Special Article

SARS-CoV-19: An Overview of the Pandemic

Dimitrios Theofanidis, MSc, PhD
Associate professor, Nursing department, International Hellenic University, Greece

Antigoni Fountouki, MSc, PhD(c)
Clinical Lecturer, Nursing department, International Hellenic University, Greece

Correspondence: Dimitrios Theofanidis, Associate professor, Nursing department, International Hellenic University, Greece, E-mail: dimitrisnoni@yahoo.gr

Abstract
Introduction: Corona viruses cause a wide range of diseases in humans and animals and generally fall into two categories, with respiratory or intestinal tropisms.
Aim: the purpose of this discussion paper is to provide an overview of the current pandemic with a solid explanation of the disease for nurses and allied health care professionals.
Discussion: Covid-19 is caused by a new corona virus (severe acute respiratory syndrome – corona virus 2 that first appeared in December 2019 and is responsible for the current pandemic, a state of international urgency concerning public health. The full clinical manifestation has been reported to range from asymptomatic cases, to mild or severe symptoms and in many cases leading to death. Moreover, different strains of the virus have evolved and now vary in transmissibility and overall death toll.
Conclusions: The primary objective of the International Health Organizations is to limit the international spread of the pandemic and prevent the spread of new added outbreaks. Due to the initial lack of effective vaccines and treatments, the main readily available method to reduce SARS-CoV-2 transmission is to identify and isolate infected patients as quickly and effectively as possible especially if a new strain of the virus is suspected or identified.

Key Words: SARS-CoV-19, corona virus, pandemic

Introduction

Within a short period of time, a new corona virus (SARS-CoV-2) developed into a threat to public health worldwide, significantly affecting the daily life of millions for the past two years. There is no doubt that lessons learned from previous corona virus epidemics, such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS), were not sufficient and the global community was not ready to face the challenges of the current Covid-19 pandemic. Yet, this has provided an opportunity for examining and implementing new practices for humanity to prepare and face future epidemics. In December 2019, an ongoing outbreak of pneumonia occurred in Wuhan, China, related to the new Severe Acute Respiratory Syndrome (SARS) corona virus. Analysis of the virus revealed that it had 88% of the same sequence identity as two SARS-type corona viruses derived from bats. Temporarily the new virus, which is a single-stranded ribonucleic acid, was named the new corona virus of 2019 (2019-nCoV) due to solar-like appearance and surface-like peaks 9-12 nm (Zu et al,2020). According to data from the European Center for Disease Prevention and Control, 1,073,947 cases of COVID-19 were identified in Europe and 103,989 deaths by April 21st, 2021. In contrast, in Greece, at that time, the figures were 2,401 cases and 121 deaths, which was due to early and strict public health measures to prevent the spread of the virus. This limited impact of the Covid-19 pandemic made our country an example to follow (Lofti et.al., 2020).

Physiology and history of coronavirus: SARS-CoV-2, is a new strain of corona virus that differs from SARS-CoV-1, i.e. the corona virus that caused the SARS epidemic in 2003, and from the other corona viruses that have been isolated by humans to date. Based on clinical experience, infection with the new corona virus usually

manifests as pneumonia, with the occurrence of acute, severe respiratory disease, high fever, cough, dyspnoea and respiratory distress. In several cases the infection has led to the development of complications of Acute Respiratory Distress Syndrome (ARDS), renal failure, multi-organ failure, coagulopathies, pericarditis and death (Hui et al., 2020). The epidemic first occurred in a cluster of mysterious cases of pneumonia in Wuhan, the capital of Hubei province in mainland China. A Wuhan hospital notified on 27 December 2019 the local center for disease control and prevention and other health committees. On December 31, the Wuhan Center admitted that there was a cluster of unknown pneumonia cases stemming from the Wuhan seafood market. On January 8, a new corona virus was identified as the cause of severe pneumonia (Khan, 2020). The virus sequence was soon published in an open access database (Cohen, 2020). The sudden rise in cases has raised questions about wildlife trade, uncertainties surrounding the virus's ability to spread and harm if the virus was circulating for longer than previously thought. The first cases were reported by December 31st, 2019, with the first cases of symptomatic disease occurring just three weeks earlier. After a specific PCR diagnostic was developed to detect the infection, the presence of 2019-nCoV was then confirmed (Cohen, Jon, 2020). Two decades earlier, i.e. in November 2002, a viral respiratory disease first appeared in southern China and quickly spread to other countries, leading to over 8,000 confirmed cases at the end of the outbreak in June 2003, with a mortality rate of 9.6%. A zoonotic beta corona virus which originated from horseshoe-bats were later evolved to infect humans. After an incubation period of 4-6 days, SARS patients developed flu-like symptoms and pneumonia, leading to acute respiratory distress syndrome and death. Although SARS-CoV affects many organs and causes systemic disease, the symptoms worsen gradually suggesting that there is an acute diversion of the immune response which in turn is the pathogenicity of SARS-CoV per se. In June 2012, MERS-CoV appeared in Saudi Arabia as the causative agent of a SARS-type respiratory disease. Although human-to-human transmission was considered limited, MERS-CoV caused two major epidemics in Saudi Arabia (2012) and South Korea (2015), with global confirmed cases of over 2,000 and a mortality rate of approximately 35%. Elderly people infected with MERS-CoV, especially those with multiple diagnoses, usually develop more severe and often fatal disease (WHO). Similar to SARS-CoV, MERS-CoV originated from bats, but later adapted to camels as an intermediate host. Currently, no vaccine or specific antiviral drug has been approved for either SARS-CoV or MERS-CoV (Weiss & Navas-Martin, 2005). Prior to the emergence of SARS-CoV, only two specific strings, i.e. HCoV-229E and HCoV-OC43 were known to cause mild upper respiratory symptoms. Together, these HCoVs probably contributed to 15-30% of common cold cases in humans globally. Yet, such mild HCoVs can sometimes cause serious lower respiratory tract infections in infants, elderly people or immune-compromised patients. Similar to SARS-CoV and MERS-CoV, HCoV-NL63 and HCoV-229E are derived from bats, while HCoV-OC43 and HCoV-HKU1 have probably originated from rodents. It is important to note that that the majority of alpha corona virus and beta corona virus were found in bats, and many phylogenetic corova viruses, associated with SARS-CoV and MERS-CoV were discovered in different species of bats (Lau et al., 2006). HCoV such as SARS-CoV and MERS-CoV probably came from bats through sequential bat mutation and recombination of bat corona viruses, underwent further mutations during intermediate hosts and eventually acquired the ability to infect human hosts (Rubin et al., 2020).
Corona viruses cause a wide range of diseases in humans and animals and generally fall into two categories, with respiratory or intestinal tropisms. Mouse hepatitis virus (MHV) and rat corona viruses are the most commonly found viruses in animals within a laboratory setting (Agostini et al., 2020).Age, genotype, immune status of mouse and MHV strain influence the type and severity of disease caused by MHV. Research on MHV has been focusing mainly in the areas of immunology and tumor biology and may reflect the ability of MHV to grow on various types of immune cells. While there are many methods to diagnose corona virus infection, serological tests, primarily ELISA and IFA, are the most commonly used. MHV is managed on a precautionary basis. Eliminating MHV from a population requires stopping reproduction and stopping the introduction of new mouse into the population (Compton et al., 1993).

SARS-CoV-2 is closely related to the original SARS-CoV (Zhu,etal.,2020) Genetic analysis revealed that corona virus is genetically related to

the genus Beta corona virus, in the B-series of the subgenus Sarbeco virus along with two strains derived from a bat. It is 96% identical throughout the genome to other corona virus samples i.e. BatCovRaTG13 (McKee et al., 2020). Bats seem to be the common natural source of SARS and MERS. The clinical characteristics are similar, but MERS progresses to respiratory failure much faster than SARS. Although the estimated pandemic potential of MERS-CoV is lower than that of SARS-CoV, the mortality rate of the MERS case is much higher and is likely related to a longer age and co-morbid disease of sporadic cases. Many knowledge gaps remain since the first discovery of MERS-CoV in 2012. More studies are needed to understand pathogenesis, viral kinetics, disease transmission way and intermediate source MERS in order to guide the common measures and treatment of control of infection (Hui et al., 2020). HCoV-22 and HCoV-OC43 were identified in the mid-1960s and are known to cause the common cold. The newly recognized SARS-CoV is the most pathogenic corona virus recognized (Fung & Liu., 2019).

Definition of coronavirus: Corona viruses are in essence a 'family' of viruses. They are named after their characteristic appearance in the electronic microscope, where they are distinguished by bulges of particles, which resemble a 'Crown'. The corona viruses are 'enveloped' viruses and bear as a genome a monoclone RNA positive (+) polarity (Murray, et al., 2012). The corona virus genome is the largest among the RNA viruses. As in SARS, S proteins attaches to the angiotensin converting enzyme (ACE-2). The protein corona, unlike other viruses, can 'survive' the conditions of the gastrointestinal system (Bachem, et al., 1996). Corona viruses are divided into three types (I, II, III) and are based on serological cross-reactivity. Group I corona viruses include animal pathogens, diarrhea virus (PEDV) and feline infectious peritonitis virus (FIPV), as well as human corona viruses HC OV229E and HKU1, which cause respiratory infections. Group II also includes pathogens of veterinary importance, such as BCoV, porcine haemagglutination encephalomyelitis, and equine corona viruses, as well as human corona viruses. OC43 and NL 63, like HCoV-229E, also cause respiratory infections. Group II also includes viruses that infect mice and rats. MHV is often studied as a prototype coronavirus. MHV is a group of related strains that cause a variety of diseases, such as intestinal disease, hepatitis and respiratory disease, as well as encephalitis and chronic demyelinating disease.There was controversy over whether SARS-CoV designates a new corona virus group or whether it is a member of Group II. It has been recorded that SARS-CoV belongs to Group III so far only includes bird corona viruses such as IBV, turkey corona virus and pheasant corona virus. Using the PCR reverse transcription (RT-PCR), corona virus sequences were detected. Phylogenetic analyzes of replicase and nucleocapsid (N) sequences indicate that these viruses are members of group III, but so far have not been characterized (Weiss & Navas-Martin, 2005).

Rationale and virology of corona virus

Corona viruses are members of the subfamily Corona virinae in the family Corona viridae and of the class Nidovirales. The subfamily consists of four genera, Alpha corona virus, Beta corona virus, Gamma corona virus and Delta corona virus, based on their phylogenetic relationships and genomic structures (Cui et al., 2019). Corona viruses are spherical or pleimorphic, with a diameter of 80-120 nm. Under the electron microscope, its surface is decorated with projections consisting of the tripartite (S) glycoprotein pin. Smaller projections consisting of the dimeric haemagglutinin-esterase (HE) protein are observed in some beta corona viruses such as HCoV-OC43 and HCoV-HV KU1. Both S and HE are type I transmembrane proteins with large resection and short endotomin. The viral envelope is supported by the glycoprotein membrane, the most abundant structural protein embodied in the envelope via three transmembrane regions. In addition, a small transmembrane protein known as envelope protein exists in a low amount. Finally, the nucleocapsid protein binds to the RNA genome one fashion with beads, forming the helical symmetrical nucleocapsid. The corona virus genome is a positive meaning, non-fragmented, monoclonal RNA, with surprisingly large size ranging from 27 to 32 kilobases. Corona virus replicase is encoded by two large overlaps; ORF (ORF1a and ORF1b) occupies about two-thirds of the genome and is directly translated by genomic RNA. Structural and auxiliary genes, however, are translated from sub-genomic RNAs (sgRNAs) that are generated during the transcription/replication of the genome

attachment and entry, translation of viral replicase, transcription and genome replication, translation of structural proteins and assembly and release of virionium. In each process, each step is briefly examined and summarizes host factors involved in the replication of corona virus (Fung & Liu., 2019). Alpha corona virus and beta corona virus only infect mammals. Gamma corona virus and delta corona virus infect birds, but some of them can also infect mammals. Alpha corona viruses and beta corona viruses usually cause respiratory disease in humans and gastroenteritis in animals. The two highly pathogenic viruses, SARS-CoV and MERS-CoV, cause severe respiratory capacity syndrome in humans and the other four human corona viruses (HCoV-NL63, HCoV-229E, HCoVC43 and HKU1) cause only mild upper respiratory diseases in immunosuppressive hosts, although some of them can cause serious infections in infants, young children and the elderly (Cui et al., 2019).

Discussion

Corona virus 2019 (Covid-19) is caused by a new corona virus (severe acute respiratory syndrome – corona virus 2 (SARS-CoV-2) that appeared in December 2019 and is responsible for the current pandemic, a state of international urgency concerning public health (Song et al., 2020).

COVID-19 is reported to be a new member of the genus beta corona virus and is closely associated with severe acute respiratory syndrome – corona virus (SARS-CoV). Compared to SARS-CoV and Middle East respiratory syndrome – corona virus (MERS-CoV), the COVID virus 19-19 shows faster human-to-human transmission, which led the World Health Organization to declare a global public health emergency (Gao et.al., 2020).SARS-CoV, SARS-CoV-2, and HCoV-NL63 use ACE2 as a cell input receptor. It seems a notable case that all known human corona virus receptors are cell surface peptidases, particularly interactions where they do not include the active location of the endopeptidase. It is worth noting in particular the presence of a specific region within ACE2, which is targeted by three corona viruses (Matheson & Lehner, 2020).

ACE2 is a transmembrane protein that is best characterized for its homeostatic role in balancing the effects of ACE on the cardiovascular system.ACE converts angiotensin I into angiotensin II, a highly active octapeptide that exhibits both a vasocomponent in vascular contraction to increase blood pressure and a pro-inflammatory effect. The carboxypeptidase activity of ACE2 converts angiotensin II into angiotensin heptapeptide-a functional angiotensin II antagonist.

Because ACE is strongly expressed in the vascular endothelial cells of the lungs, angiotensin II is also likely to be high in the pulmonary vascular system. Indeed, the deletion of ACE2 in mouse acute pulmonary injury models leads to more severe disease, which suggests a protective role for ACE2 in the pulmonary tissue. In many virus-host interactions, the expression of the viral receptor is regulated down on infected cells and the expression of ACE2 in the mouse lungs was reduced by infection with SARS-CoV. The depletion of ACE2 can therefore play a causal role in pulmonary damage caused by SARS-CoV and SARS-CoV-2, and high plasma angiotensin II refers to patients with COVID-19; however, MERS-CoV causes similar lung disease without targeting ACE2 other factors must also be important. As a respiratory virus, SARS-CoV-2 must first enter cells that align the respiratory system. The unicellular sequence and the RNA in situ mapping of the human respiratory tract indicate that the expression ACE2 and TMPRSS2 is the highest in acrylic nasal epithelial cells, with smaller amounts in bronchial epithelial This translates into greater susceptibility of epithelial cells upper and lower respiratory tract for infection with SARS-CoV-2 in vitro and matches the pathology of the disease (Matheson & Lehner, 2020). Viruses that reproduce in vitro and produce a cytopathic effect (CPE), subsequent virus identification methods may fail. Antibodies created against known viruses may not recognize the cultured virus, and specific methods for virus identification using a PCR method may not recognize the new viral genome. To solve both problems, a new method for discovering viruses was developed based on the technique of polymorphism of length-enhanced fragment cDNA (Bachem et al., 1996). Where reported to identify a new coronavirus using this Virus-Discovery-cDNAAFLP (VIDISCA) method (Hoek et al., 2004).

Clinical symptomatology: The full clinical manifestation is not yet clear as reported symptoms range from mild to severe, with some cases even leading to death (Adhikari et al.,2020). The disease is transmitted by inhalation or contact with infected droplets and the incubation period

ranges from 2 to 14 days (Singhal, 2020). Reported symptoms are fever, cough, myalgia or fatigue, pneumonia and complicated dyspnoea, while less commonly reported symptoms include headache, diarrhea, haemoptysis, runny nose and phlegm-producing cough (Adhikari et al., 2020). In addition, the American Academy of Otorhinolaryngology for surgery head and neck pain has published a statement pointing out that immunity and hypogeusia are 'significant symptoms' associated with Covid-19 (Baig, 2020).

In addition to overt respiratory and febrile symptoms of severe acute corona virus 2 respiratory syndromes (SARS-CoV-2), the symptom complex may include digestive-related symptoms such as anorexia, nausea, vomiting and diarrhea. It is important to understand the frequency of nausea and vomiting during Covid-19, because if you delay your hospitalization the clinical picture may be worse than those without digestive symptoms (Andrews et. al., 2020; Law et al., 2020). The clinical spectrum of Covid-19 varies from asymptomatic or missing symptoms in clinical conditions characterized by respiratory failure requiring mechanical ventilation and support in ICUs, to multi-organ and systemic manifestations with respect to sepsis, septic shock and Multiple Organ Dysfunction Syndrome (Choy et. al., 2020). The Chinese CDC report divided clinical manifestations of the disease according to severity into:

- Mild disease: non-pneumonia and mild pneumonia.
- Severe disease: dyspnoea, respiratory rate ≥ 30/min, blood oxygen saturation (SpO2) ≤ 93%.
- Critical disease: respiratory failure, septic shock and/or multiple organ dysfunction (Dong et al., 2020).

In those patients who show worsening inflammation caused by lung damage, there is a decrease in oxygen saturation (<93%).This indicates the criticality of the disease and there may be a rapid deterioration of respiratory functions (Dong et al., 2020).

Reports indicate that in addition to conventional respiratory symptoms of influenza, patients also display neurological signs and symptoms (Kotrotsiou et al., 2021). Several neurological manifestations in the COVID-19-related literature have been reported, classified into Central Nervous System (CNS) related events such as headache, dizziness, decreased consciousness, acute au Cerebrovascular disease, epilepsy and Peripheral Nervous System (PNS) associated manifestations such as hyposmia/anosmia, hypogeusia/ageusia, muscle pain and Guillain-Barre syndrome. In order to determine if there is CNS involvement by SARS-CoV-2, the early symptoms of smell loss, ataxia and convulsions should be evaluated (Niazkar et.al., 2020). CNS involvement may be associated with poor prognosis and worsening of the disease (Khatoon et. al, 2020). Events in patients with taxonomic SARS-CoV in the past have undoubtedly shown that corona viruses affect the brain. It would be no surprise that COVID-19 follows the same trend, as both viruses are almost identical taxonomically (Baig, 2020).Fever with headaches may occur early in Covid-19 patients. Specific manifestations related to neurological deficits such as loss of smell, taste, ataxia and convulsions have been reported. Possible entry of SARS-CoV-2 to reach the brain via plaque or after entry into systemic circulation resulting in lung infection, in early or late phases Covid-19 may lead to loss of involuntary control of breathing resulting in acute respiratory failure requiring assisted ventilation.

Along these lines, an early differential diagnosis in patients with terminal Covid-19 disease with neurological deficits would be life-saving (Sankar et al., 2020, Theofanidis, 2021). Although clinical manifestations of Covid-19 are dominated by respiratory symptoms, some patients have severe cardiovascular damage. The majority of these patients experienced heart palpitations and chest tightness rather than respiratory symptoms such as fever and cough, and were later diagnosed with Covid-19. Also, an increased risk of death may occur in Covid-19 patients with underlying cardiovascular disease (CVD), so understanding the damage caused by SARS-19 is of paramount importance CoV-2 in the cardiovascular system and underlying mechanisms. It was reported by the National Health Commission of China (NHC) that among patients who died from COVID-19 11.8% without underlying CVD had serious heart damage or cardiac arrest during hospitalization. In conclusion, the incidence of cardiovascular symptoms in patients with Covid-19 is high due to systemic inflammation immune system disorders during disease progression (Zheng et al., 2020).In the case of children, the disease appears to be milder; however this condition appears to change. Clinical symptoms are similar to any acute

respiratory viral infection with less pronounced nasal symptoms. Infants and young children have had a relatively greater worsening of the disease than older children; however, the number of deaths in children is low (Sankar et al. 2020).On the other hand, studies have shown that the elderly and those with co-morbidities, such as hypertension, cardiovascular diseases, diabetes, chronic respiratory disease and chronic renal disease, infected with the virus, have a worsening clinical picture and a higher mortality rate. After 5-7 days of infection with the virus, elderly patients with already impaired pulmonary function begin to experience shortness of breath and increased respiratory rate (Choy et al., 2020). According to a study in 21 patients with critical illness infected with SARS-CoV-2, with a mean age of 70 years, it was found that the most common symptoms were dyspnoea (76%), fever (52%) and cough (48%). Up to 86% of the elderly developed with co-morbidities, the most important being Chronic Kidney Disease (48%), congestive heart failure (43%), Chronic Obstructive Pulmonary Disease (COPD) (33%) and diabetes (33%). It was also noted that most of the fatalities to date were of elderly patients with co-morbidities (Shahid et. al., 2020).

Conclusions: The primary objective of the International Health Organizations is to limit the international spread of the pandemic and prevent the spread of new added outbreaks. Due to the initial lack of effective vaccines and treatments, the main readily available method to reduce SARS-CoV-2 transmission is to identify and isolate infected patients as quickly and effectively as possible especially if a new strain of the virus is suspected or identified.

References

Adhikari, S., Meng, S., Wu, Y.J. (2020). Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. *Infect Dis Poverty 17*;9(1):29.

Agostini, M., Andres, E., Sims, A. (2020). Coronavirus Susceptibility to the Antiviral Remdesivir (GS-5734) Is Mediated by the Viral Polymerase and the Proofreading Exoribonuclease. *mBio, 6*;9(2):e00221-18.

Andrews, P., Cai, W., Rudd, J.A., Sanger, G.J. (2020). COVID-19, nausea, and vomiting. *J Gastroenterol Hepatol. 36*(3):646-656.

Bachem, C.W., R.S., van der Hoeven, S.M., de Bruijn (1996). Visualization of differential gene expression using a novel method of RNA fingerprinting based on AFLP: analysis of gene expression during potato tuber development. *Plant J, 9*(5):745-753.

Baig, A.M. (2020). Neurological manifestations in COVID-19 caused by SARS-CoV-2. CNS *Neurosci Ther. 26*(5):499-501.

Choy, K.T., Wong, A., Kaewpreedee, P., (2020). Remdesivir, lopinavir, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro. *Antiviral Research, 178*:104786.

Cohen, J. (2020). Chinese researchers reveal draft genome of virus implicated in Wuhan pneumonia outbreak. *JAMA, 674*(12):1752-1759.

Compton, S., Barthold, S.W., Smith, A. (1993). The cellular and molecular pathogenesis of coronaviruses. *Lab Anim Sci, 43*(1):15-28.

Cui , J., Li, F., Shi, Z.L. (2019). Origin and evolution of pathogenic coronaviruses. *Nat Rev Microbiol, 17*(3):181-192.

Dong, L., Tian, J., He, S., Dong, L., Tian J., He, S., Zhu, C., Wang J., Liu C., Yang, J. (2020). Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn. *Jama, 323*(18):1846–1848.

Fung, S., Liu, DX. (2019).Human Coronavirus: Host-Pathogen Interaction. *Annu Rev Microbiol, 73*:529-557.

Gao, J., Tian., Yang, X. (2020). Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Bioscience Trends, 14*(1):72-73.

Hoek, L., Pyrc, K., Jebbink, J.F. (2004). Identification of a new human coronavirus. *Nat Med, 10*(4):368-73.

Hui, D., Memish, Z., Zumla, A. (2020).Severe acute respiratory syndrome vs. the Middle East respiratory syndrome. *Curr Opin Pulm Med, 20*(3):233-41.

Khan, N. (2020).New Virus Discovered by Chinese Scientists Investigating Pneumonia Outbreak. *Wall Street Journal, 12*(142) 0099-9660.

Khatoon, F., Prasad, K., Kumar, V.(2020). Neurological manifestations of COVID-19: available evidences and a new paradigm. *J Neurovirol. 26*(5):619-630.

Kotrotsiou, S., Theofanidis, D., Malliarou, M., Konstanti, Z., Sarafis, P., Tsioumanis, G., Paralikas, T. Investigating Nurses Stress Response Strategies During the COVID-19 Pandemic. *Mater Sociomed. 33*(3):168-173.

Lau, S., Woo, P., Yip, C., Lau, S., Woo, P., Yip, C., Tse, H., Tsoi H., Cheng V., Lee, P., Tang, B., Cheung, C., Lee, R., So, L., Lau, Y., Chan, K., Yuen K. (2006). Coronavirus HKU1 &other coronavirus infections in Hong Kong. *J Clin Microbiol, 44*(6):2063-77.

Law, S., Wingnang Leung, A., Xu C. (2020). Severe acute respiratory syndrome (SARS) and coronavirus disease-2019 (COVID-19): From causes to preventions in Hong Kong. *International Journal of Infectious Diseases, 94*:156-163.

Lofti, M., Hamblin, M., Rezaei, N. (2020). COVID-19: Transmission, prevention, and potential therapeutic opportunities. *Clinica Chimica Acta, 508*:254-266.

Matheson N.J., Lehner P.J. (2020). How does SARS-CoV-2 cause COVID-19? *Science, 31*; 369(6503):510-511.

McKee, D., Sternberg, A., Stange, U. (2020). Candidate drugs against SARS-CoV-2 and COVID-19. *Pharmacological Research, 157*:104859.

Niazkar, H.R., Zibaee, B., Nasimi, A. (2020). The neurological manifestations of COVID-19: a review article. *Neurol Sci. 41*(7):1667-1671.

Rubin, G., Ryerson, Ch., Haramati, L. (2020). The Role of Chest Imaging in Patient Management During the COVID-19 Pandemic: A Multinational Consensus Statement From the Fleischner Society. *Radiology, 158*(1):106-116.

Sankar, J., Dhochak, N., Kabra. (2020) COVID-19 in Children: Clinical Approach and Management. *Indian J Pediatr. 87*(6):433-442.

Shahid, Z., Kalayanamitra, R., McClafferty, B., Kepko, D., Ramgobin, D., Patel, R., Aggarwal, C., Vunnam, R., Sahu, N., Bhatt, D., Jones, K., Golamari, R., Jain, R. (2020). COVID-19 and Older Adults: What We Know. *J Am Geriatr Soc.68*(5):926-929.

Singhal, T. (2020) A Review of Coronavirus Disease-2019 (COVID-19). *Indian J Pediatr. 87*(4):281-286.

Song, J.Y., Yun, J.D., Noh, JY. (2020). Covid-19 in South Korea - Challenges of Subclinical Manifestations. *The New England Journal of Medicine, 382*(19):1858-1859.

Theofanidis, D. (2021). Research nurse and nurse researcher: differences and similarities. *Health & Research Journal, 7(*4):151-154.

Weiss, J., Navas-Martin, S. (2005). Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. *Microbiol Mol Biol Rev, 69*(4):635-664.

Zheng, Y.Y., Ma, Y.T., Zhang, J.Y., Xie, X. (2020). COVID-19 and the cardiovascular system. *Nat Rev Cardiol 17*:259–260.

Zu, Z., Jiang, M., Xu, P., Zu, Z., Jiang, M., Xu, P., Chen W., Ni, Q., Lu, G., Zhang, L. (2020). Coronavirus Disease 2019 (COVID-19): A Perspective from China. *Radiology, 296*(2):E15-E25.