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A scoping review on epidemiology, etiology, transmission, clinical presentation, treatment and management of coronavirus disease (COVID-19)

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ABSTRACT: *Coronavirus (COVID-19) is a highly infectious disease which has posed serious threats to global health. This viral disease was discovered in late December 2019, in Wuhan, China. Infection rates due to the pandemic amounts to over 1 million globally while death rate is over 80,000. The United States, Italy and Spain are epicenters of the disease and have recorded more deaths due to the viral infection than other countries. Since the virus is spreading worldwide, on March 11, 2020, the WHO officially described the COVID-19 outbreak as a pandemic. The virus is transmitted when people interact with each other for some time in close proximity. Precisely, this review aims to provide the evidence of early findings on the etiology, transmission, symptoms, treatment and management of COVID-19. Studies have recorded Covid-19 infection in asymptomatic patients and in those with visible symptoms. Elderly people, pregnant women, people with underlining illness and compromised immune system are very susceptible to COVID-19 than other categories of people, however, reports of deaths of people without history of underlining illness has led to controversies. The diseased due to the virus should try to seek appropriate medical help and limit their exposure to other unaffected persons. Currently, there are no vaccines for the pandemic, but the FDA has recommended hydroxyl chloroquine as a therapy for COVID-19. The likelihood of transmission can be reduced by practising hygienic measures. Frequent disinfection and cleaning are advised for groups that are at risk of contracting the virus.*

KEYWORDS*:* Covid-19, pandemic, epicenter, virus, asymptomatic, immune system, vaccines, therapy

INTRODUCTION

Human coronaviruses (COVID-19) disease is an ongoing pandemic of coronavirus disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1],affecting the lower respiratory tract of patients with pneumonia of respiratory illness in Wuhan, Hubei Province, China beginning in December 2019[2].This new virus seems to be very contagious and has quickly spread [3].As On 31 January 2020, there were 213 deaths reported globally [4].Confirmed cases were reported in the following 19 countries outside of China: Australia, Canada, Cambodia, France, Finland , Germany , India , Italy , Japan , Nepal , Malaysia, the Philippines, the Republic of Korea, Singapore, Sri Lanka , Thailand, the United States of America , United Arab Emirates and Vietnam[4].In response to the outbreak,

epidemiological and etiological investigations by WHO confirmed that the outbreak of the coronavirus epidemic was associated with the Huanan South China Seafood Market place, but no specific animal association was identified [5]. Susceptibility seems to be associated with age, biological sex, and other health conditions [6]. COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO [7].However, in the last twenty years, viral diseases continue to emerge and represent a serious issue to public health [8].Human coronaviruses (COVID-19) have long been considered inconsequential pathogens found in animals and, rarely, can be transmitted from animals to humans and then spread person to person, causing the "common cold" in otherwise healthy people [9]. Coronaviruses have been described for more than 50 years; the coronavirus belonging to a family of viruses that are common in animals worldwide, but very few cases have been known to affect humans [10]. However, in the 21st century, 2 highly pathogenic HCoVs—severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV)—emerged from animal reservoirs to cause global epidemics with alarming morbidity and mortality [11].In general, coronaviruses cause widespread respiratory, gastrointestinal, and central nervous system diseases in humans and other animals, threatening human health and causing economic loss [12]. Coronaviruses are capable of adapting to new environments through mutation and recombination with relative ease and hence are programmed to alter host range and tissue tropism efficiently [13].Therefore, health threats from coronaviruses are constant and long-term [14].Understanding the virology of coronaviruses and controlling their spread have important implications for global health and economic stability [15] This review aims to provide the evidence of early and recent findings on the etiology, transmission, symptoms, treatment and management of COVID-19.This may support government decision-making process on development of coherent strategies to handle this public health emergency at the community, national, and international levels. It can also lead to a better understanding and mechanism of developing a first-line therapy.

Epidemiology

Health authorities in Wuhan, the capital of Hubei province, China, reported a cluster of pneumonia cases of unknown cause on 31 December 2019 and an investigation was launched in early January 2020[16]. The cases mostly had links to the Huanan Seafood Wholesale Market and so the virus is thought to have a zoonotic origin [17].The virus that caused the outbreak is known as SARS-CoV-2, a newly discovered virus closely related to bat coronaviruses pangolin coronaviruses, [18] and SARS-CoV[19]. The earliest known person with symptoms was later discovered to have fallen ill on 1 December 2019 without any visible connections with the later wet market cluster[20,21] Of the early cluster of cases reported in December 2019, two-thirds were found to have a link with the market [22,23]. On 13 March 2020, an unverified report from the *South China Morning Post* suggested that a case traced back to 17 November 2019, in a 55-year-old from Hubei province, may have been the first [24, 25] .

On 26 February 2020, the WHO reported that, as new cases reportedly declined in China but suddenly increased in Italy, Iran, and South Korea, the number of new cases outside China had exceeded the number of new cases within China for the first time [26]. There may be substantial

underreporting of cases, particularly among those with milder symptoms [27, 28]. By 26 February, 2020, relatively few cases had been reported among youths 2.4% of cases worldwide. [29].Government sources in Germany and the United Kingdom estimate that 60–70% of the population will need to become infected before effective herd immunity can be achieved [30, 31, 32].

Etiology

The Coronaviruses (CoVs) are the largest group of viruses belonging to the Nidovirales order, which includes Coronaviridae, Arteriviridae, Roniviridae and Mesoniviridae families [33]. The classification of Coronaviruses has been based on genomic organization, similarities in genomic sequence, antigenic properties of viral proteins, replication strategies, and structural characteristics of virions, pathogenic, cytopathogenic and physicochemical properties [34].

The Coronaviridae family is the largest one of the four families, by its genomic sizes of coronaviridae range from 26 to 32 kb [35]. Coronaviridae virus family subdivided into two subfamilies, coronavirinae and torovirinae [36]. It is now divided into four genera, Alpha coronavirus, Beta coronavirus, Gamma coronavirus and Delta coronavirus .They can be classified into four genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*. Among them, alpha-and betacoronaviruses infect mammals, gammacoronaviruses infect avian species, and deltacoronaviruses infect both mammalian and avian species [37]. Representative alphacoronaviruses include human coronavirus NL63 (HCoV-NL63), porcine transmissible gastroenteritis coronavirus (TGEV), PEDV, and porcine respiratory coronavirus (PRCV). Representative betacoronaviruses include SARS-CoV, MERS-CoV, bat coronavirus HKU4, mouse hepatitis coronavirus (MHV), bovine coronavirus (BCoV), and human coronavirus OC43[38]. Representative gamma-and deltacoronaviruses include avian infectious bronchitis coronavirus (IBV) and porcine deltacoronavirus (PdCV), respectively. Coronaviruses are large, enveloped, positive-stranded RNA viruses. They have the largest genome among all RNA viruses, typically ranging from 27 to 32 kb. The genome is packed inside a helical capsid formed by the nucleocapsid protein (N) and further surrounded by an envelope. Associated with the viral envelope are at least three structural proteins: The membrane protein (M) and the envelope protein (E) are involved in virus assembly, whereas the spike protein (S) mediates virus entry into host cells. Some coronaviruses also encode an envelope-associated hemagglutinin-esterase protein (HE) [39].

Among these structural proteins, the spike forms large protrusions from the virus surface, giving coronaviruses the appearance of having crowns (hence their name; *corona* in Latin means crown). In addition to mediating virus entry, the spike is a critical determinant of viral host range and tissue tropism and a major inducer of host immune responses [40].

To date, seven human CoVs (HCoVs) — capable of infecting humans — have been identified. Some of HCoVs were identified in the mid-1960s, while others were only detected in the new millennium [41]. Common human CoVs: HCoV-OC43, and HCoV-HKU1 (betaCoVs of the A

lineage); HCoV-229E, and HCoV-NL63 (alphaCoVs). They can cause common colds and self-limiting upper respiratory infections in immunocompetent individuals. In immunocompromised subjects and the elderly, lower respiratory tract infections can occur [42].

Other human CoVs: SARS-CoV, SARS-CoV-2, and MERS-CoV (betaCoVs of the B and C lineage, respectively). These cause epidemics with variable clinical severity featuring respiratory and extra-respiratory manifestations. Concerning SARS-CoV, MERS-CoV, the mortality rates are up to 10% and 35%, respectively [43]. Thus, SARS-CoV-2 belongs to the betaCoVs category. It has round or elliptic and often pleomorphic form, and a diameter of approximately 60–140 nm. Like other CoVs, it is sensitive to ultraviolet rays and heat. Furthermore, these viruses can be effectively inactivated by lipid solvents including ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform except for chlorhexidine [44].

Transmission

Some details about how the disease is spread are still being determined. [45].Because the first cases of the CoVID-19 disease were linked to direct exposure to the Huanan Seafood Wholesale Market of Wuhan, the animal-to-human transmission was presumed as the main mechanism [46]. Nevertheless, subsequent cases were not associated with this exposure mechanism [46]. Therefore, it was concluded that the virus could also be transmitted from human-to-human, and symptomatic people are the most frequent source of COVID-19 spread. The disease is believed to spread during close contact and by small droplets produced when people cough, sneeze, or talk [47] with close contact being within 1 to 2 meters (3 to 6 feet) [48]. Studies have found that an uncovered coughing can lead to droplets travelling up to 4.5 metres (15 feet) to 8.2 metres (27 feet) [49].The virus is most contagious when people are symptomatic; while spread may be possible before symptoms appear, this risk is low.[50]. The European Centre for Disease Prevention and Control (ECDC) states that while it is not entirely clear how easily the disease spreads, one person generally infects two to three others [51]. The virus survives for hours to days on surfaces [52]. Specifically, the virus was found to be detectable for up to three days on plastic and stainless steel, for one day on cardboard, and for up to four hours on copper. This, however, varies based on the humidity and temperature [53].
Further studies are needed to understand the mechanisms of transmission, the incubation times and the clinical course, and the duration of infectivity.

Clinical Presentation

Incubation period

These symptoms may appear 2-14 days after exposure (based on the incubation period of MERS-CoV viruses). with a median time of 4-5 days from exposure to symptoms onset [54]. One study reported that 97.5% of persons with COVID-19 who develop symptoms will do so within 11.5 days of SARS-CoV-2 infection [54].

Presentation

The signs and symptoms of COVID-19 present at illness onset vary, but over the course of the disease, most persons with COVID-19 will experience the following:Fever (83–99%),Cough (59–82%), Shortness of breath (31–40%),Fatigue (44–70%),Anorexia (40–84%),Sputum production (28–33%),Myalgias (11–35%)[55].

Atypical presentations have been described and older adults and persons with medical comorbidities may have delayed presentation of fever and respiratory symptoms[56].Headache, confusion, rhinorrhea, sore throat, hemoptysis, vomiting, and diarrhea have been reported but are less common (<10%) [57].Some persons with COVID-19 have experienced gastrointestinal symptoms such as diarrhea and nausea prior to developing fever and lower respiratory tract signs and symptoms. Anosmia or ageusia preceeding the onset of respiratory symptoms has been anecdotally reported, but more information is needed to understand its role in identifying COVID-19[58].

Asymptomatic and Pre-Symptomatic Infection

Several studies have documented SARS-CoV-2 infection in patients who never develop symptoms (asymptomatic) and in patients not yet symptomatic (pre-symptomatic) [59]. Since asymptomatic persons are not routinely tested, the prevalence of asymptomatic infection and detection of pre-symptomatic infection is not well understood [60].Although transmission of SARS-CoV-2 from asymptomatic or pre-symptomatic persons has been reported risk of transmission is thought to be greatest when patients are symptomatic [61].

Clinical Course

Illness Severity

The largest cohort of >44,000 persons with COVID-19 from China showed that illness severity can range from mild to critical [62].

- Mild to moderate (mild symptoms up to mild pneumonia): 81%
- Severe (dyspnea, hypoxia, or >50% lung involvement on imaging): 14%
- Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%

Risk Factors for Severe Illness

Age is a strong risk factor for severe illness, complications, and death[63].Among more than 44,000 confirmed cases of COVID-19 in China, the case fatality rate was highest among older persons: ≥80 years: 14.8%, 70–79 years: 8.0%, 60–69 years: 3.6%, 50–59 years: 1.3%, 40–49 years: 0.4%, <40 years: 0.2%[64] .Early U.S. epidemiologic data suggests that the case fatality was highest in persons aged ≥85 years (range 10%–27%), followed by 3%–11% for ages 65–84 years, 1%–3% for ages 55–64 years, and <1% for ages 0–54 years[65].

Patients with no reported underlying medical conditions had an overall case fatality of 0.9%, but case fatality was higher for patients with comorbidities: 10.5% for those with cardiovascular disease, 7.3% for diabetes, and approximately 6% each for chronic respiratory disease,

hypertension, and cancer [66].Heart disease, hypertension, prior to stroke, diabetes, chronic lung disease, and chronic kidney disease have all been associated with increased illness severity and adverse outcomes [67].

Treatment / Management

There is no vaccines currently available for the treatment of COVID-19. The treatment is symptomatic, and oxygen therapy represents the major treatment intervention for patients with severe infection. Mechanical ventilation may be necessary in cases of respiratory failure refractory to oxygen therapy, whereas hemodynamic support is essential for managing septic shock [68].
On January 28, 2020, the WHO released a document summarizing WHO guidelines and scientific evidence derived from the treatment of previous epidemics from HCoVs. This document addresses measures for recognizing and sorting out patients with severe acute respiratory disease; strategies for infection prevention and control; early supportive therapy and monitoring; a guideline for laboratory diagnosis; management of respiratory failure and acute respiratory distress syndrome (ARDS); management of septic shock; prevention of complications; treatments; and considerations for pregnant patients [69].
Among these recommendations, we report the strategies for addressing respiratory failure, including protective mechanical ventilation and high-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV).

Precautions: WHO recommends multiple steps to prevent the transmission and risk of Covid-19:
1. Regularly and thoroughly washing of hands with soap and water, and alcohol-based hand sanitiser.
2. Maintaining at least 1 & half metres (5 feet) distance between yourself and anyone who is coughing or sneezing.
3. Persistent coughing or sneezing persons should stay home or keep a social distance, not mixing in crowd.
4. Ensuring that you and people around you are following good respiratory hygiene which means covering of mouth and nose with a disposable tissue while sneezing.
5. staying at home when a person feels unwell with symptoms like fever, cough and difficulty in breathing. Avoidance of engagements in self-medication.
6. Staying informed on the latest developments about COVID-19 through official channels on TV and Radio, State Ministry of Health, NCDC and Federal Ministry of Health [69]

CONCLUSIONS AND FUTURE DIRECTIONS

Coronaviruses (CoVs) are a diverse family of viruses that interact at multiple levels with components of host cells taking the advantage of some of the cellular machineries for replication and proliferation. Various techniques are known about the molecular biology of CoVs but more information is needed. For example, many of the nonstructural and accessory proteins encoded by these viruses remain uncharacterized with no known function, and it will be important to identify mechanisms of actions for these proteins as well as defining their role in viral replication and

pathogenesis. The challenge now is that no effective medication has been implicated. Developing technology is going to be getting important insight about structure of CoVs protein to define the mechanism of how these proteins cause disease, understanding the protein-protein and protein RNA interaction will significantly improve our ability to design vaccines. In the meantime, molecular modeling methods provide important solutions to the struggle. Although these studies are relevant to control the current public emergency, the need for more high-quality and actual research is high to providing valid and reliable ways for the management of this kind of public health emergency in both the short- and long-term basis.

REFERENCES

[1] "Coronavirus disease 2019". World health organization. Retrieved 15 march 2020.
[2] Li Q., Guan, X., Wu, P., Wang X., Zhou L and Tong Y., *et al* (2020). Early Transmission Dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *New England Journal of Medicine*, 382, (13):1199-1207.
[3]CDC (2019).Novel coronavirus, Wuhan, China. 2020. *Https://www.cdc.gov/coronavirus/2019-ncov/summary*.html. Accessed 1 Feb 2020.
[4] WHO. Novel coronavirus 2019-ncovid situation report-11.2020.
[5] WHO (2020). Novel Coronavirus–China. *Https://www.who.int/csr/don.*
[6] Fehr, A.R., Channappanavar, R and Perlman, S. (2017). Middle East Respiratory Syndrome: Emergence of a Pathogenic Human Coronavirus. *Annual* Review of *Medicine*, 68:387–99.
[7]WHO (2019). Statement on the second meeting of the international health regulations, emergency committee regarding the outbreak of novel coronavirus (2019-ncov). Https://www.who.int/news-room/detail/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov).
[8]"WHO (2020). Director-general's opening remarks at the media briefing on covid-19—11 March 2020".
[9] Peiris, J.S.M., Lai,S.T., Poon,L.L.M., Guan,Y., Yam,L.Y.C *et al* (2003). Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet*, 361:1319–25.
[10] Fehr, A.R., channappanavar r, perlman s. Middle east respiratory syndrome: emergence of a pathogenic human coronavirus. *Annual* Review of *Medicine*, 2017, 68:387–99.
[11] Poudel Adhikari, S.; Meng, S.; Wu, Y.; Mao, Y.; Ye, R.; Wang, Q.; Sun, C.; Sylvia, S.; Rozelle, S.; Raat, H.; Zhou, H (2020). A Literature Review of 2019 Novel Coronavirus during the Early Outbreak Period: Epidemiology, Causes, Clinical Manifestation and Diagnosis, Prevention and Control. *Preprints*, 2020, 2020020060.
[12] Enjuanes, L., Almazan, F., Sola, I., Zuniga, S (2006). Biochemical aspects of Coronavirus replication and virus-host interaction. *Annual* Review of *Microbiology*; 60:211–30.
[13] Perlman, S and Netland, J (2009). Coronaviruses post-sars: update on replication and pathogenesis. *Nature Reviews Microbiology*, 7:439–50.

[14] Graham R.L and Baric, R.S (2010). Recombination, reservoirs, and the modular spike: mechanisms of coronavirus cross-species transmission. *Journal of Virology*, 84:3134–46.]
[15] Li, F (2013). Receptor recognition and cross-species infections of SARS Coronavirus. *Antiviral Research*; 100:246–54.
[16] "Mystery Pneumonia Virus probed in China". BBC news. 3 January 2020. Archived from the original on 5 January 2020. Retrieved 29 January 2020
[17] Zhonghua, Liu., Xing, Bing., Xue Za Zhi (2020). The Epidemiological Characteristics of an outbreak of 2019 novel Coronavirus diseases (covid-19) in China]".*PubMed*, 41 (2): 145–151.
[18] Perlman, S (2020). "Another decade, another Coronavirus". *The New England Journal of Medicine*. 382 (8): 760–762.
[19] Wong, M.C., Cregeen, S. J., Ajami, N. J., Petrosino, J. F. (2020). "Evidence of recombination in coronaviruses implicating pangolin origins of ncov-2019". *Biorxiv*(preprint). Doi:10.1101/2020.02.07.939207.
[20]"outbreak of severe acute respiratory syndrome coronavirus 2 (sars-cov-2): increased transmission beyond china—fourth update" (pdf*). European Centre for disease prevention and control*. 14 February 2020. Retrieved 8 march 2020.
[21] Cohen, Jon (2020). "Wuhan seafood market may not be source of novel virus spreading globally". Science. Doi:10.1126/science.abb0611.
[22] Wang, C., Horby, P. W., Hayden, F. G and Gao, G. F. (2020). "a novel coronavirus outbreak of Global Health Concern". *Lancet*, 395 (10223): 470–473.
[23] Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y *et al* (2020). "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China". *Lancet*, 395 (10223): 497–506.
[24] Chan, I.F, Yuan, S, Kok, K.H, To, K.K Chu, H and Yang J *et al* (2020). "a familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster". *Lancet*, 395 (10223): 514–523.
[25] Ma, Josephina (2020). "China's first confirmed Covid-19 case traced back to November 17". South china morning post. Archived from the original on 19 march 2020.
[26] "WHO Director-General's opening remarks at the mission briefing on covid-19—26 February 2020". World health organization. 26 February 2020.
[27] Li, Ruiyun., Pei, Sen., Chen, Bin., Song, Yimeng., Zhang, Tao., Yang, Wan and Shaman, Jeffrey (2020). "substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (Covid-19)''Medrvix (preprint).2020.02.14.20023127.

[28] Sun, D., Borame L., Chen, M., Cook, Alex Richard and Clapham, H.E (2020). "estimating number of global importations of covid-19 from Wuhan, risk of transmission outside mainland china and covid-19 introduction index between countries outside mainland china". Medrxiv (preprint): 2020.02.17.20024075. Doi:10.1101/2020.02.17.20024075.
[29] "report of the WHO-China joint mission on coronavirus disease 2019 (covid-19) (report). World health organization. 2020".

[30]"interview with Christian Drosten: "we have to bring down the number of cases now. Otherwise we won't be able to handle it"". *Die Zeit*. 21 march 2020.
[31]"60% of UK population need to get coronavirus so country can build 'herd immunity', chief scientist says". The independent. 13 march 2020. Retrieved 20 march 2020.
[32]"up to 70% of Germany could contract virus—merkel".BBC news. 11 march 2020.
[33] Enjuanes, L., Almazan, F., Sola, I and Zuniga, S (2006). Biochemical aspects of Coronavirus replication and virus-host interaction. Annual *Review of* Microbiology, 60:211–30.
[34] Lai, M.M and Cavanagh, D (1997). The molecular biology of coronaviruses. *Advances in Virus Research*, 48: 1-100. https://goo.gl/AUaxWf
[35] Zirkel, F., Kurth, A., Quan, P.L., Briese, T., Ellerbrok, H and Pauli, G, *et al* (2011). An Insect Nidovirus Emerging from a Primary Tropical Rainforest. *mBio*, 2: e00077-11.
[36] Gorbalenya, A.E., Enjuanes, L., Ziebuhr, J and Snijder, E.J (2006). *Nidovirales*: evolving the largest RNA virus genome. *Virus Research*, 117: 17-37.
[37] Weiss and Leibowitz (2011).Coronavirus Pathogenesis, A*dvances in Virus Research*, 81:85-164.
[38] Li, F. (2016). Structure, Function, and Evolution of Coronavirus Spike Proteins. *Annual review of virology*, *3*(1), 237–261.
[39] Weiss, S. R., & Navas-Martin, S. (2005). Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. *Microbiology and molecular biology review, Microbiology and Molecular Biology Reviews*, *69*(4), 635–664.
[40] Perlman, S and Netland, J (2009). Coronaviruses post-SARS: update on replication and pathogenesis. *Nature Reviews Microbiology*, 7:439–50.
[41] Chan, J.F., To, K.K, Tse, H., Jin, D.Y and Yuen, K.Y (2013). Interspecies transmission and emergence of novel viruses: lessons from bats and birds. *Trends in Microbiology*, *21*(10):544-55.
[42]Chen, Y., Liu, Q and Guo, D (2020). Emerging coronaviruses: Genome structure, replication, and pathogenesis. *Journal of Medical Virology*, 92(4):418-423.
[43] Chan, J.F., Kok, K.H., Zhu, Z., Chu, H., To, K.K., Yuan, S and Yuen, K.Y (2020). Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerging Microbes & Infections*, 9(1):221-236.
[44].Marra, M.A., Jones, S.J.M., Astell, C.R., Holt, R.A and Brooks-Wilson A, *et al* (2003). The genome sequence of the SARS-associated coronavirus. *Science*, 300:1399–404.
[45] Coronavirus Disease 2019 (COVID-19)—Transmission". Centers for Disease Control and Prevention. 17 March 2020. Retrieved 23 March 2020.
[46] Zhou, M., Zhang, X. & Qu, J. Coronavirus disease 2019 (COVID-19): a clinical update. *Front. Med.* (2020). https://doi.org/10.1007/s11684-020-0767-8
[47] "Q&A on coronaviruses". World Health Organization. 11 February 2020. Retrieved 24 February 2020.
[48] Coronavirus Disease 2019 (COVID-19)—Transmission". Centers for Disease Control and Prevention. 17 March 2020. Retrieved 23 March 2020.

[49] Loh, Ne-Hooi W, Tan, Y., Taculod, J H *et al*. (2020). "The Impact of High-Flow Nasal Cannula (HFNC) on Coughing Distance: Implications on Its Use during the Novel Coronavirus Disease Outbreak". *Canadian Journal of Anesthesia*. doi:10.1007/s12630-020-01634-3. PMC 7090637. PMID 32189218.
[50] "Coronavirus Disease 2019 (COVID-19)—Transmission". Centers for Disease Control and Prevention. 17 March 2020. Retrieved 23 March 2020.
[51] Q & A on COVID-19". European Centre for Disease Prevention and Control. Retrieved 23 March 2020.
[52] "Coronavirus Disease 2019 (COVID-19)—Environmental Cleaning and Disinfection Recommendations". Centers for Disease Control and Prevention. 11 February 2020. Retrieved 24 March 2020.
[53] "New coronavirus stable for hours on surfaces". National Institutes of Health (NIH). 17 March 2020. Retrieved 24 March 2020.
[54] Lauer, S.A., Grantz, K.H and Bi, Q, *et al* (2020). The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Annals of Internal Medicine*, 2020.
[55] Chen, N., Zhou, M and Dong, X, *et al* (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* (London, England), 395(10223):507-513.
[56] Yang, X., Yu, Y and Xu, J *et al* (2020). Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*. 2020.
[57] Chen, N., Zhou, M and Dong, X, *et al* (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* (London, England), 395(10223):507-513.
[58] Pan, L., Mu, M and Ren, H.G *et al (*2020). Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. *American Journal of Gastroenterology*; [Epub ahead of print].
[59] Chan, J.F., Yuan, S and Kok, K.H et al (2020). A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* (London, England), 395(10223):514-523.
[60] Wang, Y., Liu, Y., Liu, L., Wang, X., Luo, N and Ling, L (2020). Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China. *The Journal of infectious diseases*.
[61] Bai, Y., Yao, L and Wei, T *et al* (2020). Presumed Asymptomatic Carrier Transmission of COVID-19. *Jama*. 2020.
[62] 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*. 2020.
[63] Livingston, E and Bucher, K. Coronavirus Disease 2019 (COVID-19) in Italy. *Jama*. 2020.

[64] Zhonghua, Liu, Xing, Bing and Xue Za Zh (2020). Novel Coronavirus Pneumonia Emergency Response Epidemiology T. [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China], 41(2):145-151.
[65] CDC COVID-19 Response Team. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020. *MMWR Morbidity and mortality weekly report*. 2020.
[66] Zhonghua, Liu, Xing, Bing and Xue Za Zh (2020). Novel Coronavirus Pneumonia Emergency Response Epidemiology T. [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China], 41(2):145-151.
[67] Wei, M., Yuan, J., Liu, Y., Fu, T., Yu, X and Zhang, Z.J (2020). Novel Coronavirus Infection in Hospitalized Infants Under 1 Year of Age in China. *Jama*. 2020.
[68] World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020 (Accessed on February 12, 2020).
[69]WHO. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). 2020V.