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Multidisciplinary Academic Journal Publisher

Coronavirus disease 2019 (COVID-19)

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Abstract: Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Common symptoms include fever, cough, and shortness of breath. Other symptoms may include muscle pain, sputum production, diarrhea, sore throat, loss of smell, and abdominal pain. While the majority of cases result in mild symptoms, some progress to viral pneumonia and multi-organ failure. As of 28 March 2020, the overall rate of deaths per number of diagnosed cases is 4.7 percent; ranging from 0.2% to 15% according to age group and other health problems. In comparison, the mortality rate of the 1918 flu pandemic was approximately 3% to 5%. This article introduces recent research reports as references in the related studies.
[Mark Herbert. **Coronavirus disease 2019 (COVID-19).** *Researcher* 2020;12(4):14-23]. ISSN 1553-9865 (print); ISSN 2163-8950 (online). http://www.sciencepub.net/researcher. 3. doi:10.7537/marsrsj120420.03.

Key words: coronavirus; disease; COVID-19; lung; stem cell; life; research

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Lin, Zhao et al. 2020). Common symptoms include fever, cough, and shortness of breath. Other symptoms may include muscle pain, sputum production, diarrhea, sore throat, loss of smell, and abdominal pain. While the majority of cases result in mild symptoms, some progress to viral pneumonia and multi-organ failure. As of 28 March 2020, the overall rate of deaths per number of diagnosed cases is 4.7%; ranging from 0.2% to 15% according to age group and other health problems. In comparison, the mortality rate of the 1918 flu pandemic was approximately 3% to 5% (Kakodkar, Kaka et al. 2020).

The following introduces recent reports as references in the related studies.

The virus is spread mainly through close contact and via respiratory droplets produced when people cough or sneeze. Respiratory droplets may be produced during breathing but the virus is not generally airborne. However, a recent study by the American National Institute of Health (NIH) indicates that the virus remains viable in aerosoles for up to 3 hours. For healthcare professionals caring for patients with confirmed Covid-19 infection or suspected Covid-19 infection, the CDC recommends placing the patient in an Airborne Infection Isolation Room (AIIR) in addition to using standard precautions, contact precautions, and airborne precautions. People may also contract COVID-19 by touching a contaminated surface and then their face. It is most contagious when people are symptomatic, although spread may be possible before symptoms appear. The virus can survive on surfaces up to 72 hours. Time from exposure to onset of symptoms is generally between two and fourteen days, with an average of five days. The standard method of diagnosis is by reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab. The infection can also be diagnosed from a combination of symptoms, risk factors and a chest CT scan showing features of pneumonia (Lauer, Grantz et al. 2020).

The emergence of SARS-CoV-2 has once again exposed the weaknesses of global health systems preparedness, ability to respond to an infectious threat, the rapidity of transmission of infections across international borders and the ineffectiveness of knee-jerk policy responses to emerging/re-emerging infectious disease threats. With the key learning points from the ongoing efforts to prevent and contain COVID-19 and identifies the need to invest in health systems, community-led response mechanisms and the need for preparedness and global health security (Chatterjee, Nagi et al. 2020).

The emergence of SARS-CoV-2, since the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012, marked the third introduction of a highly pathogenic and large-scale epidemic coronavirus into the human population in the twenty-first century. As of 1 March 2020, a total of 87,137 confirmed cases globally, 79,968 confirmed in China and 7169 outside of China, with 2977 deaths (3.4%) had been reported by WHO. Meanwhile,

several independent research groups have identified that SARS-CoV-2 belongs to beta-coronavirus, with highly identical genome to bat coronavirus, pointing to bat as the natural host. The novel coronavirus uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as that for SARS-CoV, and mainly spreads through the respiratory tract. Importantly, increasingly evidence showed sustained human-to-human transmission, along with many exported cases across the globe. The clinical symptoms of COVID-19 patients include fever, cough, fatigue and a small population of patients appeared gastrointestinal infection symptoms. The elderly and people with underlying diseases are susceptible to infection and prone to serious outcomes, which may be associated with acute respiratory distress syndrome (ARDS) and cytokine storm. Currently, there are few specific antiviral strategies, but several potent candidates of antivirals and repurposed drugs are under urgent investigation. In this review, we summarized the latest research progress of the epidemiology, pathogenesis, and clinical characteristics of COVID-19, and discussed the current treatment and scientific advancements to combat the epidemic novel coronavirus (Guo, Cao et al. 2020).

In the WHO European Region, COVID-19 surveillance was implemented 27 January 2020. We detail the first European cases. As at 21 February, nine European countries reported 47 cases. Among 38 cases studied, 21 were linked to two clusters in Germany and France, 14 were infected in China. Median case age was 42 years; 25 were male. Late detection of the clusters' index cases delayed isolation of further local cases. As at 5 March, there were 4,250 cases (Spiteri, Fielding et al. 2020).

Recommended measures to prevent infection include frequent hand washing, social distancing, covering coughs and sneezes with a tissue or inner elbow, and keeping unwashed hands away from the face. The use of masks is recommended for those who suspect they have the virus and their caregivers. Recommendations for mask use by the general public vary, with some authorities recommending against their use, some recommending their use, and others requiring their use. Currently, there is no vaccine or specific antiviral treatment for COVID-19. Management involves treatment of symptoms, supportive care, isolation, and experimental measures. Local transmission of the disease has been recorded in many countries across all six WHO regions (Kim 2020).

Those infected with the virus may be asymptomatic or develop flu-like symptoms, including fever, cough, fatigue, and shortness of breath. Emergency symptoms include difficulty breathing, persistent chest pain or pressure, confusion, difficulty waking, and bluish face or lips; immediate medical attention is advised if these symptoms are present (Scott, Zabel et al. 2020). Less commonly, upper respiratory symptoms, such as sneezing, runny nose, or sore throat may be seen. Symptoms such as nausea, vomiting, and diarrhea have been observed in varying percentages. Some cases in China initially presented only with chest tightness and palpitations. In March 2020 there were reports indicating that anosmia may be a common symptom among those who have mild disease, although not as common as initially reported. In some, the disease may progress to pneumonia, multi-organ failure, and death. In those who develop severe symptoms, time from symptom onset to needing mechanical ventilation is typically eight days (Rello, Tejada et al. 2020).

As is common with infections, there is a delay between the moment when a person is infected with the virus and the time when they develop symptoms. This is called the incubation period. The incubation period for COVID-19 is typically five to six days but may range from two to 14 days. 97.5% of people who develop symptoms will do so within 11.5 days of infection. Scientists are endeavoring to find antivirals specific to the virus. Several drugs such as chloroquine, arbidol, remdesivir, and favipiravir are currently undergoing clinical studies to test their efficacy and safety in the treatment of coronavirus disease 2019 (COVID-19) in China; some promising results have been achieved thus far. This article summarizes agents with potential efficacy against SARS-CoV-2 (Dong, Hu et al. 2020).

Reports indicate that not all who are infected develop symptoms, but their role in transmission is unknown. Preliminary evidence suggests asymptomatic cases may contribute to the spread of the disease. The proportion of infected people who do not display symptoms is currently unknown and being studied, with South Korea's CDC reporting that 20% of all confirmed cases remained asymptomatic during their hospital stay.

SARS-CoV-2 infection can cause mild illness and result in positive tests for up to 18 days after diagnosis, without evidence of transmission to close contacts. These data might inform public health strategies to manage individuals with asymptomatic infection or mild illness (Scott, Zabel et al. 2020).

The disease is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is primarily spread between people during close contact and via respiratory droplets from coughs and sneezes. A study investigating the rate of decay of the virus found no viable viruses after four hours on copper, 24 hours on cardboard, 72 hours on stainless steel, and 72 hours on plastic. However, detection rates did not reach 100% and varied between surface type.

Estimation of the rate of decay with a Bayesian regression model suggests that viruses may remain viable up to 18 hours on copper, 55 hours on cardboard, 90 hours on stainless steel, and over 100 hours on plastic. The virus remained viable in aerosols throughout the time of the experiment. The virus has also been found in faeces, and transmission through faeces is being researched. The virus has been found in the faeces of as many as 53% of hospitalised people and more anal swab positives have been found than oral swab positives in the later stages of infection. The virus was found in faeces from one to twelve days, and seventeen percent of patients continued to present the virus in faeces after no longer presenting them in respiratory samples, indicating that the viral gastrointestinal infection and the potential fecal-oral transmission can last even after viral clearance in the respiratory tract. Reoccurrence of the virus has also been detected through anal swabs suggesting a shift from more oral positive during the early stages of the disease to more anal positive during later periods.

The disease spreads faster where people are close together or travel between areas. Travel restrictions can reduce the basic reproduction number from 2.35 to 1.05, allowing the epidemic to be more manageable. An observational study of nine people found no vertical transmission from mother to the newborn. The virus spreads faster than its two ancestors the SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), but has lower fatality. The global impact of this new epidemic is yet uncertain (Singhal 2020).

The lungs are the organs most affected by COVID-19 because the virus accesses host cells via the enzyme ACE2, which is most abundant in the type II alveolar cells of the lungs. The virus uses a special surface glycoprotein called a spike to connect to ACE2 and enter the host cell. The density of ACE2 in each tissue correlates with the severity of the disease in that tissue and some have suggested that decreasing ACE2 activity might be protective, though another view is that increasing ACE2 using angiotensin II receptor blocker medications could be protective and that these hypotheses need to be tested. As the alveolar disease progresses, respiratory failure might develop and death may follow. The virus also affects gastrointestinal organs as ACE2 is abundantly expressed in the glandular cells of gastric, duodenal and rectal epithelium as well as endothelial cells and enterocytes of the small intestine.

The current scientific data and status of governing bodies such as the Center of Disease Control (CDC) and the WHO on the usage of controversial therapies such as angiotensin-converting enzyme (ACE) inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs) (Ibuprofen), and corticosteroids usage in COVID-19 are discussed. The composite collection of accredited studies on each of these subtopics of COVID-19 within this review will enable clarification and focus on the current status and direction in the planning of the management of this global pandemic (Kakodkar, Kaka et al. 2020).

The WHO has published several testing protocols for the disease. The standard method of testing is real-time reverse transcription polymerase chain reaction (rRT-PCR). The test is typically done on respiratory samples obtained by a nasopharyngeal swab, however a nasal swab or sputum sample may also be used. Results are generally available within a few hours to two days. Blood tests can be used, but these require two blood samples taken two weeks apart and the results have little immediate value. Chinese scientists were able to isolate a strain of the coronavirus and publish the genetic sequence so laboratories across the world could independently develop polymerase chain reaction (PCR) tests to detect infection by the virus. As of 19 March 2020, there were no antibody tests though efforts to develop them are ongoing. The FDA approved the first point-of-care test on 21 March 2020 for use at the end of that month.

Diagnostic guidelines released by Zhongnan Hospital of Wuhan University suggested methods for detecting infections based upon clinical features and epidemiological risk. These involved identifying people who had at least two of the following symptoms in addition to a history of travel to Wuhan or contact with other infected people: fever, imaging features of pneumonia, normal or reduced white blood cell count, or reduced lymphocyte count.

A March 2020 review concluded that chest X-rays are of little value in early stages, whereas CT scans of the chest are useful even before symptoms occur. Typical features on CT include bilateral multilobar ground-glass opacificities with a peripheral, asymmetric and posterior distribution. Subpleural dominance, crazy paving and consolidation develop as the disease evolves. As of March 2020, the American College of Radiology recommends that CT should not be used to screen for or as a first-line test to diagnose COVID-19. Preventive measures to reduce the chances of infection include staying at home, avoiding crowded places, washing hands with soap and water often and for at least 20 seconds, practicing good respiratory hygiene and avoiding touching the eyes, nose, or mouth with unwashed hands. The CDC recommends covering the mouth and nose with a tissue when coughing or sneezing and recommends using the inside of the elbow if no tissue is available. They also recommend proper hand hygiene after any cough or sneeze. Social distancing strategies aim to reduce contact of infected persons with large groups by closing schools and workplaces, restricting travel,

and canceling mass gatherings. Social distancing also includes that people stay at least six feet apart (about 1.80 meters).

Because a vaccine against SARS-CoV-2 is not expected to become available until 2021 at the earliest, [98] a key part of managing the COVID-19 pandemic is trying to decrease the epidemic peak, known as flattening the curve, through various measures seeking to reduce the rate of new infections. Slowing the infection rate helps decrease the risk of health services being overwhelmed, allowing for better treatment of current cases, and delaying additional cases until therapeutics or a vaccine become available.

According to the WHO, the use of masks is recommended only if a person is coughing or sneezing or when one is taking care of someone with a suspected infection. Some countries also recommend healthy individuals to wear face masks, including China, Thailand, Czech Republic, and Austria, etc. In order to meet the need for masks, the WHO estimates that global production will need to increase by 40%. Hoarding and speculation have worsened the problem, with the price of masks increasing six fold, N95 respirators tripled, and gowns doubled. Some health experts consider wearing non-medical grade masks and other face coverings like scarves or bandanas a good way to prevent people from touching their mouths and noses, even if non-medical coverings would not protect against a direct sneeze or cough from an infected person.

Those diagnosed with COVID-19 or who believe they may be infected are advised by the CDC to stay home except to get medical care, call ahead before visiting a healthcare provider, wear a face mask before entering the healthcare provider's office and when in any room or vehicle with another person, cover coughs and sneezes with a tissue, regularly wash hands with soap and water, and avoid sharing personal household items. The CDC also recommends that individuals wash hands often with soap and water for at least 20 seconds, especially after going to the toilet or when hands are visibly dirty, before eating and after blowing one's nose, coughing, or sneezing. It further recommends using an alcohol-based hand sanitiser with at least 60% alcohol, but only when soap and water are not readily available.

For areas where commercial hand sanitisers are not readily available, WHO provides two formulations for local productions. In these formulations, the antimicrobial activity arises from ethanol or isopropanol. Hydrogen peroxide is used to help eliminate bacterial spores in the alcohol; it is not an active substance for hand antisepsis. Glycerol is added as a humectant. People are managed with supportive care, which may include fluid, oxygen support, and supporting other affected vital organs. The CDC recommends that those who suspect they carry the virus wear a simple face mask. Extracorporeal membrane oxygenation (ECMO) has been used to address the issue of respiratory failure, but its benefits are still under consideration. The WHO and Chinese National Health Commission have published recommendations for taking care of people who are hospitalised with COVID-19. Intensivists and pulmonologists in the U.S. have compiled treatment recommendations from various agencies into a free resource, the IBCC.

Some medical professionals recommend paracetamol (acetaminophen) over ibuprofen for first-line use. The WHO does not oppose the use of non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen for symptoms, and the FDA says currently there is no evidence that NSAIDs worsen COVID-19 symptoms. While theoretical concerns have been raised about ACE inhibitors and angiotensin receptor blockers, as of 19 March 2020, these are not sufficient to justify stopping these medications. Steroids such as methylprednisolone are not recommended unless the disease is complicated by acute respiratory distress syndrome.

Precautions must be taken to minimise the risk of virus transmission, especially in healthcare settings when performing procedures that can generate aerosols, such as intubation or hand ventilation. CDC outlines the specific guidelines for the use of personal protective equipment (PPE) during the pandemic. The recommended gear includes: respirator or facemask, gown, medical gloves and eye protection. When available, respirators are preferred. N95 respirators are approved for industrial settings but the FDA has authorised the masks for use under an Emergency Use Authorization (EUA). They are designed to protect from airborne particles like dust but effectiveness against a specific biological agent is not guaranteed for off-label uses. When masks are not available the CDC recommends using face shields, or as a last resort homemade masks.

Most cases of COVID-19 are not severe enough to require mechanical ventilation (artificial assistance to support breathing), but a percentage of cases do. Some Canadian doctors recommend the use of invasive mechanical ventilation because this technique limits the spread of aerosolised transmission vectors. Severe cases are most common in older adults (those older than 60 years and especially those older than 80 years). Many developed countries do not have enough hospital beds per capita, which limits a health system's capacity to handle a sudden spike in the number of COVID-19 cases severe enough to require hospitalization. This limited capacity is a significant driver of the need to flatten the curve. One study in China found 5% were admitted to intensive care units,

2.3% needed mechanical support of ventilation, and 1.4% died. Around 20-30% of the people in hospital with pneumonia from COVID-19 needed ICU care for respiratory support.

Mechanical ventilation becomes more complex as ARDS develops in COVID-19 and oxygenation becomes more difficult. Ventilators capable of pressure control modes and high PEEP are needed to maximise oxygen delivery while minimizing the risk of ventilator-associated lung injury and pneumothorax. High PEEP may not be available on older ventilators. No medications are approved to treat the disease by the WHO although some are recommended by individual national medical authorities. Research into potential treatments started in January 2020, and several antiviral drugs are in clinical trials. Although new medications may take until 2021 to develop, several of the medications being tested are already approved for other uses, or are already in advanced testing. Antiviral medication may be tried in people with severe disease. The WHO recommended volunteers take part in trials of the effectiveness and safety of potential treatments.

In February 2020, China launched a mobile app to deal with the disease outbreak. Users are asked to enter their name and ID number. The app is able to detect close contact using surveillance data and therefore a potential risk of infection. Every user can also check the status of 3 other users. If a potential risk is detected, the app not only recommends self-quarantine, it also alerts local health officials. Big data analytics on cellphone data, facial recognition technology, mobile phone tracking and artificial intelligence are used to track infected people and people whom they contacted in South Korea, Taiwan, and Singapore. In March 2020, the Israeli government enabled security agencies to track mobile phone data of people supposed to have coronavirus. The measure was taken to enforce quarantine and protect those who may come into contact with infected citizens. Also in March 2020, Deutsche Telekom shared aggregated phone location data with the German federal government agency, Robert Koch Institute, in order to research and prevent the spread of the virus. Russia deployed facial recognition technology to detect quarantine breakers. Italian regional health commissioner Giulio Gallera said he has been informed by mobile phone operators that 40% of people are continuing to move around anyway. German government conducted a 48 hours weekend hackathon with more than 42,000 participants. Also the president of Estonia, Kersti Kaljulaid, made a global call for creative solutions against the spread of coronavirus.

Individuals may experience distress from quarantine, travel restrictions, side effects of treatment, or fear of the infection itself. To address these concerns, the National Health Commission of China published a national guideline for psychological crisis intervention on 27 January 2020. The disease may take a mild course with few or no symptoms, resembling other common upper respiratory diseases such as the common cold. Mild cases typically recover within two weeks, while those with severe or critical diseases may take three to six weeks to recover. Among those who have died, the time from symptom onset to death has ranged from two to eight weeks.

Children are susceptible to the disease, but are likely to have milder symptoms and a lower chance of severe disease than adults; in those younger than 50 years, the risk of death is less than 0.5%, while in those older than 70 it is more than 8%. Pregnant women may be at higher risk for severe infection with COVID-19 based on data from other similar viruses, like SARS and MERS, but data for COVID-19 is lacking.

In some people, COVID-19 may affect the lungs causing pneumonia. In those most severely affected, COVID-19 may rapidly progress to acute respiratory distress syndrome (ARDS) causing respiratory failure, septic shock, or multi-organ failure. Complications associated with COVID-19 include sepsis, abnormal clotting, and damage to the heart, kidneys, and liver. Clotting abnormalities, specifically an increase in prothrombin time, have been described in 6% of those admitted to hospital with COVID-19, while abnormal kidney function is seen in 4% of this group. Liver injury as shown by blood markers of liver damage is frequently seen in severe cases. Some studies have found that the neutrophil to lymphocyte ratio (NLR) may be helpful in early screening for severe illness.

Many of those who die of COVID-19 have pre-existing conditions, including hypertension, diabetes mellitus, and cardiovascular disease. The Istituto Superiore di Sanità (ISS) reported that 88% of overall deaths in Italy had at least one comorbidity. An additional report by the ISS reported that out of 10.4% of deaths where medical charts were available for review, there were at least one comorbidity in 97.9% of sampled patients with the average patient having 2.7 diseases. According to the same report, the median time between onset of symptoms and death was nine days, with five being spent hospitalised. However, patients transferred to an ICU had a median time of six days between hospitalization and death. In a study of early cases, the median time from exhibiting initial symptoms to death was 14 days, with a full range of six to 41 days. In a study by the National Health Commission (NHC) of China, men had a death rate of 2.8% while women had a death rate of 1.7%. Histopathological examinations of post-mortem lung samples show diffuse alveolar damage with cellular

fibromyxoid exudates in both lungs. Viral cytopathic changes were observed in the pneumocytes. The lung picture resembled acute respiratory distress syndrome (ARDS). In 11.8% of the deaths reported by the National Health Commission of China, heart damage was noted by elevated levels of troponin or cardiac arrest.

Availability of medical resources and the socioeconomics of a region may also affect mortality. Estimates of the mortality from the condition vary because of those regional differences, but also because of methodological difficulties. The under-counting of mild cases can cause the mortality rate to be overestimated. However, the fact that deaths are the result of cases contracted in the past can mean the current mortality rate is underestimated.

In April 2020 in the Austrian village of Ischgl the Medical University of Innsbruck will conduct tests how many persons have corona virus antibodies, as the village was hit early and hard. The researchers said they want to find out how many people had COVID-19 without noticing, to judge if herd immunity is there. They also said that the high number of fatalities in Italy is caused by a high percentage of ACE inhibitors used to treat high blood pressure, and at the same time they warn to change medication as it may lead to heart attacks. It is unknown if past infection provides effective and long-term immunity in people who recover from the disease. Immunity is likely, based on the behavior of other coronaviruses, but cases in which recovery from COVID-19 have been followed by positive tests for coronavirus at a later date have been reported. It is unclear if these cases are the result of reinfection, relapse, or testing error.

The virus is thought to be natural and have an animal origin, through spillover infection. The origin is unknown but by December 2019 the spread of infection was almost entirely driven by human-to-human transmission. The earliest reported infection has been unofficially reported to have occurred on 17 November 2019 in Wuhan, China. A study of the first 41 cases of confirmed COVID-19, published in January 2020 in The Lancet, revealed the earliest date of onset as 1 December 2019. Official publications from the WHO reported the earliest onset of symptoms as 8 December 2019.

Several measures are commonly used to quantify mortality. These numbers vary by region and over time, and are influenced by the volume of testing, healthcare system quality, treatment options, time since initial outbreak, and population characteristics such as age, sex, and overall health. In late 2019, WHO assigned the emergency ICD-10 disease codes U07.1 for deaths from lab-confirmed SARS-CoV-2 infection and U07.2 for deaths from clinically or epidemiologically diagnosed COVID-19 without lab-confirmed SARS-CoV-2 infection. The death-to-case ratio reflects the number of deaths divided by the number of diagnosed cases within a given time interval. Based on WHO statistics, the global death-to-case ratio was 4.7% as of 29 March. The number varies by region.

Other measures include the case fatality rate (CFR), which reflects the percent of diagnosed individuals who die from a disease, and the infection fatality rate (IFR), which reflects the percent of infected individuals who die from a disease. These statistics are not time bound and follow a specific population from infection through case resolution. A number of academics have attempted to calculate these numbers for specific populations. While the disease is named COVID-19, the virus that causes it is named severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2. The virus was initially referred to as the 2019 novel coronavirus or 2019-nCoV. The WHO additionally uses the COVID-19 virus and the virus responsible for COVID-19 in public communications. Coronaviruses were named in 1968 for their appearance in electron micrographs which was reminiscent of the solar corona, corona meaning crown in Latin.

There is no available vaccine, but research into developing a vaccine has been undertaken by various agencies. Previous work on SARS-CoV is being utilised because SARS-CoV-2 and SARS-CoV both use the ACE2 receptor to enter human cells. There are three vaccination strategies being investigated. First, researchers aim to build a whole virus vaccine. The use of such a virus, be it inactive or dead, aims to elicit a prompt immune response of the human body to a new infection with COVID-19. A second strategy, subunit vaccines, aims to create a vaccine that sensitizes the immune system to certain subunits of the virus. In the case of SARS-CoV-2, such research focuses on the S-spike protein that helps the virus intrude the ACE2 enzyme receptor. A third strategy is that of the nucleic acid vaccines. Experimental vaccines from any of these strategies would have to be tested for safety and efficacy. On 16 March 2020, the first clinical trial of a vaccine started with four volunteers in Seattle. The vaccine contains a harmless genetic code copied from the virus that causes the disease.

Several existing antiviral medications are being evaluated for treatment of COVID-19 and some have moved into clinical trials. In March 2020, WHO launched a multi-country trial involving 10 countries called Solidarity in response to COVID-19 pandemic. Remdesivir, chloroquine and hydroxychloroquine, lopinavir/ritonavir and lopinavir/ritonavir combined with interferon beta are the experimental treatments currently being researched under Solidarity Trial. There is tentative evidence for remdesivir as of March

2020. Remdesivir inhibits SARS-CoV-2 in vitro. Phase 3 clinical trials are being conducted in the U.S., in China, and in Italy.

Chloroquine, previously used to treat malaria, was studied in China in February 2020, with positive preliminary results. However, there are calls for peer review of the research. The Guangdong Provincial Department of Science and Technology and the Guangdong Provincial Health and Health Commission issued a report stating that chloroquine phosphate improves the success rate of treatment and shortens the length of person's hospital stay and recommended it for people diagnosed with mild, moderate and severe cases of novel coronavirus pneumonia.

On 17 March, the Italian Pharmaceutical Agency included chloroquine and hydroxychloroquine in the list of drugs with positive preliminary results for treatment of COVID-19. Korean and Chinese Health Authorities recommend the use of chloroquine. However, the Wuhan Institute of Virology, while recommending a daily dose of one gram, notes that twice that dose is highly dangerous and could be lethal. On 28 March 2020, the FDA issued an emergency use authorization for hydroxychloroquine and chloroquine at the discretion of physicians treating people with COVID-19. In 2020, a trial found that lopinavir/ritonavir was ineffective in the treatment of severe illness. Nitazoxanide has been recommended for further in vivo study after demonstrating low concentration inhibition of SARS-CoV-2.

Unlike other acute infectious diseases progressing to sepsis, the severe courses of COVID19 seemingly show prolonged progression from onset of first symptoms to life-threatening deterioration of (primarily) lung function. Diagnosis relies on PCR using specimens from the respiratory tract. Severe ARDS reflects the hallmark of a critical course of the disease. Preventing nosocomial infections (primarily by correct use of personal protective equipment) and maintenance of hospitals' operational capability are of utmost importance. Departments of Anaesthesia, Intensive Care and emergency medicine will envisage major challenges (Thomas-Ruddel, Winning et al. 2020).

Studies have demonstrated that initial spike protein priming by transmembrane protease serine 2 (TMPRSS2) is essential for entry of SARS-CoV-2 via interaction with the ACE2 receptor. These findings suggest that the TMPRSS2 inhibitor camostat approved for use in Japan for inhibiting fibrosis in liver and kidney disease might constitute an effective off-label treatment. In February 2020, favipiravir was being studied in China for experimental treatment of the emergent COVID-19 disease. Cytokine storm, a life-threatening medical condition, can be a complication in the later stages of severe COVID-19. There is evidence that hydroxychloroquine has anti-cytokine storm properties.

Tocilizumab has been included in treatment guidelines by China's National Health Commission after a small study was completed. It is undergoing a phase 2 non randomized test at the national level in Italy after showing positive results in people with severe disease. Combined with a serum ferritin blood test to identify cytokine storms, it is meant to counter such developments, which are thought to be the cause of death in some affected people. The interleukin-6 receptor antagonist was approved by the FDA for treatment against cytokine release syndrome induced by a different cause, CAR T cell therapy, in 2017. The Feinstein Institute of Northwell Health announced in March a study on a human antibody that may prevent the activity of IL-6.

During the novel coronavirus pandemic, organ transplant recipients represent a frail susceptible category due to long-term immunosuppressive therapy. For this reason, clinical manifestations may differ from general population and different treatment approaches may be needed. We present the case of a 36-year-old kidney transplanted woman affected by Senior-Loken syndrome diagnosed with COVID-19 pneumonia after a contact with her positive mother. Initial symptoms were fatigue, dry cough and coryza; she never had fever nor oxygen supplementation. Hydroxychloroquine and lopinavir/ritonavir were started, and the antiviral drug was replaced with darunavir/cobicistat after two days for diarrhea. Immunosuppressant levels were closely monitored, and we observed very high tacrolimus trough levels despite initial dose reduction. The patient was left with steroid therapy alone. The peculiarity of clinical presentation and the management difficulties represent the flagship of our case-report. We stress the need for guidelines in transplant recipients with COVID-19 infection with particular regard to the management of therapy (Bartiromo, Borchi et al. 2020).

The lung virus titre was between 105-107 TCID50/g. Challenged index hamsters consistently infected naive contact hamsters housed within the same cage, resulting in similar pathology but not weight loss. All infected hamsters recovered and developed mean serum neutralising antibody titre >/=1:427 fourteen days post-challenge. Immunoprophylaxis with early convalescent serum achieved significant decrease in lung viral load but not in lung pathology. No consistent non-synonymous adaptive mutation of the spike was found in viruses isolated from infected hamsters. Besides satisfying the Koch's postulates, this readily available hamster model is an important tool for studying transmission, pathogenesis, treatment, and vaccination against SARS-CoV-2 (Chan, Zhang et al. 2020).

Transferring donated blood containing antibodies produced by the immune systems of those who have recovered from COVID-19 to people who need them is being investigated as a non vaccine method of immunisation. This strategy was tried for SARS. Viral neutralization is the anticipated mechanism of action by which passive antibody therapy can mediate defense against SARS-CoV-2. Other mechanisms however, such as antibody-dependent cellular cytotoxicity and/or phagocytosis, may be possible. Other forms of passive antibody therapy, for example, using manufactured monoclonal antibodies, are in development. Production of convalescent serum, which consists of the liquid portion of the blood from recovered patients and contains antibodies specific to this virus, could be increased for quicker deployment (Wikipedia, 2020).

IN a paper by Dashraath, P., et al., it describes "The current coronavirus disease 2019 (COVID-19) pneumonia pandemic, caused by the severe acute respiratory syndrome 2 (SARS-CoV-2) virus, is spreading globally at an accelerated rate, with a basic reproduction number (R0) of 2 - 2.5, indicating that 2 - 3 persons will be infected from an index patient. A serious public health emergency, it is particularly deadly in vulnerable populations and communities in which healthcare providers are insufficiently prepared to manage the infection. As of March 16, 2020, there are more than 180,000 confirmed cases of COVID-19 worldwide, with over 7,000 related deaths. The SARS-CoV-2 virus has been isolated from asymptomatic individuals, and affected patients continue to be infectious two weeks after cessation of symptoms. The substantial morbidity and socioeconomic impact have necessitated drastic measures across all continents, including nationwide lockdowns and border closures. Pregnant women and their fetuses represent a high-risk population during infectious disease outbreaks. To date, the outcomes of 55 pregnant women infected with COVID-19 and 46 neonates have been reported in the literature, with no definite evidence of vertical transmission. Physiological and mechanical changes in pregnancy increase susceptibility to infections in general, particularly when the cardiorespiratory system is affected, and encourage rapid progression to respiratory failure in the gravida. Furthermore, the pregnancy bias towards T-helper 2 (Th2) system dominance which protects the fetus, leaves the mother vulnerable to viral infections, which are more effectively contained by the Th1 system. These unique challenges mandate an integrated approach to pregnancies affected by SARS-CoV-2. Here we present a review of COVID-19 in pregnancy, bringing together the various factors integral to the understanding of pathophysiology and susceptibility, diagnostic challenges with real-time reverse transcriptase polymerase chain reaction (RT-PCR) assays, therapeutic controversies, intrauterine transmission and maternal-fetal complications. We discuss the latest options in antiviral therapy and vaccine development, including the novel use of chloroquine in the management of COVID-19. Fetal surveillance, in view of the predisposition to growth restriction and special considerations during labor and delivery are addressed. Additionally, we focus on keeping frontline obstetric care providers safe while continuing to provide essential services. Our clinical service model is built around the principles of workplace segregation, responsible social distancing, containment of cross-infection to healthcare providers, judicious use of personal protective equipment and telemedicine. Our aim is to share a framework which can be adopted by tertiary maternity units managing pregnant women in the flux of a pandemic while maintaining the safety of the patient and healthcare provider at its core" (Dashraath, Jing Lin Jeslyn et al. 2020).

Due to the large infection population, broad transmissibility and high mortality, it is urgent to find out the efficient and specific methods to prevent and treat COVID-19. As biological products have broadly applied in the prevention and treatment of severe epidemic diseases, they are promising in blocking novel coronavirus infection. According to the research advances of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), we reviewed the potential application of biological products such as interferon, convalescent plasma, intestinal micro-ecological regulators, vaccines and therapeutic antibodies, etc., on prevention and treatment of COVID-19 (Yan, Li et al. 2020).

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating and sharing.

References

1. Baidu. http://www.baidu.com. 2020.
2. Cancer Biology. http://www.cancerbio.net. 2020.
3. Google. http://www.google.com. 2020.
4. Journal of American Science. http://www.jofamericanscience.org. 2020.
5. Life Science Journal. http://www.lifesciencesite.com. 2020.
6. Ma H, Chen G. Stem cell. The Journal of American Science 2005;1(2):90-92. doi:10.7537/marsjas010205.14. http://www.jofamericanscience.org/journals/am-sci/0102/14-mahongbao.pdf.
7. Ma H, Cherng S. Eternal Life and Stem Cell. Nature and Science. 2007;5(1):81-96. doi:10.7537/marsnsj050107.10.

http://www.sciencepub.net/nature/0501/10-0247-mahongbao-eternal-ns.pdf.
8. Ma H, Cherng S. Nature of Life. Life Science Journal 2005;2(1):7-15. doi:10.7537/marslsj020105.03. http://www.lifesciencesite.com/lsj/life0201/life-0201-03.pdf.
9. Marsland Press. http://www.sciencepub.net. 2020.
10. Marsland Press. http://www.sciencepub.org. 2020.
11. National Center for Biotechnology Information, U.S. National Library of Medicine. http://www.ncbi.nlm.nih.gov/pubmed. 2020.
12. Nature and Science. http://www.sciencepub.net/nature. 2020.
13. Stem Cell. http://www.sciencepub.net/stem. 2020.
14. Wikipedia. The free encyclopedia. http://en.wikipedia.org. 2020.
15. Wikipedia. Coronavirus. The free encyclopedia. https://en.wikipedia.org/wiki/Coronavirus. 2020.
16. Wikipedia. Coronavirus disease 2019. The free encyclopedia. https://en.wikipedia.org/wiki/Coronavirus_disease_2019. 2020.
17. Bartiromo, M., B. Borchi, A. Botta, A. Bagala, G. Lugli, M. Tilli, A. Cavallo, B. Xhaferi, R. Cutruzzula, A. Vaglio, S. Bresci, A. Larti, A. Bartoloni and C. Cirami (2020). "Threatening drug-drug interaction in a kidney transplant patient with Coronavirus Disease 2019 (COVID-19)." Transpl Infect Dis.
18. Chan, J. F., A. J. Zhang, S. Yuan, V. K. Poon, C. C. Chan, A. C. Lee, W. M. Chan, Z. Fan, H. W. Tsoi, L. Wen, R. Liang, J. Cao, Y. Chen, K. Tang, C. Luo, J. P. Cai, K. H. Kok, H. Chu, K. H. Chan, S. Sridhar, Z. Chen, H. Chen, K. K. To and K. Y. Yuen (2020). "Simulation of the clinical and pathological manifestations of Coronavirus Disease 2019 (COVID-19) in golden Syrian hamster model: implications for disease pathogenesis and transmissibility." Clin Infect Dis.
19. Chatterjee, P., N. Nagi, A. Agarwal, B. Das, S. Banerjee, S. Sarkar, N. Gupta and R. R. Gangakhedkar (2020). "The 2019 novel coronavirus disease (COVID-19) pandemic: A review of the current evidence." Indian J Med Res.
20. Dashraath, P., W. Jing Lin Jeslyn, L. Mei Xian Karen, L. Li Min, L. Sarah, A. Biswas, M. Arjandas Choolani, C. Mattar and S. L. Lin (2020). "Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy." Am J Obstet Gynecol.
21. Dong, L., S. Hu and J. Gao (2020). "Discovering drugs to treat coronavirus disease 2019 (COVID-19)." Drug Discov Ther 14(1): 58-60.
22. Guo, Y. R., Q. D. Cao, Z. S. Hong, Y. Y. Tan, S. D. Chen, H. J. Jin, K. S. Tan, D. Y. Wang and Y. Yan (2020). "The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status." Mil Med Res 7(1): 11.
23. Kakodkar, P., N. Kaka and M. N. Baig (2020). "A Comprehensive Literature Review on the Clinical Presentation, and Management of the Pandemic Coronavirus Disease 2019 (COVID-19)." Cureus 12(4): e7560.
24. Kim, J. Y. (2020). "Letter to the Editor: Case of the Index Patient Who Caused Tertiary Transmission of Coronavirus Disease 2019 in Korea: the Application of Lopinavir/Ritonavir for the Treatment of COVID-19 Pneumonia Monitored by Quantitative RT-PCR." J Korean Med Sci 35(7): e88.
25. Lauer, S. A., K. H. Grantz, Q. Bi, F. K. Jones, Q. Zheng, H. R. Meredith, A. S. Azman, N. G. Reich and J. Lessler (2020). "The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application." Ann Intern Med.
26. Lin, Q., S. Zhao, D. Gao, Y. Lou, S. Yang, S. S. Musa, M. H. Wang, Y. Cai, W. Wang, L. Yang and D. He (2020). "A conceptual model for the coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China with individual reaction and governmental action." Int J Infect Dis 93: 211-216.
27. Rello, J., S. Tejada, C. Userovici, K. Arvaniti, J. Pugin and G. Waterer (2020). "Coronavirus Disease 2019 (COVID-19): A critical care perspective beyond China." Anaesth Crit Care Pain Med.
28. Scott, S. E., K. Zabel, J. Collins, K. C. Hobbs, M. J. Kretschmer, M. Lach, K. Turnbow, L. Speck, J. R. White, K. Maldonado, B. Howard, J. Fowler, S. Singh, S. Robinson, A. P. Pompa, K. Chatham-Stephens, A. Xie, J. Cates, S. Lindstrom, X. Lu, M. A. Rolfes, M. Flanagan, R. Sunenshine and C.-C. I. T. Maricopa County (2020). "First Mildly Ill, Non-Hospitalized Case of Coronavirus Disease 2019 (COVID-19) Without Viral Transmission in the United States - Maricopa County, Arizona, 2020." Clin Infect Dis.
29. Singhal, T. (2020). "A Review of Coronavirus Disease-2019 (COVID-19)." Indian J Pediatr 87(4): 281-286.
30. Spiteri, G., J. Fielding, M. Diercke, C. Campese, V. Enouf, A. Gaymard, A. Bella, P. Sognamiglio, M. J. Sierra Moros, A. N. Riutort, Y. V. Demina, R. Mahieu, M. Broas, M. Bengner, S. Buda, J. Schilling, L. Filleul, A. Lepoutre, C. Saura, A.

Mailles, D. Levy-Bruhl, B. Coignard, S. Bernard-Stoecklin, S. Behillil, S. van der Werf, M. Valette, B. Lina, F. Riccardo, E. Nicastri, I. Casas, A. Larrauri, M. Salom Castell, F. Pozo, R. A. Maksyutov, C. Martin, M. Van Ranst, N. Bossuyt, L. Siira, J. Sane, K. Tegmark-Wisell, M. Palmerus, E. K. Broberg, J. Beaute, P. Jorgensen, N. Bundle, D. Pereyaslov, C. Adlhoch, J. Pukkila, R. Pebody, S. Olsen and B. C. Ciancio (2020). "First cases of coronavirus disease 2019 (COVID-19) in the WHO European Region, 24 January to 21 February 2020." Euro Surveill 25(9).

31. Thomas-Ruddel, D., J. Winning, P. Dickmann, D. Ouart, A. Kortgen, U. Janssens and M. Bauer (2020). "Coronavirus disease 2019 (COVID-19): update for anesthesiologists and intensivists March 2020." Anaesthesist.
32. Yan, C. X., J. Li, X. Shen, L. Luo, Y. Li and M. Y. Li (2020). "[Biological Product Development Strategies for Prevention and Treatment of Coronavirus Disease 2019]." Sichuan Da Xue Xue Bao Yi Xue Ban 51(2): 139-145.

4/16/2020