Review Article

Transmission, stability, symptoms, diagnosis and management of COVID 19

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Abstract

COVID 19 can be considered as the most devastating pandemics that happened in the 21st century. Many researches on its virology, epidemiology, transmission, diagnosis, and treatments are ongoing. Studies on the causative virus of COVID 19 has been successfully carried out. Its genome has been sequenced, analyzed and compared with other corona viruses in those studies. Some studies on disease transmission also been carried out and as an outcome of those studies, information about the stability of the virus in different conditions and sources of disease transmission are available. Symptoms of the disease also been successfully identified and diagnosis methods to identify infected patients are also been developed. Preventive measures for the disease also been published and implemented in many countries. However, at the time of writing, there is no permanent cure for this viral infection and it would take time to develop a vaccine and/or other medicine for this disease.

Key words: COVID 19, Corona virus, Symptoms, Diagnosis

1. Introduction

COVID 19 is the present pandemic caused by beta corona viruses after Severe Acute Respiratory Syndrome (SARS) in 2003 and the Middle East respiratory syndrome (MERS) in 2012 from the same group of viruses. According to the United Nations' secretary general the current corona virus outbreak is the biggest challenge for the world since World War Two. This is a viral infection caused by a novel corona virus called SARS CoV2 and the first case appeared in Wuhan, China at the end of 2019. Thereafter, the infection rapidly spread in many countries within a short period affecting global health, supplies, economy, and social life.

As this virus disease is new to mankind, researches are conducted throughout the world on different aspects of the disease. As such, the knowledge on virology, epidemiology, clinical features, treatments, etc. upgrade day by day and some facts are still at the experimental

level. This article is reviewing on the presently available findings of the symptoms and risk factors of the disease, stability and transmission of the virus, techniques used to diagnose COVID 19, and treatments and management of the disease.

2. Coronavirus

Coronaviruses (CoV) are a group of enveloped, positive sense, single-stranded RNA (+ssRNA) viruses belonging to the family *Coronaviridae* (Poutanen, 2012). They are well-established pathogens of mammalians and birds. Members of the virus family can cause respiratory, enteric, hepatic, and neurological diseases in different animal species, including camels, cattle, cats, and bats. To date, seven human CoVs (HCoVs) capable of infecting humans have been identified (Cascella et al., 2020). Among them, only three CoVs in genus beta-coronavirus namely; SARS-CoV (Severe Acute Respiratory Syndrome coronavirus), MERS-CoV (Middle East Respiratory Syndrome coronavirus), and SARS-CoV2 (Severe acute respiratory syndrome coronavirus 2) are known to cause severe infections to human. HKU1, NL63, OC43 and 229E are other four HCoVs associated with mild symptoms as a common cold (D. X. Liu et al., 2020). SARS-CoV emerged in southern China from palm civet cats in 2003, MERS-CoV emerged in Saudi Arabia from dromedary camels in 2012, and SARS-CoV2 originally tentatively named 2019-nCoV (2019 new corona virus) emerged in December 2019 in China possibly from bats or pangolins (still under investigation) (Banerjee et al., 2019).

3. COVID-19

Corona virus disease 2019 (COVID-19) or the disease caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) arose in one of the largest cities, Wuhan, which is in Hubei province of China, in early December 2019. This is initially diagnosed as pneumonia of an unknown etiology. Later on, identified the etiology of the illness is attributed to a novel, virus belongs to the coronavirus (CoV) family, named as SARS-CoV-2 due to the close similarities with SARS-CoV (Cascella et al., 2020). Because most of the infected people found initially were exposed to the wet animal market of Hubei, this is considered as a potential zoonotic virus so as SARS-CoV (Rothan & Byrareddy, 2020).

COVID19 considered a rapidly contagious and severe disease and the number of confirmed cases and deaths is constantly increasing daily. Therefore, WHO has declared COVID 19 as the sixth public health emergency of international concern on 30 January 2020, a one month after diagnosing the first case on 31 December 2019 (Ahmed et al., 2020; Gu et al., 2020). In

the first week of May 2020, the virus affected nearly 212 countries and territories around the world and reported over 4 million patients, among, nearly 0.25 million were died(Worldometer, 2020). United States, Brazil, Russia, the United Kingdom, Spain, Italy, France, Germany, Turkey, and India are considered as the ten most impacted countries from the disease to date with highest total positive cases (Worldometer,2020).

4. SARS-CoV-2 virus

SARS-CoV-2 is the virus responsible for COVID 19 outbreak. The genetic sequence of SARS CoV2 is closely linked to the SARS CoV. MERS CoV is distance related to these genomes Further, it is approximately 70% genetic similarity to the SARS-CoV. The virus has a 96% similarity to a bat coronavirus, so it is widely suspected to originate from bats (D. Wu et al., 2020). The SARS-CoV 2 virus is ~125 nm in diameter, and its genome ranges from ~30 kilobases, the largest for an RNA virus. It has 4 structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N) (Ahmed et al., 2020) (figure 1).

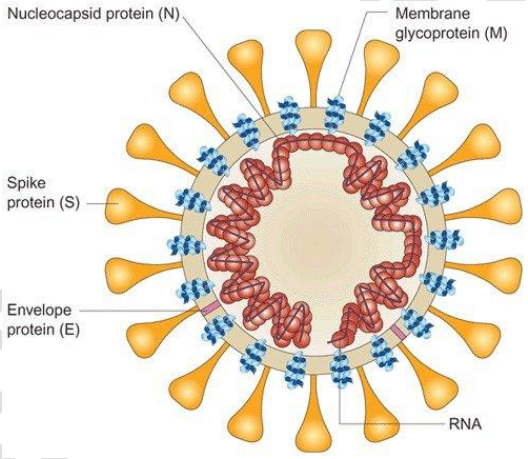

Figure1: Structure of SARS CoV2

Source : (Peiris et al., 2004)

The S protein bind to a receptor protein in the surface of host cells called angiotensin-converting enzyme 2 (ACE2). ACE2 is commonly present in the intestine, kidney, blood vessels, and most abundantly in type II alveolar cells of the lungs. The spike protein of SARS-CoV-2 is primed by human enzyme transmembrane protease, serine 2 (TMPRSS2) (Hoffmann et al., 2020).

5. Symptoms and risk factors of the disease

COVID 19 showed various levels of severity from mild upper respiratory illness to severe pneumonia and acute respiratory distress syndrome (ARDS). Huang et al. (2020) reported the clinical features of 41 patients confirmed with SARS CoV2 infection in Wuhan, China by 2nd January 2020. Among, 98% showed fever as the common symptoms at the onset of illness. Cough, headache, hemoptysis (coughing up of blood), diarrhea, dyspnea (difficulty in breathing), myalgia (muscle pain), lymphopenia (having an abnormally low level of lymphocytes in the blood), were some other exhibited symptoms. All 41 patients had pneumonia with abnormal findings on chest CT.

Besides the respiratory symptoms, non-respiratory syndromes also reported in the patients (Vetter et al., 2020). The virus can infect the gastrointestinal tract and causes vomiting and diarrhea. Virus RNA has been detected in stool samples, sometimes at high levels (Han et al., 2020). Loss of smell and taste (anosmia) is another symptom detect in COVID 19 that may be due to attack and invade olfactory nerve endings by coronaviruses (Menni et al., 2020). Studies using animal models showed that coronaviruses might pass into the brain via the olfactory nerve or bulb or both, causing neuronal damage or death (Vetter et al., 2020). Patients with COVID-19 in China and US acquired other neurological symptoms such as impair consciousness, skeletal muscle injury, cerebrovascular disease, hemorrhagic stroke, dizziness, headache, etc. without evidence of direct viral invasion into the brain (Mao et al., 2020; Vetter et al., 2020). The virus also may be causing secondary infections as heart inflammation, acute kidney disease, neurological malfunction, blood clots, intestinal damage, and liver problems. It has been reported to reduce sperm concentration as well (Bernstein et al., 2020; Segars et al., 2020).

Normally, the infected patients had at least one symptom but it is possible to have infected persons without symptoms (silent patients) who are fueling the pandemic. A study of Kimball, (2020) showed that nearly half of 23 infected health-care workers had no symptoms (asymptomatic or pre-symptomatic period) at the point of detection. According to some researchers, nearly 2% of the population are healthy carriers of a CoV(Cascella et al., 2020). ..In this sense, symptoms-based screening is not fully reliable. Therefore, isolation and active monitoring of persons with contact history are practicing by many countries as a precaution. However, the current understanding of the incubation period of the virus is controversial and limited.

Severity and fatality rates of the disease are induced by specific health conditions of the patient. Older patients and patients with comorbidities have a higher rate of fatality. It appears people over 65 with coronary heart diseases or hypertension are more likely to be infected and to develop more severe symptoms (G. Li et al., 2020). G. Li et al. (2020) showed that COVID 19 induced hypertension and serious myocardial damage which triggers the mortality. Hypertension, chronic obstructive pulmonary diseases, diabetic, cardiovascular disease, and cancers considered as underline health conditions which increase the COVID 19 susceptibility (Guo et al., 2020; Jordan et al., 2020). Male sex, leukocytosis, high LDH level, and high-dose corticosteroid use were also associated with death in patients with severe COVID-19 (X. Li et al., 2020). Smoking also assumed to be possibly associated with the progression of the disease. Smoking adversely affects lung health, immune system, make the smoker more vulnerable to the disease (Vardavas & Nikitara, 2020). Moreover, there are shreds of evidence that atmospheric pollution became a co factor for enamors deaths in Italy and US due to COVID 19 (Conticini et al., 2020; X. Wu et al., 2020). Big differences between Chinese and Italian mortality indicate ethnicity might affect disease outcomes, but there is little to no data to support this claim (Pareek et al., 2020). Behaviors, comorbidities, immune profiles, hence the risk of infection can be varying in different ethnicities. Mitigation efforts and health infrastructure also vary from country to country.

It is assumed that a high inoculum dose at the time of infection makes the disease more severe (Petrosillo et al., 2020). Liu et al. (2020) found a strong association between disease severity and the amount of virus present in the nose. However, no obvious difference in viral load and severity of illness was reported by He et al. (2020).

6. Stability and transmission of the virus

Live coronavirus can survive anywhere from three hours to seven days on surfaces, depending on the material (Table 1). The stability of the virus varies with different environmental conditions (Harmooshi et al., 2020). SARS-CoV-2 is extremely stable in a wide range of pH values (pH 3–10) at room temperature (Chin et al., 2020). The survival rates decreased with elevated atmospheric temperatures (Chin et al., 2020) and high relative humidity (J. Wang et al., 2020). Therefore, summer and rainy seasons might facilitate the viral spread.

Table 1: Survival of SARS CoV2 in different surfaces

Material	**Duration of survival**
printing and tissue papers	3 h
treated wood and cloth	2 days
glass and banknote	4 days
stainless steel and plastic	7 days
outer layer of a surgical mask	~0·1% of the original inoculum survive on day 7

**at room temperature (22°C) with a relative humidity of around 65%*
Source: (Chin et al., 2020)

SARS-CoV2 is a novel virus and the transmitting modes and ability is need to be further asses (Chen, 2020). Normally, a respiratory virus is transmitted in one of three ways as;

- contact (direct or indirect)
- droplet spray in short range transmission
- aerosol in long-range transmission (airborne transmission)

Initially, the infection was believed to be transmitted from animal to human at the wet fish market of Hubei. Currently, most cases of COVID 19 reported as a direct transition from person to person by respiratory droplets from coughing, sneezing, and talking (J. Chen, 2020). Therefore, a social distance of 1 m is advised by the World Health Organization (WHO), Singapore, and Hong Kong. In Australia, its 1.5 m and the USA advise 1.8 m (the equivalent of 6 feet), and the UK, Ireland, and New Zealand favor 2 m (Williams, 2020). However, respiratory droplets can spread over 6 feet as well and the best way to protect is to stay indoors and self-isolation. Morawska and Cao (2020) suggested that the virus spreads through the air, and recommend that adequate control measures be implemented to prevent further spread.

Emerging indications suggested that the virus may also be transmitted through the contact of infected surfaces (J. Chen, 2020). Therefore, hand washing recommended by WHO as the main protection measure. Except for a 5 minute washing with hand soap, no infectious virus could be detected after a 5 minute washing at room temperature (22°C) with disinfectants as household bleach, ethanol, povidone iodine, chloroxylenol, chlorhexidine, benzalkonium

chloride (Chin et al., 2020). Kampf et al. (2020) also showed 0.1% sodium hypochlorite or 62–71% ethanol significantly reduces coronavirus infectivity on surfaces within 1 min exposure time. Therefore, washing hands with disinfectants are even effective (Chin et al., 2020). The envelope of coronavirus composed of lipid is attached with the hydrophobic ends of soap micelles and washed away (D'Souza & Banerjee, 2020). Further, contaminated hands can transfer the virus to a person's body through eyes, nose, or mouth. Therefore, the WHO recommends not to touch them at public before washing the hands (WHO-Advice for Public, 2020).

The gastrointestinal route of transmission SARS CoV2 also assumed but further investigations needed before confirming this mode of transmission (Petrosillo et al., 2020). Postpartum neonatal transmission from mother to child has been reported (Segars et al., 2020). The first case of a corpse transmitting the coronavirus to a medical examiner was reported by scientists in Thailand in the second week of April 2020 (Tucker, 2020).

7. Techniques used to diagnose COVID 19

Symptoms of COVID 19 are not unique, therefore, they cannot be considered as accurate measures for diagnosing the disease. Patients with suspected symptoms, contact history, and radiological changes in the chest are undergoing biochemical tests to confirm the disease. Basically, two types of tests are undergoing to confirm COVID 19 as Nucleic acid amplification tests (NAAT) and serology/antibody test.

In NAAT methods, measure the presence of SARS CoV2 virus's RNA in patient's respiratory tract specimens. Real-time reverse transcription-polymerase chain reaction (RT-PCR) is the abundantly used and standard NAAT method recommended by WHO. RT PCR detects the presence of virus RNA in the specimens of upper (the first choice is nasopharyngeal swab if not oropharyngeal swab) or lower (coughed up sputum, Bronchial and tracheal secretions, or bronchoalveolar lavage) respiratory tract of patients. After first week of infection, the virus might not present in the upper respiratory tract and gain negative results for such specimens (Richardson et al., 2004). Loop-mediated isothermal amplification (LAMP) also another NAAT method such as RT-PCR but is novel, technically simple, and easy with compare to RT-PCR. However, this method is not widely used yet (Green et al., 2020). The sensitivity and specificity of the real-time RT-PCR test is not 100% and sometimes false-negative and false-positive results may also obtain. Therefore, it suggests to

testing different specimens as stool or blood at different stages of infection (Tahamtan & Ardebili, 2020).

In Serological/antibody tests, the presence and amount of IgM/IgG antibodies in the blood serum are detected. Patients developed antibodies to a detectable level at 7 to 10 days or more after the onset of symptoms. Therefore, this test is not suitable for early case detection. However, this test is comparatively rapid and cheaper (Green et al., 2020). So, this method can be used to test the patients admitted to hospitals some days after they show symptoms as an initial detection step so that positive patients can be separated and go for RT-PCR test.

In addition, regular laboratory testing and imaging are necessary for the assessment of disease progression and complications such as white blood cell count, liver markers (AST and ALT), inflammatory markers (LDH and ferritin), and chest x ray and CT scans (El-Lababidi et al., 2020).

8. Treatments and management of the disease

At the time of writing, there are no specific, effective, proven drugs to treat COVID-19 and some drugs are under clinical trials to test the efficacy and safety. Therefore, infection prevention and control (IPC) is considered as the best management method to date. At least one-meter distance among two individuals, lock-downs/curfews, travel restrictions, quarantine the persons who are having contact history, using face masks, using sanitizers, hand washing are some important precautions for IPC.

For the victims, oxygen therapy, ventilatory support, and conservative fluid management used according to the severity of the disease. Since the pandemic has not a permanent cure, traditional and complementary medicine are also tested. Yonesi and Rezazadeh, (2020) have reviewed the potential of utilizing plant sources as natural, cost effective and with less side effects approach against SARS CoV2. In some cases, nearly, 85% of COVID-19 patients received combined treatment with regular medication and traditional remedies (Liang & Litscher, 2020). convalescent plasma therapy is another promising treatment for this disease. Once a person infected with SARS CoV2, their immune system starts producing antibodies. That antibodies are remaining even after recovering the patient. This antibody containing blood can be transfusion to another COVID patient which called convalescent plasma therapy. This approach helps to fend off the disease until their immune systems start to produce own antibodies. This method was successfully implemented against SARS,MERS, Ebola and H1N1 viruses (L. Chen et al., 2020).

Chloroquine, a broadly used, antimalarial has been suggested for treating COVID 19. There are pre-clinical rationales and evidence regarding the effectiveness of chloroquine for the treatment of COVID-19 (Cortegiani et al., 2020; Gao et al., 2020). Some in-vitro studies showed that remdesivir can inhibit coronaviruses replication such as SARS-CoV and MERS-CoV (Al-Tawfiq et al., 2020). M. Wang et al. (2020) evaluated the antiviral efficiency of five FDA approved drugs (ribavirin, penciclovir, nitazoxanide, nafamostat, chloroquine) and two antiviral drugs remdesivir , and favipiravir against clinical isolate of 2019-nCoV in vitro. Their findings revealed that remdesivir and chloroquine are highly effective in controlling SARS CoV2 infection, in vitro. However, all these medicines should go through further testing before use them as medicine for the disease.

Bacillus Calmette–Guerin (BCG), the vaccine used for tuberculosis has been suggested as a possible agent to prevent coronavirus disease 2019 (Redelman-Sidi, 2020). According to Miller et al. (2020), countries without universal policies of BCG vaccination such as Italy, Netherlands, USA have been more severely affected by COVID 19. This gives a clue that the BCG vaccine may help to develop immunity against the disease.

It is an urgent mission to find a specific vaccine for COVID 19. Several new and tailored vaccines against SARS CoV2 are developing and testing by dozens of companies, institutions, and universities including Pfizer and its German partner BioNTech, the Chinese company CanSino and the University of Oxford, which is working with AstraZeneca (Grady, 2020). Hinder the replication of the virus inside the host cells is a key requirement for such a vaccine. However, it is a big challenge as viruses are known to be a tricky target for medicines with compare to infectious agents like bacteria and fungi since they are mutating quickly.

9. Conclusion

COVID 19 is the most devastating pandemics that happened in 21st century. Still, the facts on its virology, epidemiology, transmission, and diagnosis are updating. At the time of writing, there is no permanent cure for this viral infection. Many type of research have been conducted as well as carrying out on COVID 19 and related topics by many researchers in different parts of the world. However, the results of some of their research are controversial, particularly for clinical studies. Therefore, combine research with the assistance of scientists throughout the world is needed to better understand the picture of this disease by using the maximum possible sample size. There is a good progress in some aspects such as virus

identification studies including virus genome sequencing, comparison and analysis, disease symptom identification, diagnosis method development, and introduction of preventive measures. However, it would take more time to develop vaccines and/or other medicine for this disease.

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