



Review

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2):
Emergence, history, basic and clinical aspects

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ABSTRACT

In late December 2019, the world woke to a reality of a pandemic of Coronavirus Disease (COVID-19), elicited by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which belongs to a group of β -coronavirus. The potential to cause life-threatening respiratory failure and rapid transmission puts COVID-19 in the list of Public Health Emergency of International Concern (PHEIC). In the last two decades, this is the 3rd deadliest Coronavirus pandemic, following SARS which lasted between 2002 and 2003 and Middle East Respiratory Syndrome (MERS) from 2012 till date. Globally and as of April 23rd 2020, COVID-19 has affected 2,544,792 individuals in over 200 countries, causing 175,694 fatalities. While the SARS-CoV-2 originated in China with 84,302 confirmed cases and 4642 deaths as at the time of writing this review, the rapid transmission of SARS-CoV-2 has resulted in exponential increase in the number of cases outside of China to about 10 times the report case and death in mainland China. SARS-CoV-2 is suspected to be zoonotic in nature as genetic studies have shown sequence similarity to viruses originating from bats. Extreme precautionary measures, such as curfew, shutting of borders and quarantining of individuals suspected to be infected have been instituted with immediate effect; however, due to individuals that are asymptomatic, uncontrolled human-to-human transmission has resulted in exponential infection rate and numerous loss of lives even with this lockdown measures. This review article summarizes the developing situation surrounding the SARS-CoV-2 pandemic with respect to its epidemiology, unique genomic structure, possible origins, transmission, pathogenesis, comparison with other deadly species of Coronaviruses (CoV) and emerging treatment strategies built on informed literature.

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1. Introduction

In late December 2019, the People's Republic of China (Wuhan City of Hubei Province) evidenced pneumonia cases of unknown etiology (Riou and Althaus, 2020), which was later confirmed as the 2019 novel Coronavirus (2019-nCoV) by Chinese authorities on 7th of January 2020 (WHO, 2020b). The 2019-nCoV took the entire China by storm and transcended international borders in no time, reaching the worldwide tally of 2,544,792 confirmed cases and 175,694 deaths, reported as per World Health Organization (WHO) Situation Report-94 of 23rd of April 2020 (WHO, 2020). Ever since, the entire world has been caught off guard by the unsuspecting increase in the number of new cases due to the exponential increase in the rate of transmission of 2019-nCoV, now formally referred to as SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) by the International Committee on Taxonomy of Viruses, the causative agent of Coronavirus Disease 2019 (COVID-19) (Ceraolo and Giorgi, 2020).

Upon declaration of SARS-CoV-2 as a Public Health Emergency of International Concern (PHEIC) by WHO and the mounting evolutionary data surrounding the SARS-CoV-2 pandemic, more than 1000 scientific papers have been documented in PubMed alone. Perhaps, extensive research is the ideal way forward, since this is what led to sequencing of the virus genome, development of COVID-19 diagnostic kit, characterization of the disease and possible effective development of vaccine in near future, in an attempt to eradicate the continued infection of SARS-CoV-2. Here, we comprehensively review the developing phenomenon of SARS-CoV-2 pandemic with respects to its epidemiological landscape, unique genomic structure, possible origins, transmission, pathogenesis, comparison with other deadly species of Coronaviruses (CoV) and informed deductions on possible treatment built on evidence from the literature. As a matter of fact, this review article will also address the key precautionary measures taken across the world to halt the outbreak of SARS-CoV-2.

2. Epidemiological landscape

Based on the preliminary findings from the outbreak of SARS-CoV-2 in China around 10th to 24th of January 2020, the epidemiological trend of a snowballing incidence mainly followed the exponential growth was borne. The mean reproduction number (R_0) which is the anticipated number of secondary infection cases triggered by a single infectious case in at-risk population, was projected to fall between 2.24 [95% confidence interval (CI) 1.96–2.55] and 3.58 (95% CI 2.89–4.39), indicating a two to eight times greater infectious rate associated with SARS-CoV-2 (Bai et al., 2020; Zhang et al., 2020b; Zhao et al., 2020). According to WHO situation reports, by 23rd of April 2020, the SARS-CoV-2 pandemic has affected 2,544,792 individuals (confirmed cases) and claimed 175,694 lives globally (WHO, 2020). The current figures of SARS-CoV-2 pandemic are clearly in agreement with the pattern suggested through initial data by calculating the mean R_0 . Obviously, this unprecedented outbreak created way more chaos than the infections caused by the former strains of Coronaviruses. Severe Acute Respiratory Syndrome (SARS) resulted in 8096 morbidities and 774 mortalities in 2003 and the Middle East Respiratory Syndrome (MERS) resulted in 2494 cases and 858 deaths since 2013 till present (Lu et al., 2020c; Wang et al., 2020c; Wu and McGoogan, 2020).

The SARS-CoV-2 has been transmitted to more than 200 countries thus far with dreadful impact in almost all affected regions of the world defined by the WHO (Fig. 1). Moreover, 712 COVID-19 cases have also been confirmed in International Conveyance (Diamond Princess Cruise Ship). Within China, the province of Hubei suffered the most with 67,794 COVID-19 cases, followed by Guangdong ($n = 1357$), Henan ($n = 1273$), Zhejiang ($n = 1231$) and Hunan ($n = 1018$) (WHO, 2020c, d). Till 17th of February 2020, there was steep rise in the number of COVID cases in China. However, a reduction in the rate of new cases began to decline resulting in a plateau of the curve for the total number of cases. Outside of mainland China, the situation is much worse by the fact the COVID-9 cases are proliferating at a very extraordinary speed (Figs. 2 and 3) (WHO, 2020).

3. Possible origins of SARS-CoV-2

In late December 2019, a group of novel pneumonia cases (now called COVID-19) were reported by the Wuhan Municipal Health Commission, China. It was suspected that the first 27 COVID-19 cases originated in the Southern China Animal and Seafood Wholesale Market in Wuhan, Hubei Province. The early COVID-19 cases were either proprietors of the shop or individuals who had visited the market. It is a huge market of 50,000 square meters that deals in sales of fresh meat, seafood and a wide range of live wild animals of different types and species caged in close proximity for human consumption (Tan et al., 2020; Zhu et al., 2020).

The SARS-CoV-2 belongs to a group of β -coronavirus, which is an enveloped positive-sense RNA virus of subgenus sarbecovirus (Subfamily: Orthocoronavirinae) (Zhu et al., 2020). Coronaviruses are classified into four genera; α -CoV, β -CoV, γ -CoV and δ -CoV. The α -CoV and β -CoV are capable of infecting mammals, whereas γ -CoV and δ -CoV have a tendency to infect birds. Formerly, six Coronaviruses have been recognized as causative agent for

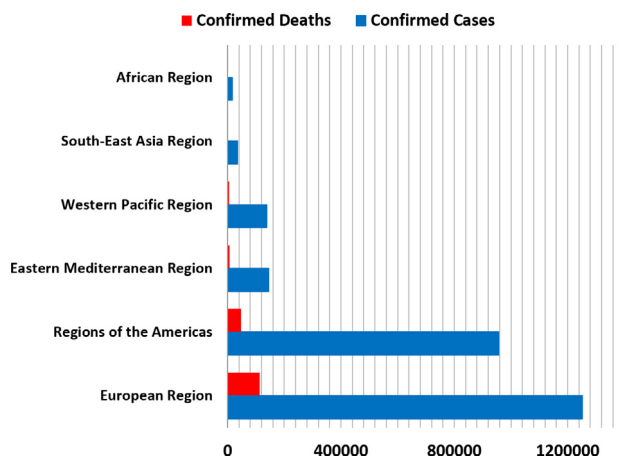


Fig. 1. Regional Distribution of COVID-19 (WHO Situation Report-94, as of 23rd of April 2020).

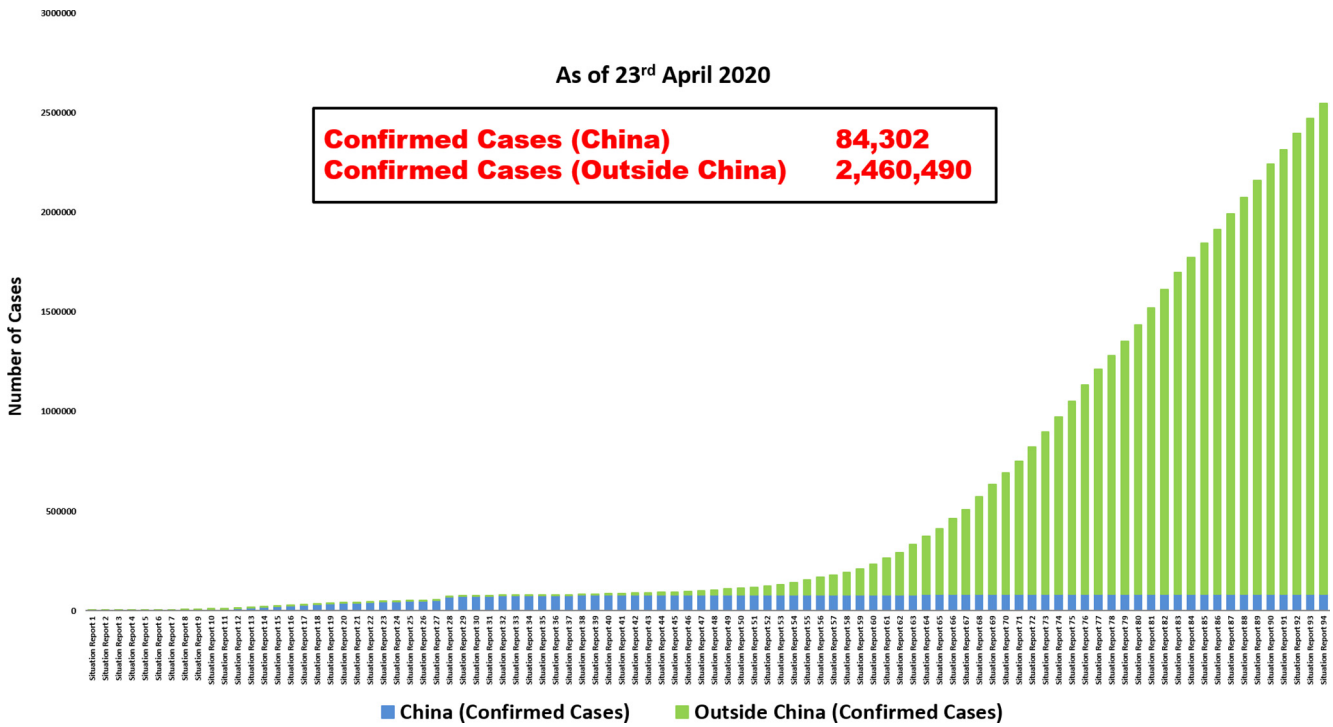


Fig. 2. Epidemiological Trend of Confirmed COVID-19 Cases in China and Outside China [WHO Situation Reports (1–94) as of 23rd of April 2020].

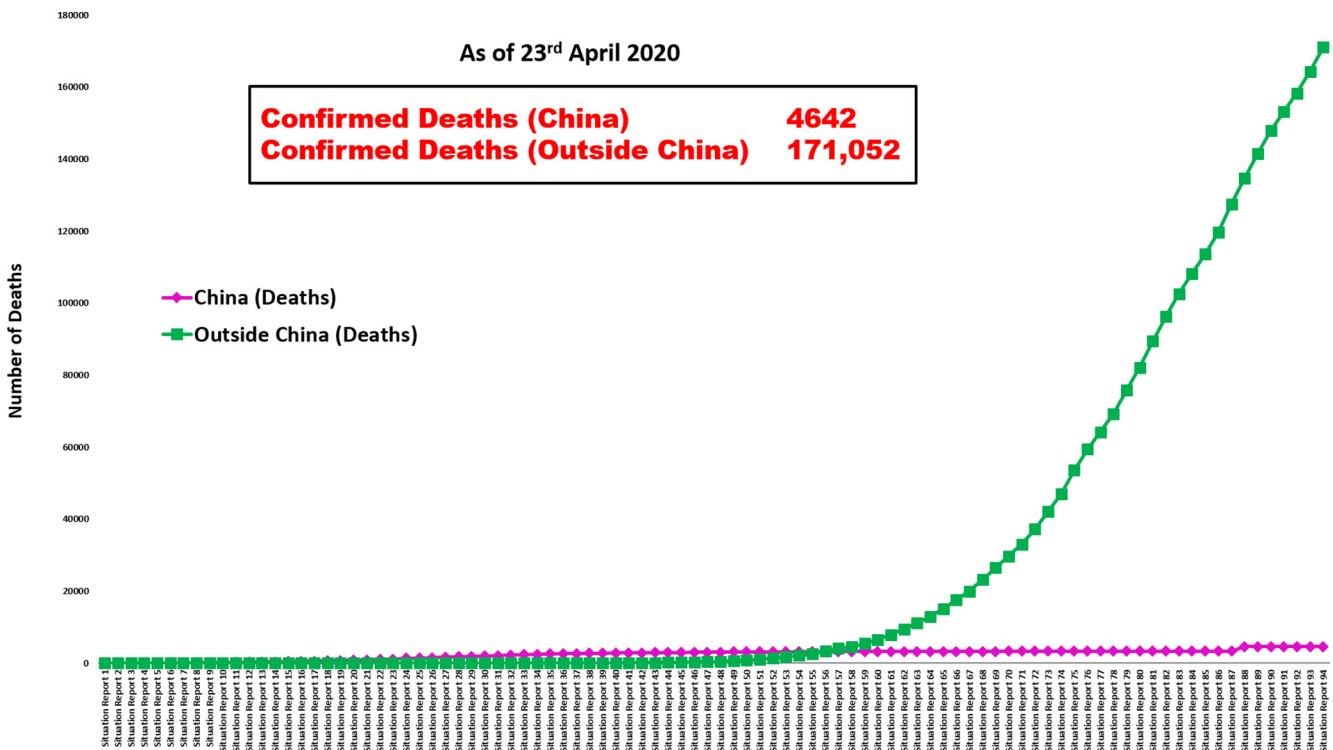


Fig. 3. Epidemiological Curve of Confirmed Deaths due to COVID-19 in China and Outside China [WHO Situation Reports (1–94) as of 23rd of April 2020].

infection in humans. Among them, the α -CoV strains (HCoV-229E and HCoV-NL63) and β -CoV strains (HCoV-HKU1 and HCoV-OC43) possess low infectivity and produce only mild respiratory infection akin to the common cold. The two much known β -CoV of which SARS-CoV and MERS-CoV belong, can cause severe and possibly life-threatening respiratory infection (Yin and

Wunderink, 2018). It is confirmed that 96.2% of the genomic sequence of SARS-CoV-2 is identical to bat CoV RaTG13. Earlier reports have documented this also in *Rhinolophus affinis*, Bat-SL-CoVZC21 and then Bat-SL-CoVZC45, which indicates a common ancestry and that the SARS-CoV-2 originated from Chinese chrysanthemum bat. The virus also shares 79.5% of the genome

sequence with SARS-CoV. Based on available evidence of genome sequencing and evolutionary analysis, bat has been suggested as the natural reservoir and origin of the SARS-CoV-2. Bats may transmit the virus to humans via anonymous intermediate hosts (Guo et al., 2020). Lately, pangolin has also been suggested to play a role in the viral infection as an intermediate host because about 99% of sequence similarity exist between pangolin species (>1000 samples metagenomic data) and SARS-CoV-2 (Guo et al., 2020).

4. Mode of transmission

Coronaviruses can easily move across species (Guo et al., 2020). The major component of Coronavirus transmission is the Spike glycoprotein S1 that firmly binds to Angiotensin Converting Enzyme 2 (ACE2) receptor and enters the host cell (Lu et al., 2015). Most importantly, Coronavirus gateway mainly depends on ACE2 and transmembrane protease/serine subfamily member 2 (TMPRSS2) cleavages, specifically in airway and alveolar areas. A handful of studies previously explained the mutant nature of these proteins (Shereen et al., 2020). The Spike glycoprotein S1 endured significant evolution during the earlier Coronavirus outbreak (Li, 2016). The protein showed high positive selection in both intraspecies and interspecies transmissions (Song et al., 2005; Woo et al., 2009; Zhang et al., 2006). Substantial variability in the protein was reported in human and civet isolates (Song et al., 2005). The SARS Spike proteins can identify ACE2 receptors in civet, mouse, bat and raccoon dog, highlighting the ease of SARS-CoV transmission across species (Hou et al., 2010; Sheahan et al., 2008; Xu et al., 2009). The high genetic variability between Coronaviruses across the species enhances the risk of interspecies spread (Salata et al., 2020).

The first few COVID-19 patients affected with SARS-CoV-2 in Wuhan were linked to a wholesale seafood market exposure, signifying the animal-to-human classical transmission. Later, a huge number of COVID-19 patients who supposedly did not have prior association with the wet animal wholesale and seafood markets were reported, indicating the development of human-to-human or communal spread (Chan et al., 2020; Huang et al., 2020a; Lu et al., 2020b; Nishiura et al., 2020). The SARS-CoV-2 is appeared to be disseminated among humans through respiratory droplets while coughing and/or sneezing. Transmission through droplet can take place when a COVID-19 person coughs or sneezes, as a result of which SARS-CoV-2 containing droplets are pushed up to 3 feet (Guo et al., 2020). These droplets then can be collected at the mucous membranes of the eyes, nose or mouth of the adjacent person. A recent study reported that ocular surface does have the potential to carry SARS-CoV-2 and therefore can transmit the infection (Lu et al., 2020a). Other means of SARS-CoV-2 spread include handshaking with infected person, contact with an object/surface containing virus, repeated touching of the face (eyes, nose or mouth) or exposure to excreta of infected patient. Another recently confirmed mode of transmission is "hidden transmission", defined as the unintentional spread of SARS-CoV-2 by asymptomatic virus carriers to close contacts (Chan et al., 2020).

5. Dynamics of SARS-CoV-2 infection (COVID-19)

The disease produced by SARS-CoV-2, originated in China, was termed as COVID-19 (a respiratory disease). The clinical presentation of COVID-19 is highly variable and may not manifest as in asymptomatic virus carrier, a form with Acute Respiratory Disease (ARD) and typical pneumonia of protean severity. Earlier reports suggest that asymptomatic patients whom show no symptoms of COVID-19, such as fever, cough and sneezing, and no chest radiograph abnormalities were spotted through positive viral nucleic

acid testing (Bai et al., 2020; Team, 2020). The person-to-person transmission of COVID-19 by asymptomatic SARS-CoV-2 carriers has been widely documented in the literature (Bai et al., 2020; Chan et al., 2020; Liu et al., 2020; Rothe et al., 2020). In contrast, laboratory-diagnosed COVID-19 patients had respiratory symptoms of ARD; nonetheless, their chest computed tomography (CT) was not remarkable for pneumonia signs (Guan et al., 2020). Finally, COVID-19 patients with pneumonia presented with both respiratory symptoms and chest abnormalities consistent with pneumonia. This class is indicative of severe pneumonia (respiratory rate ≥ 30 /minute, PaO₂/FiO₂ ≤ 300 mmHg, or SpO₂ $\leq 93\%$, and a grave respiratory complication such as respiratory failure needing mechanical ventilation, shock, or permanent end-organ damage necessitating management in Intensive Care Unit (ICU) (Team, 2020).

6. High-risk population

The exact risk factors for COVID-19 are not yet established. However, several studies have reported that a substantial percentage of COVID-19 occurrence are in patients who had underlying comorbidities (Huang et al., 2020a; Team, 2020; Wang et al., 2020a; Guan et al., 2020). For instance, it was demonstrated that 50.5% of COVID-19 patients had chronic health conditions, which included cerebrovascular and cardiovascular diseases (Wang et al., 2020a). Guan et al (2020) reported at least one comorbid condition among 23.2% of the COVID-19 cases. Among coexisting diseases, Hypertension was the most frequent illness (14.9%), followed by diabetes mellitus (7.4%) (Guan et al., 2020). Likewise, a report from China Centre for Disease Control (CDC) Weekly also revealed hypertension as the most prevalent underlying health condition (12.8%), followed by diabetes mellitus (5.3%) and cardiovascular disease (4.2%) in COVID-19 patients (Team, 2020). Besides, COVID-19 severity were significantly associated with presence of coexisting diseases in comparison with those having non-severe COVID-19 (37.6% versus 20.5%, $P < 0.001$) (Guan et al., 2020). In agreement with this, other reports also stated similar trend in their study of 138 COVID-19 patients. They found that 46.4% of the COVID-19 cases had simultaneously other health conditions, and in fact ICU cases were more prone to have underlying comorbidities than non-ICU cases (72.2% versus 37.3%, $P < 0.001$) (Guan et al., 2020). The earlier deaths reported due to COVID-19 have also been attributed to old age, perhaps owing to immune suppression that allows virus to reproduce at much higher rate (Guan et al., 2020; Wu et al., 2020b).

7. Genomic configuration of SARS-CoV-2 and viral factors

While SARS-CoV (27.9 kb) and MERS-CoV (30.1 kb) both have positive-sense RNA genetic material (de Wit et al., 2016), the sequencing of whole genome of Wuhan-Hu-1 coronavirus (WHCV), one important strain of SARS-CoV-2, isolated from the first COVID-19 patient was 29.9 kilo base (kb) (Wu et al., 2020b). Coronaviruses' genomes possess highly variable open reading frames (ORFs) (Song et al., 2019). The first ORF (ORF1a/b) contains two-thirds of RNA and encodes two polyproteins; pp1a and pp1ab, and also translates 16 non-structural proteins (NSP). On the other hand, the residual ORFs codes for structural and accessory proteins. The remaining of the genome translates four critical structural proteins, which are small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein and spike (S) glycoprotein, including a number of accessory proteins that suppress host's innate immune response (Cui et al., 2019) (Fig. 4). A study by Wu et al. (2020a,b) lately conducted in-depth meta-transcriptomic sequencing analysis on WHCV, which revealed 16 NSP (Wu et al., 2020a). The WHCV

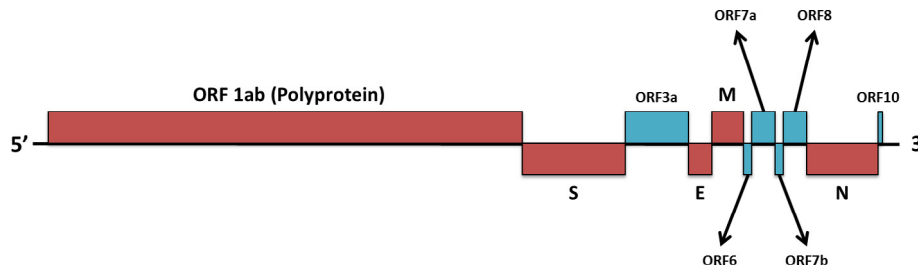


Fig. 4. A diagram showing the genomic structure of the SARS-CoV-2 (COVID-19). Structural Proteins in Maroon (S = Spike, E = Envelope, M = Membrane, and N = Nucleocapsid) and Accessory Proteins in Aqua (ORFs = Open Reading Frames).

also shows certain phylogenetic and genomic resemblance to SARS-CoV, predominantly in the gene encoding the S-glycoprotein and receptor-binding domain (RBD), signifying their competence for human-to-human transmission. With regards to the whole genome sequencing, SARS-CoV-2 is very similar to the SARS-like bat Coronaviruses in contrast to the known genomes of SARS-CoV and MERS-CoV which are of non-bat ancestry. In addition, most of the encoded proteins by genome of SARS-CoV-2 are comparable to SARS-CoV, however, few variances also exist. From proteomics perspective, no substitutions of amino acid were present in envelope, NSP7, NSP13, matrix, or other accessory proteins such as p6 and 8b, excluding spike protein, NSP2 and NSP3 (Wu et al., 2020a). Angeletti et al. (2020) highlighted that NSP2 and NSP3 mutation might play an important role in infective potential and viral differentiation processes of SARS-CoV-2. This drove scientists to probe the host tropism and transmission differences between SARS-CoV-2 and SARS-CoV, and carry out more research to identify the possible drug targets (Angeletti et al., 2020). Zhang et al. (2020a,b) also found mutations in the SARS-CoV-2 genome of different patients from several provinces of China (Zhang et al., 2020a). Tang et al. (2020) performed population-based genetic analyses on 103 genomes of SARS-CoV-2. They categorized two common types; L type (~70%) and S type (~30%) of SARS-CoV-2. The strains in L type of SARS-CoV-2 which is cultivated from the S type are far more hostile and transmissible (Tang et al., 2020).

8. Pathogenesis and viral replication

The precise mechanism by which SARS-CoV-2 ensues COVID-19 still remains to be elucidated. However, a few findings that could contribute to the pathogenicity have been suggested. Globally, the increasing fatalities in recent outbreak of SARS-CoV-2 can be attributed to severity of symptoms in COVID-19 patients. It was demonstrated that COVID-19 patients are presented with elevated levels of leukocytes, anomalous respiratory manifestations and high plasma pro-inflammatory cytokines (Rothan and Byrareddy, 2020). A case report found high grade fever (39.0 °C) in previous 5 days accompanied with cough and rough breathing sounds in both lungs of COVID-19 patient. Real-time polymerase chain reaction (RT-PCR) of DNA extracted from patients' sputum sample established COVID-19 diagnosis. Contrary to typical infections, the laboratory findings indicated leukopenia (2.91×10^9 cells/L, of them 70% were neutrophils). Moreover, a blood C-reactive protein (CRP) was notably higher (16.16 mg/L) than the usual range (0–10 mg/L). D-dimer and erythrocyte sedimentation rate (ESR) were also raised in these patients (Zhou et al., 2020). A study by Huang and colleagues (2020) reported that the primary pathogenic mechanism of COVID-19 infection to cause respiratory system insult is RNAemia, severe pneumonia, incidence of ground-glass opacities and acute cardiac injury. The study also found significantly elevated blood levels of chemokines and cytokines in COVID-19 patients, which includes IL-7, IL-8, IL-9, IL-10, IL1RA,

IL1- β , GCSF, GMCSF, basic FGF2, IP10, MCP1, MIP1 α , MIP1 β , IFN γ , TNF α , PDGFB and VEGFA. COVID-19 patients admitted in ICU displayed raised pro-inflammatory cytokines that are associated with severity of disease; IL-2, IL-7, IL-10, IP10, MCP1, MIP1 α , GCSF and TNF α (Huang et al., 2020b).

Angiotensin Converting Enzyme-2 (ACE2), which is present in the human's lower respiratory tract, is the well-known receptor utilized by SARS-CoV (Guo et al., 2020) and controls both human-to-human and cross-species transmission (Huang et al., 2020b). Zhou et al. (2020) confirmed through the bronchoalveolar lavage fluid (BALF) of a COVID-19 case patient that the SARS-CoV-2 also utilizes the ACE2 cellular receptor (Zhou et al., 2020). The S-glycoprotein of the Coronavirus can bind to the ACE2 receptor of the human respiratory cells (Tortorici and Veesler, 2019). The S-glycoprotein has two subunits; S1 and S2 (Zhang et al., 2014). While S1 regulates the cellular tropism, the virus and host range, S2 facilitates virus and cell membrane fusion through tandem domains; heptad repeats 1 (HR1) (Ji et al., 2020) and HR2 (Yu et al., 2020). Membrane fusion results in release of the viral RNA into the cytoplasm and the RNA (uncoated) encode two polyproteins; pp1a and pp1ab (de Wilde et al., 2018), which translate the NSP sequence, and collectively make replication-transcription complex (RTC) in double-layered vesicle (Sawicki and Sawicki, 2005). RTC continuously replicates and form a network of subgenomic RNAs, which translates structural and accessory proteins (Hussain et al., 2005). These envelope glycoproteins, nucleocapsid proteins and new genomic RNA amalgamate together to produce virus particles. Finally, the vesicles containing virion fuse with the cell membrane to discharge the new viruses. Since SARS-CoV-2 S-glycoprotein and ACE2 receptor binding is necessary for the entry of the virus, virus-receptor drug target research is underway.

9. Relationship with SARS-CoV and MERS coronaviruses

Recent COVID-19 pandemic from SARS-CoV-2 can be compared with the two previous outbreaks of severe respiratory infections; SARS (2002–2003) and MERS (2012–till present). SARS-CoV, the causative organism of SARS, originated in the market of Guangdong Province, China from the bats through palm civets (zoonotic transmission). MERS (MERS-CoV) was also found to emerge through zoonosis from bats through dromedary camels in Saudi Arabia. Interestingly, symptoms of SARS-CoV, MERS-CoV and SARS-CoV-2 frequently manifest as high grade fever, cough and sneezing, and subsequently severe respiratory tract infection with poor prognosis for the elderly, immunocompromised and individuals with underlying comorbidities. The diagnosis is established via the RNA testing of sputum and throat swab samples.

The WHO affirmed that the outbreak of SARS ceased on 5th of July 2003. A total number of 8096 SARS morbidities and 774 mortalities across 29 nations were published with case-fatality rate of 9.6%. MERS is yet to halt and has so far infected 2494 individuals

and claimed 858 lives across 27 nations with case-fatality rate of 34.4%. While SARS-CoV and MERS-CoV had significantly high case-fatality rate, SARS-CoV-2 has done more damage in terms of mortality. This could be explained by high number of documented and undocumented cases. In this regard, Li et al. (2020), through a metadata analysis and Bayesian inference, suggested that substantial number of undocumented COVID-19 cases might assist in rapid spread of SARS-CoV-2. They observed transmission capacity rate (per person) of 55% in documented COVID-19 cases from undocumented COVID-19 patients, and according to them, this rate could reach up to 79% (Li et al., 2020). The secondary dissemination of SARS-CoV and MERS-CoV arose mostly in the hospital environment and so did with SARS-CoV-2. One report suggested that 1716 cases of COVID-19 transmission among healthcare personnel, of which 5 deaths were informed (Team, 2020). However, unlike SARS and MERS infection, COVID-19 patients biochemically present with elevated viral loads, even when asymptomatic (Holshue et al., 2020). Similar, findings were also observed for SARS-CoV-2 infected patients who visited Wuhan, United States, Germany and other countries (Wang et al., 2020d).

10. Treatment for COVID-19

Presently, there is no known antiviral treatment for COVID-19. However, research studies are ongoing to develop novel therapy. Current therapeutic options mostly focused on symptomatic and supportive management of COVID-19 as per recent guidelines (Jin et al., 2020). All patients receive oxygen therapy and WHO endorses extracorporeal membrane oxygenation (ECMO) to COVID-19 cases presenting with refractory hypoxemia (WHO, 2020a). Also, plasma and immunoglobulin G showed promising results in treating severe cases (Chen et al., 2020). As far as antiviral treatment strategy is concerned, several studies have shown promising results. A study demonstrated Remdesivir to be effective in treating the first COVID-19 case in the United States (Holshue et al., 2020). Another study proved Remdesivir and Chloroquine combination to be effective in antagonizing the in vitro replication of SARS-CoV-2 (Wang et al., 2020b). A systematic review also attested the effectiveness of Chloroquine in COVID-19. The study comprehensively listed clinical trials at various stages assessing the potential role of Chloroquine in COVID-19. However, high-end clinical trials are still needed for safe clinical implementation (Cortegiani et al., 2020). According to one report from WHO, nearly 500 clinical trials are being conducted to explore for therapeutic options in China, of which 13 are assessing the efficacy of Chloroquine in COVID-19 (WHO, 2020e). A report from South Korea showed significantly reduced SARS-CoV-2 viral loads in COVID-19 patient upon administration of Lopinavir/Ritonavir treatment (Lim et al., 2020). Passive immunization is one of the elapsed immunological treatment entities. Earlier, a meta-analysis on use of convalescent plasma for SARS-CoV and MERS-CoV infection has shown encouraging results (Mair-Jenkins et al., 2015). In particular, administration of convalescent plasma, obtained from recovered COVID-19-infected patients, showed promising results in treating patients with clinical complication related to the infection (Shen et al., 2020).

11. Precautionary measures taken worldwide to combat the spread of SARS-CoV-2

The virus is being transmitted at a high rate in nations outside of mainland China, with USA is now the epicenter of the outbreak. The latest WHO figures for the number of people with SARS-CoV-2 internationally might be an underestimation given the fact that many of the cases with mild symptoms may go unnoticed, while

circulating the virus at the same time. The WHO has labeled SARS-CoV-2 a pandemic and as a result, international government organizations have naturally been tasked to ramp up safety measures to dampen both imported cases and local transmission, ever mindful of “at-risk” groups. Each and every country, at their own level, is leaving no stone unturned to thoroughly test for the SARS-CoV-2 infection. The underlined pointers are the collective summary of steps taken across the globe to counter the spread of SARS-CoV-2. These include hand washing with soap or an alcohol-based hand rub, regularly disinfecting surfaces with 70% Ethyl Alcohol or 0.5% bleach solution, refraining from touching your eyes, nose and mouth with soiled hands, exercising respiratory hygiene such as coughing or sneezing into a bent elbow or tissue, disposing contaminated tissue immediately, wearing medical or surgical mask for individuals with respiratory symptoms, performing hand hygiene after disposing off medical or surgical mask, self-quarantining of individuals with respiratory symptoms, avoiding close contact in large gatherings and maintaining a person-to-person distance of 6.5 feet, drinking plenty of water, avoiding smoking, travel screening, worldwide travel ban, closure of educational institutions, working from home wherever possible and remaining abreast of the developing situation regarding SARS-CoV-2.

12. Conclusion

The SARS-CoV-2 pandemic is now a global crisis, with human lives and global economy at stake. This review article is an extension of previously published data on COVID-19. The SARS-CoV-2 has zoonotic origin and patients present with typical pneumonia signs and symptoms. Individuals that are elderly, immunocompromized or with existing health conditions are more likely to contract SARS-CoV-2. While China might have reached the plateau with regards to incidence of new COVID-19 cases, other countries are still struggling to flatten the curve of reported cases and in fact, numbers of cases and fatalities have surpassed that of China. Till date, no effective therapy is available except for supportive disease management. However, the similarity of genomic sequences between SARS-CoV-2 and SARS-CoV and MERS might assist in development of novel treatments. Presently, concerted efforts to promote and exercise infection control and other established measures such as social distancing are the only tactic adopted to slow the spread of this highly communicable virus.

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References

- Angeletti, S., Benvenuto, D., Bianchi, M., Giovanetti, M., Pascarella, S., Ciccozzi, M., 2020. COVID-2019: The role of the nsp2 and nsp3 in its pathogenesis. *J. Med. Virol.* <https://doi.org/10.1002/jmv.25719>. Online ahead of print.
- Bai, Y., Yao, L., Wei, T., Tian, F., Jin, D.-Y., Chen, L., Wang, M., 2020. Presumed asymptomatic carrier transmission of COVID-19. *JAMA* 323 (14), 1406–1407. <https://doi.org/10.1001/jama.2020.2565>.
- Ceraolo, C., Giorgi, F.M., 2020. Genomic variance of the 2019-nCoV coronavirus. *J. Med. Virol.* 92 (5), 522–528. <https://doi.org/10.1002/jmv.25700>.
- Chan, J.F.-W., Yuan, S., Kok, K.-H., To, K.K.-W., Chu, H., Yang, J., Xing, F., Liu, J., Yip, C. C.-Y., Poon, R.W.-S., Tsoi, H.-W., Lo, S.K.-F., Chan, K.-H., Poon, V.K.-M., Chan, W.-M., Ip, J.D., Cai, J.-P., Cheng, V.C.-C., Chen, H., Hui, C.K.-M., Yuen, K.-Y., 2020. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *The Lancet* 395, 514–523.

- Chen, L., Xiong, J., Bao, L., Shi, Y., 2020. Convalescent plasma as a potential therapy for COVID-19. *Lancet Infect. Dis.* 20 (4), 398–400. [https://doi.org/10.1016/S1473-3099\(20\)30141-9](https://doi.org/10.1016/S1473-3099(20)30141-9).
- Cortegiani, A., Ingoglia, G., Ippolito, M., Giarratano, A., Einav, S., 2020. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. *J. Crit. Care* S0883-9441 (20), 30390–30397. <https://doi.org/10.1016/j.jcrr.2020.03.005>.
- Cui, J., Li, F., Shi, Z.L., 2019. Origin and evolution of pathogenic coronaviruses. *Nat. Rev. Microbiol.* 17, 181–192.
- de Wilde, A.H., Snijder, E.J., Kikkert, M., van Hemert, M.J., 2018. Host factors in coronavirus replication. *Curr. Top Microbiol. Immunol.* 419, 1–42.
- de Wit, E., van Doremalen, N., Falzarano, D., Munster, V.J., 2016. SARS and MERS: recent insights into emerging coronaviruses. *Nat. Rev. Microbiol.* 14, 523–534.
- Guan, W.-j., Ni, Z.-y., Hu, Y., Liang, W.-h., Ou, C.-q., He, J.-x., Liu, L., Shan, H., Lei, C.-l., Hui, D.S., Du, B., Li, L.-j., Zeng, G., Yuen, K.-y., Chen, R.-c., Tang, C.-l., Wang, T., Chen, P.-y., Xiang, J., Li, S.-y., Wang, J.-l., Liang, Z.-j., Peng, Y.-x., Wei, L., Liu, Y., Hu, Y.-h., Peng, P., Wang, J.-m., Liu, J.-y., Chen, Z., Li, G., Zheng, Z.-j., Qiu, S.-q., Luo, J., Ye, C.-j., Zhu, S.-y., Zhong, N.-s., 2020. Clinical characteristics of 2019 novel coronavirus infection in China. *medRxiv*, 2020.2002.2006.20020974.
- Guo, Y.-R., Cao, Q.-D., Hong, Z.-S., Tan, Y.-Y., Chen, S.-D., Jin, H.-J., Tan, K.-S., Wang, D.-Y., Yan, Y., 2020. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. *Mil. Med. Res.* 7, 11.
- Holshue, M.L., DeBolt, C., Lindquist, S., Lofy, K.H., Wiesman, J., Bruce, H., Spitters, C., Ericson, K., Wilkerson, S., Tural, A., Diaz, G., Cohn, A., Fox, L., Patel, A., Gerber, S.I., Kim, L., Tong, S., Lu, X., Lindstrom, S., Pallansch, M.A., Weldon, W.C., Biggs, H.M., Uyeki, T.M., Pillai, S.K., 2020. First case of 2019 novel coronavirus in the United States. *N. Engl. J. Med.* 382, 929–936.
- Hou, Y., Peng, C., Yu, M., Li, Y., Han, Z., Li, F., Wang, L.-F., Shi, Z., 2010. Angiotensin-converting enzyme 2 (ACE2) proteins of different bat species confer variable susceptibility to SARS-CoV entry. *Arch. Virol.* 155, 1563–1569.
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., 2020a. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 395, 497–506.
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M., Xiao, Y., Gao, H., Guo, L., Xie, J., Wang, G., Jiang, R., Gao, Z., Jin, Q., Wang, J., Cao, B., 2020b. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 395, 497–506.
- Hussain, S., Pan, J.a., Chen, Y., Yang, Y., Xu, J., Peng, Y., Wu, Y., Li, Z., Zhu, Y., Tien, P., Guo, D., 2005. Identification of novel subgenomic RNAs and noncanonical transcription initiation signals of severe acute respiratory syndrome coronavirus. *J. Virol.* 79, 5288–5295.
- Ji, W., Wang, W., Zhao, X., Zai, J., Li, X., 2020. Cross-species transmission of the newly identified coronavirus 2019-nCoV. *J. Med. Virol.* 92, 433–440.
- Jin, Y.-H., Cai, L., Cheng, Z.-S., Cheng, H., Deng, T., Fan, Y.-P., Fang, C., Huang, D., Huang, L.-Q., Huang, Q.J.M.M.R., 2020. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version), 7, 4.
- Li, F., 2016. Structure, function, and evolution of coronavirus spike proteins. *Annu. Rev. Virol.* 3, 237–261.
- Li, R., Pei, S., Chen, B., Song, Y., Zhang, T., Yang, W., Shaman, J., 2020. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). *Science* 3221.
- Lim, J., Jeon, S., Shin, H.Y., Kim, M.J., Seong, Y.M., Lee, W.J., Choe, K.W., Kang, Y.M., Lee, B., Park, S.J., 2020. Case of the index patient who caused tertiary transmission of COVID-19 infection in Korea: the application of lopinavir/ritonavir for the treatment of COVID-19 infected pneumonia monitored by quantitative RT-PCR. *J. Korean Med. Sci.* 35, e79.
- Liu, Y.-C., Liao, C.-H., Chang, C.-F., Chou, C.-C., Lin, Y.-R., 2020. A locally transmitted case of SARS-CoV-2 infection in Taiwan. *N. Engl. J. Med.* 382, 1070–1072.
- Lu, G., Wang, Q., Gao, G.F., 2015. Bat-to-human: spike features determining ‘host jump’ of coronaviruses SARS-CoV, MERS-CoV, and beyond. *Trends Microbiol.* 23, 468–478.
- Lu, C.-W., Liu, X.-F., Jia, Z.-F., 2020a. 2019-nCoV transmission through the ocular surface must not be ignored. *The Lancet* 395 (10224), e39. [https://doi.org/10.1016/S0140-6736\(20\)30313-5](https://doi.org/10.1016/S0140-6736(20)30313-5).
- Lu, H., Stratton, C.W., Tang, Y.-W., 2020b. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *J. Med. Virol.* 92, 401–402.
- Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., Wang, W., Song, H., Huang, B., Zhu, N., Bi, Y., Ma, X., Zhan, F., Wang, L., Hu, T., Zhou, H., Hu, Z., Zhou, W., Zhao, L., Chen, J., Meng, Y., Wang, J., Lin, Y., Yuan, J., Xie, Z., Ma, J., Liu, W.J., Wang, D., Xu, W., Holmes, E.C., Gao, G.F., Wu, G., Chen, W., Shi, W., Tan, W., 2020c. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet (London, England)* 395, 565–574.
- Mair-Jenkins, J., Saavedra-Campos, M., Baillie, J.K., Cleary, P., Khaw, F.-M., Lim, W.S., Makki, S., Rooney, K.D., Group, C.P.S., Nguyen-Van-Tam, J.S., 2015. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. *J. Infect. Dis.* 211, 80–90.
- Nishiura, H., Linton, N.M., Akhmetzhanov, A.R., 2020. Initial cluster of novel coronavirus (2019-nCoV) infections in Wuhan, China is consistent with substantial human-to-human transmission. *Multidisciplinary Digital Publishing Institute*.
- Riou, J., Althaus, C.L., 2020. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Euro surveillance : bulletin European sur les maladies transmissibles = European communicable disease bulletin* 25, 2000058.
- Rothan, H.A., Byrareddy, S.N., 2020. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J. Autoimmun.* 109, 102433. <https://doi.org/10.1016/j.jaut.2020.102433>.
- Rothe, C., Schunk, M., Sothmann, P., Bretzel, G., Froeschl, G., Wallrauch, C., Zimmer, T., Thiel, V., Janke, C., Guggemos, W., Seilmaier, M., Drosten, C., Vollmar, P., Zwirgmaier, K., Zange, S., Wölfel, R., Hoelscher, M., 2020. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N. Engl. J. Med.* 382, 970–971.
- Salata, C., Calistri, A., Parolin, C., Palù, G., 2020. Coronaviruses: a paradigm of new emerging zoonotic diseases. *Pathogens and Disease* 77.
- Sawicki, S.G., Sawicki, D.L., 2005. Coronavirus transcription: a perspective. *Curr. Top Microbiol. Immunol.* 287, 31–55.
- Sheahan, T., Rockx, B., Donaldson, E., Corti, D., Baric, R., 2008. Pathways of cross-species transmission of synthetically reconstructed zoonotic severe acute respiratory syndrome coronavirus. *J. Virol.* 82, 8721–8732.
- Shen, C., Wang, Z., Zhao, F., Yang, Y., Li, J., Yuan, J., Wang, F., Li, D., Yang, M., Xing, L., Wei, J., Xiao, H., Yang, Y., Qu, J., Qing, L., Chen, L., Xu, Z., Peng, L., Li, Y., Zheng, H., Chen, F., Huang, K., Jiang, Y., Liu, D., Zhang, Z., Liu, Y., Liu, L., 2020. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. *JAMA*, e204783. <https://doi.org/10.1001/jama.2020.4783>.
- Shereen, M.A., Khan, S., Kazmi, A., Bashir, N., Siddique, R., 2020. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. *J. Adv. Res.* 24, 91–98.
- Song, H.-D., Tu, C.-C., Zhang, G.-W., Wang, S.-Y., Zheng, K., Lei, L.-C., Chen, Q.-X., Gao, Y.-W., Zhou, H.-Q., Xiang, H., 2005. Cross-host evolution of severe acute respiratory syndrome coronavirus in palm civet and human. *Proc. Natl. Acad. Sci.* 102, 2430–2435.
- Song, Z., Xu, Y., Bao, L., Zhang, L., Yu, P., Qu, Y., Zhu, H., Zhao, W., Han, Y., Qin, C., 2019. From SARS to MERS, thrusting coronaviruses into the spotlight. *Viruses* 11 (1), 59. <https://doi.org/10.3390/v11010059>.
- Tan, W., Zhao, X., Ma, X., Wang, W., Niu, P., Xu, W., Gao, G., Wu, G.J.C.C.W., 2020. A novel coronavirus genome identified in a cluster of pneumonia cases—Wuhan, China 2019–2020 (2), 61–62.
- Tang, X., Wu, C., Li, X., Song, Y., Yao, X., Wu, X., Duan, Y., Zhang, H., Wang, Y., Qian, Z., Cui, J., Lu, J., 2020. On the origin and continuing evolution of SARS-CoV-2. *Natl. Sci. Rev.* <https://doi.org/10.1093/nsr/nwaa036>.
- Team, T., 2020. Vital surveillances: The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China, 2020. *China CDC Weekly* 2, 113–122.
- Tortorici, M.A., Veesler, D., 2019. Structural insights into coronavirus entry. *Adv. Virus Res.* 105, 93–116.
- Wang, M., Cao, R., Zhang, L., Yang, X., Liu, J., Xu, M., Shi, Z., Hu, Z., Zhong, W., Xiao, G., 2020b. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res.* 30, 269–271.
- Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X., Zhang, J., Wang, B., Xiang, H., Cheng, Z., Xiong, Y., Zhao, Y., Li, Y., Wang, X., Peng, Z., 2020a. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*, e201585. <https://doi.org/10.1001/jama.2020.1585>.
- Wang, Y., Wang, Y., Chen, Y., Qin, Q., 2020c. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. *J. Med. Virol.* <https://doi.org/10.1002/jmv.25748>.
- WHO, 2020a. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance, 28 January 2020. *World Health Organization*.
- WHO, 2020b. Coronavirus disease 2019 (COVID-19) Situation Report – 52.
- WHO, 2020c. Coronavirus disease 2019 (COVID-19) Situation Report – 56.
- WHO, 2020d. 2020. Coronavirus disease 2019 (COVID-19) Situation Report – 94.
- WHO, 2020e. Informal consultation on the potential role of chloroquine in the clinical management of COVID 19 infection.
- Woo, P.C., Lau, S.K., Huang, Y., Yuen, K.-Y., 2009. Coronavirus diversity, phylogeny and interspecies jumping. *Exp. Biol. Med.* 234, 1117–1127.
- Wu, A., Peng, Y., Huang, B., Ding, X., Wang, X., Niu, P., Meng, J., Zhu, Z., Zhang, Z., Wang, J., Sheng, J., Quan, L., Xia, Z., Tan, W., Cheng, G., Jiang, T., 2020a. Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. *Cell Host Microbe* 27, 325–328.
- Wu, F., Zhao, S., Yu, B., Chen, Y.-M., Wang, W., Song, Z.-G., Hu, Y., Tao, Z.-W., Tian, J.-H., Pei, Y.-Y., Yuan, M.-L., Zhang, Y.-L., Dai, F.-H., Liu, Y., Wang, Q.-M., Zheng, J.-J., Xu, L., Holmes, E.C., Zhang, Y.-Z., 2020b. A new coronavirus associated with human respiratory disease in China. *Nature* 579, 265–269.
- Wu, Z., McGoogan, J.M., 2020. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese center for disease control and prevention. *JAMA*. <https://doi.org/10.1001/jama.2020.2648>.
- Xu, L., Zhang, Y., Liu, Y., Chen, Z., Deng, H., Ma, Z., Wang, H., Hu, Z., Deng, F., 2009. Angiotensin-converting enzyme 2 (ACE2) from raccoon dog can serve as an efficient receptor for the spike protein of severe acute respiratory syndrome coronavirus. *J. Gen. Virol.* 90, 2695–2703.
- Yin, Y., Wunderink, R.G., 2018. MERS, SARS and other coronaviruses as causes of pneumonia. *Respirology* 23, 130–137.
- Yu, F., Du, L., Ojcius, D.M., Pan, C., Jiang, S., 2020. Measures for diagnosing and treating infections by a novel coronavirus responsible for a pneumonia outbreak originating in Wuhan, China. *Microbes Infect.* 22, 74–79.

- Zhang, L., Shen, F.-M., Chen, F., Lin, Z., 2020a. Origin and evolution of the 2019 novel coronavirus. *Clin. Infect. Dis.* ciaa112. <https://doi.org/10.1093/cid/ciaa112>.
- Zhang, C.-Y., Wei, J.-F., He, S.-H., 2006. Adaptive evolution of the spike gene of SARS coronavirus: changes in positively selected sites in different epidemic groups. *BMC Microbiol.* 6, 88.
- Zhang, N., Jiang, S., Du, L., 2014. Current advancements and potential strategies in the development of MERS-CoV vaccines. *Expert Rev. Vaccines* 13, 761–774.
- Zhang, W., Du, R.-H., Li, B., Zheng, X.-S., Yang, X.-L., Hu, B., Wang, Y.-Y., Xiao, G.-F., Yan, B., Shi, Z.-L., Zhou, P., 2020b. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerging Microbes Infect.* 9, 386–389.
- Zhao, S., Lin, Q., Ran, J., Musa, S.S., Yang, G., Wang, W., Lou, Y., Gao, D., Yang, L., He, D., Wang, M.H., 2020. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. *Int. J. Infect. Dis.* 92, 214–217.
- Zhou, P., Yang, X.-L., Wang, X.-G., Hu, B., Zhang, L., Zhang, W., Si, H.-R., Zhu, Y., Li, B., Huang, C.-L., Chen, H.-D., Chen, J., Luo, Y., Guo, H., Jiang, R.-D., Liu, M.-Q., Chen, Y., Shen, X.-R., Wang, X., Zheng, X.-S., Zhao, K., Chen, Q.-J., Deng, F., Liu, L.-L., Yan, B., Zhan, F.-X., Wang, Y.-Y., Xiao, G.-F., Shi, Z.-L., 2020. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 579, 270–273.
- Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., Zhao, X., Huang, B., Shi, W., Lu, R., Niu, P., Zhan, F., Ma, X., Wang, D., Xu, W., Wu, G., Gao, G.F., Tan, W., 2020. A novel coronavirus from patients with pneumonia in China, 2019. *N. Engl. J. Med.* 382, 727–733.