-19 patients contained live viruses. Therefore, the transmission rate of the virus is high and may allow easy transmission via saliva. Hence, it can be suggested that the risk of transmission of SARS-CoV-2 via saliva directly or indirectly even among patients without respiratory symptoms is greater than other transmission routes.

So far, there are no strong documents on fecal-oral transmission and thus further studies are needed [12]. Recently, Xiao et al. provided evidence of gastrointestinal infection of SARS-CoV-2 and showed the risk of virus transmission via the fecal-oral route, which can be as a driver for SARS-CoV-2 transmission [18]. Consequently, concerning the approved and investigated transmission route of SARS-CoV-2, it seems that the risk of transmission of the virus is greater than what we think.

To date, no evidence of the vertical transmission of mother-to-infant has been reported. In this regard, several studies have investigated possible mother-to-infant transmission. For example, Zhu et al. analyzed the clinical characterization of 10 cases of neonates born to mothers with COVID-19 infection. According to their findings, although COVID-19 infection may have adverse effects on newborns, there is no sufficient evidence for the risk of vertical transmission of SARS-CoV-2. Moreover, Chen et al. found no evidence of vertical transmission in women with COVID-19 pneumonia in late pregnancy. These originals findings are in line with the vertical transmission of SARS-CoV and MERS-CoV, for which there was no supporting evidence. Therefore, it can be concluded that the risk of vertical transmission in pregnant women with COVID-19 is very low. However, this hypothesis needs to be further investigated.

### NOSOCOMIAL TRANSMISSION

Consistent with SARS-CoV and MERS-CoV, the nosocomial transmission is a severe problem in COVID-19 and even worse. Nosocomial transmission of COVID-19 is facilitated by mobile phones of health care workers and hospital equipment [27]. According to several studies, the nosocomial transmission has been a hallmark of COVID-19 infections. Analysis of data in the Hong Kong Special Administrative Region suggested that COVID-19 is not spread by an airborne route. Moreover, the results showed that nosocomial transmissions could be prevented through vigilant basic infection control measures, including hand and environmental hygiene, and wearing of surgical masks [28]. A retrospective study showed that a total of 1716 health workers were infected by the virus, accounting for 3.84% of total cases. This finding is consistent with the person-to-person transmission of this novel coronavirus in hospital settings [29]. In another study in the Zhongnan hospital of the Wuhan University, 29.0% (n=40) of medical staff involving with COVID-19 during hospitalization was reported

[19]. Therefore, the greatest risk for COVID-19 is transmission to healthcare workers. COVID-19 has been detected in a neonate born to a pregnant woman with COVID-19 infection 36h after birth at Wuhan Tongji Hospital. So, it is reasonable to assume that a newborn could be infected by COV-ID-19 and hence, newborns should be placed in separate rooms to avoid exposure to any source of infection [30]. In this regard, there is no evidence of perinatal infection of COVID-19 during pregnancy [31, 32].

### MORTALITY

During the 2002-2003 SARS-CoV epidemic, more than 8,000 people were infected, of which 774 died representing a mortality rate of 10%. Later, in 2012, MERS-CoV infected more than 857 cases with 334 deaths resulting in a mortality rate of 35%. At the end of 2019, the epidemic of COV-ID-19 occurred. This outbreak is expanding with remarkable morbidity and mortality in the last 4 months. As recorded by the WHO, by May 18th, 2020, there had been more than 4,618,821 confirmed cases and more than 31,2000 deaths due to COVID-19, with an average mortality of about 4.08% [33]. Therefore, it seems that the mortality rate of COVID-19 is higher than influenza, especially seasonal influenza. Although regarding the rapid spread of COVID-19, it is still too early to estimate the mortality rate, there are several reports on the mortality rate in different studied populations. Su Yu et al. reported 14-15% death in hospitalized COVID-19 patients [34]. Huang et al. and Wang et al. reported mortality rates of 14.6% [35] and 4.3% [13], respectively. Moreover, in a study conducted in China, the mortality of the 27 included patients infected by SARS-CoV-2 was 37%.

However, these mortality rates do not represent the actual death rate. The most important reason for this discrepancy is undetectable data on asymptomatic cases or patients with very mild symptoms that are not notified.

Overall, the mortality of COVID-19 is associated with underlying health conditions. Similar to an outbreak caused by SARS, several host factors may be associated with mortality in the COV-ID-19 outbreak including older age (>60 years), smoking history, pre-existing pneumonia, and significant comorbid illnesses (such as immunocompromised states, chronic heart, lung, and kidney disease, and diabetes mellitus) [36].

Accordingly, there is strong evidence to suggest that diabetes might be associated with mortality, while there is not sufficient evidence to display that hypertension might be associated with an increased risk of mortality [37]. Leung et al. suggested the possible role of cardiovascular, cerebrovascular, and pulmonary disease at a higher risk of mortality [37, 38]. Peng et al. concluded that fulminant inflammation, lactic acid accumulation, and thrombotic events are associated with a higher risk of mortality in COVID-19 patients [39]. According to previous studies, acute respiratory distress syndrome is the major cause of death in patients with COVID-19. This syndrome is the major indication for transferring patients to the Intensive Care Unit (ICU). Hence, the delay of hospital admission of patients with COVID-19 is significantly associated with a higher mortality rate [37, 40]. Leung et al. showed that although 67.4% of all death cases were male, gender was not associated with mortality [37].

Fever and cough are the most frequent symptoms associated with death. However, there is not sufficient documentation to show the association of this fatality with fever [37].

In a hospital-based case-cohort study, comorbidities, older age, lower oxygenation index, the serum urea nitrogen, AST/ALT ratio, TBIL, LDH, and several markers of extrapulmonary organ injuries were positively associated with death risk of COVID-19 patients [41]. In this study, among dead cases, 80% had at least one of comorbidities including hepatic disease, diabetes, cardiac disease, hypertension, and chronic pulmonary disease. There is a significant correlation between comorbidities and elevated death risk of COVID-19 patients [41].

In a prospective cohort study, four potential risk factors including age ≥65 years, preexisting concurrent cardiovascular or cerebrovascular diseases, cardiac troponin I ≥0.05 ng/mL and CD3+ CD8+ T cells ≤75 cell/µL were identified as predictors for mortality of COVID-19 patients with pneumonia [42].

### MORBIDITY

Although there are no biological markers to predict the susceptibility of humans to COVID-19, several risk factors have been identified to predict the susceptibility of patients to COVID-19.

Initial data revealed that males, pregnant women, elderly, and underlying conditions are often associated with higher morbidity and mortality and also might be at risk for a severe infection of COV-ID-19 [34, 35, 43]. The most predominant related comorbidities are old age, smoking, diabetes, and pulmonary disease.

Previous reports have found that the disease tends to develop quicker in elderly male people [44]. In this regard, in a retrospective cohort study, Shi et al. investigated host risk factors associated with severe COVID-19. According to their findings, among 487 studied patients, elder age, male, and presence of hypertension are independently related to severe disease at admission. In comparison, COVID-19 is much more predominant among males, with a male to female ratio of 2.7:1 [1]. Moreover, the concurrency of hypertension, diabetes, cardiovascular diseases, and malignancy was higher among severe cases at admission [45].

In a meta-regression study, it was reported that hypertension is related to ~2.5-fold-increased risk of both increased mortality and severity [46]. Moreover, hypertension should be accounted for as a clinical predictor of COVID-19 severity among older individuals [46].

Some studies have demonstrated that smoker cases are related to higher expression and the potential of upregulating the ACE2, which is known as the receptor of SARS-CoV- 2 and may be considered as a risk factor [47]. In this regard, Zhang et al. found that there was an association between smoking and the severity of COVID-19 [48]. Moreover, Liu et al. reported that in patients with the progression of COVID-19 pneumonia, a history of smoking was significantly higher in comparison with improvement patients. They suggested that smoking may be related to disease progression [49]. In a recent systematic review, it was concluded that "smoking is most likely associated factor with negative progression and adverse outcomes of COVID-19" [50].

However, according to the literature review, there are no reliable and strong data to support that smoking is a predisposing factor in men or another subgroup for infection with SARS-CoV-2 [51]. Although several studies revealed the clinical characteristics of pregnant women with COV-

ID-19 infection are compatible with those reported for non-pregnant adults, some studies described that clinical characteristics of pregnant women are atypical [52].

Liu et al. investigated clinical and CT imaging features of the COVID-19 among pregnant women. They showed that the clinical symptoms of pregnant women were atypical and they had high complication rates compared with the non-pregnant women [52].

In a systematic review, the clinical symptoms and maternal and perinatal outcomes of COVID-19 were assessed during pregnancy. Among 108 survey pregnant cases, most mothers were discharged without any main complications; however, severe maternal morbidity as a result of COV-ID-19 and perinatal deaths were reported, as well [53].

Accordingly, despite the lack of any maternal deaths, one intrauterine death and one neonatal death were observed. Therefore, there is evidence on the possibility of severe maternal morbidity requiring ICU admission and perinatal death with COVID-19 infection in pregnancy [53].

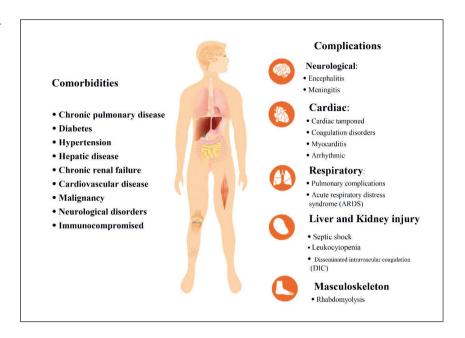
Studies have shown that children are less affected than adults and clinical attack rates in the 0-19 age group are low and usually present as a mild disease [52]. Reports suggest that children are infected from the household transmission of adults. However, neonates and elderly people need more attention, due to their effete immune system and chronic underlying diseases.

Recently, it has been reported that blood group A had a significantly higher risk for COVID-19. Zhao et al. investigated the relationship between the blood group and the COVID-19 among 2.173 patients and compared them with normal patients in Wuhan and Shenzhen, China. The results showed that the proportion of blood group A in COVID-19 patients was significantly higher such that it is accounted as a risk factor [54].

Devarajan et al. studied the single-nucleotide polymorphism rs12252-C/C in the gene IFITM3 as a factor associated with severe influenza in patients with COVID-19. According to their results, this polymorphism may be a risk factor in COVID-19 patients. However, they suggested that further examination of the IFITM3-rs12252-C/C allele in a large population is needed.

Among the host factor, the platelet count can be a simple and commonly available biomarker in as-

Figure 2 - Comorbidity and complication related to COVID-19.



sociation with disease severity. In the SARS outbreak, thrombocytopenia was recognized as an important risk factor for mortality.

In a meta-analysis, Lippi et al. showed that the level of platelet was remarkably lower in patients with more severe COVID-19. Therefore, thrombocytopenia could be a clinical indicator and is also considered as a risk for severe disease and mortality in patients with COVID-19 [55]. The more prevalent comorbidity and complication related to COVID-19 are presented in Figure 2.

# ■ POSSIBLE ORIGINS, SOURCES AND RESERVOIRS

The disease caused by SARS-CoV-2 in humans is a public health emergency of international concern. However, so far, the origin and the source of the causative virus and its intermediate host of the virus is yet to be fully determined [2].

CoVs of bat origin have caused tree pandemics in 21<sup>th</sup> century. SARS-CoV, MERS-CoV and SARS-CoV-2, all three originated from bats [11]. Previous studies revealed that the SARS-CoV spreading from bats to palm civets to humans and the MERS-CoV spreading from bats to camels to humans and also like many other coronaviruses, the SARS-CoV-2 may have been transmitted to humans by an intermediate animal host. To date, a

large number of studies suggested, on the basis of phylogenomic analysis of the recently released genomic data of SARS-CoV-2 that the human was the most similar to Bat coronavirus isolates such as BaT-CoV RaTG13 with 96.2% identical in complete genome sequence [3, 56]. Their findings suggesting that the bats' CoV and the human SARS-CoV-2 share a recent common ancestor and SARS-CoV-2 might be transmitted from bats via unknown intermediate animal hosts (such as pangolins) to humans. According to the report, the SARS-CoV-2 virus, which is responsible for the current outbreak of COVID-19, did not come directly from pangolins. However, due to incomplete sequence of pangolin coronavirus published in GenBank, they cannot exclude that other pangolins from China may contain coronaviruses that exhibit greater similarity to the SARS-CoV-2 [57, 58]. Summary of the possible reservoir, intermediate and target hosts for SARS-CoV, MERS-CoV, and SARS-CoV-2 is presented in Figure 3.

SARS-CoV-2 binds to ACE2 with high affinity as an entry receptor to infect humans. However, some amino acid residues are different in the receptor-binding domain (RBD) of SARS-CoV compared to SARS-CoV-2. It seems that humans are infected with the virus directly from intermediate animal hosts via contact [59-61]. It is clear now that the animal may serve as a key interme-

diate host for the recombination and evolution of SARS-CoV-2. Nevertheless, further investigation and analysis may be needed to find the intermediate hosts and other sources.

Frequent host-shifting cases likely characterize coronaviruses, whether they are animal-to-animal, animal-to-human (zoonosis), or human-to-animal (reverse zoonosis). Many studies speculated that snake is a possible reservoir for SARS-CoV-2 but it was dismissed by other scholars [61-63]. In other more advanced molecular analysis and virological studies, it was shown that bats are the primary reservoir of SARS-CoV and MERS-CoV [63-65]. A similar study suggests that pangolin species are natural reservoirs of SARS-CoV-2like CoVs, but there is no conclusive evidence that SARS-CoV-2 has a specific wildlife host as a virus reservoir [62, 66].

### INCUBATION PERIOD

The incubation period of an infectious disease is the time interval between the exposures to an infectious agent until signs and symptoms of the disease appear. The incubation period of a disease can widely vary from one person to another. The incubation period data are used in estimating the size of the transmission potential and the epidemic. These data also help assess the effectiveness of entry screening and contact tracing. The reported estimate of the novel coronavirus incubation time is based on limited case data. Using data from many public reports, the incubation period for the novel coronavirus is estimated to be in the range of 2-14 days; however, two cases with an incubation period of 19 and 27 days have been reported [67, 68]. The median incubation period is 6 (interquartile range of 3 to 8) days and also the median time from the first visit to a doctor to confirm the diagnosis is about 1 (interquartile range of 1 to 2) day [69, 70]. Besides, the median time from onset of symptoms to dyspnea was 5 days, hospitalization was 7 days, and acute respiratory distress syndrome (ARDS) was 8 days [71].

### GLOBAL DISTRIBUTION

WHO has described four levels of COVID-19 transmission with varying social measures and public health based on the evolution of the COV-ID-19 pandemic in countries or local areas with:

- 1) no cases reported;
- 2) sporadic cases;
- 3) clusters of cases (grouped in time and place);
- 4) community transmission [72].

On 29 December 2019, the first four cases of COV-ID-19 were reported in Wuhan City, Hubei Province, China, where the outbreak was believed to have begun at a wildlife market. Immediately after, it quickly spread to other parts of the world. Due to the lack of drugs against COVID-19, the

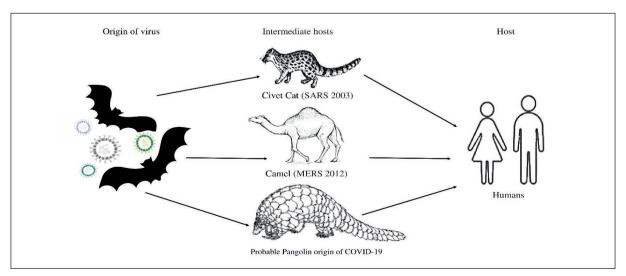
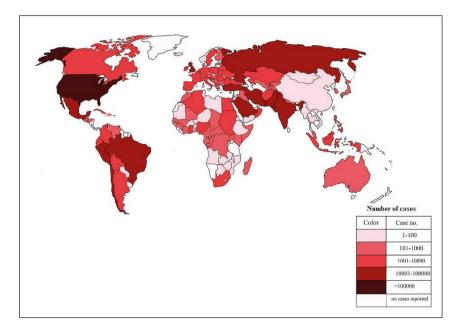


Figure 3 - Summary of potential interspecies transmission cycle of SARS-CoV, MERS-CoV, and SARS-CoV-2.

Figure 4 - The global distribution of COVID-19 patients (18 May 2020).



disease spreads rapidly and the fatality rate is relatively high [73]. In China, 82,052 were confirmed as cases and 3,339 were total deaths in 34 provinces as of 12:25, 13 April 2020. In the early days, the highest rate of spread and mortality was in mainland China where the outbreak began. But, the vast majority of cases and deaths of coronavirus are now being reported in the United States, which is currently a global hotspot, Spain, Italy, and France [74].

Studies based on modeling revealed that the transmissibility of SARS-CoV-2 was higher than the MERS in the Middle East countries, similar to SARS, but lower than MERS in the Republic of Korea [75]. The latest update in April, the global distribution of COVID-19 patients is summarized in Figure 4.

### CONCLUSIONS

This study is a picture of the current research on epidemiology in response to the outbreak of COVID-19. In this review, we summarized the latest reports of transmission rout and risk of transmission, mortality and morbidity risk factor and clinical features caused by SARS-CoV-2 infection. However, further research on all aspects of the disease is needed to better understand the infection.

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### **Conflicts of Interest**

None

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