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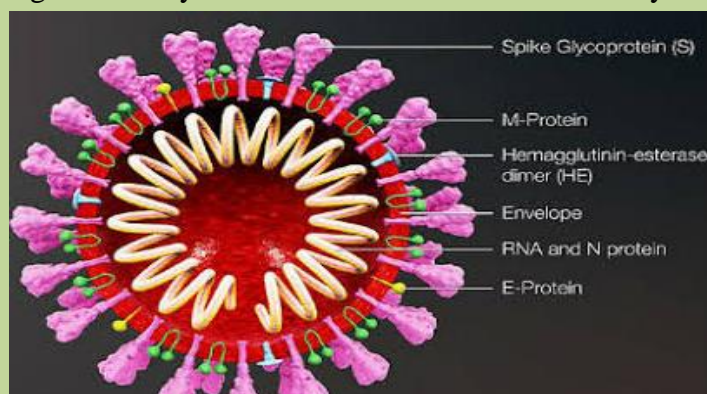
nCOVID 19 – Facts to Know

T Saranya, Pharm D Internee



Introduction:

The purpose of this communication is to provide relevant clinical information and treatment guidelines on the COVID-19 pandemic .Since December 2019, an outbreak of COVID-19 is the disease caused by the new virus SARS-CoV-2. Most people who are infected get mild respiratory symptoms that will disappear on their own, but some people develop more severe illness, like pneumonia. The virus is transmitted through contact with an infected person or via respiratory droplets when an infected person coughs or sneezes. There is a higher risk of infection if you have been in an area where the virus is spreading, or if you have been in close contact with a person infected with the new coronavirus. There is also a higher risk if you suffer from comorbidities already.



Coronavirus infections can be prevented and an outbreak can be stopped through the active engagement of decision-makers, healthcare professionals, the media and the community. This was demonstrated in previous coronavirus outbreaks such as in 2003 with SARS-CoV .This article aims to assist pharmacists and the pharmacy workforce in preventing the spread of the disease and contributing to its efficient management in the healthcare system.

SARS-CoV-2 CORONA VIRUS

Corona viruses (CoVs) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). A novel coronavirus (nCoV) is a new strain that has not been previously identified in humans.

Corona viruses are large, enveloped, positive-stranded RNA viruses. They have the largest genome among all RNA viruses. The genome is packed inside a helical capsid formed by the nucleocapsid protein and further surrounded by an envelope. Associated with the viral envelope are at least three structural proteins: the membrane protein and the envelope protein are involved in virus assembly, whereas the spike protein mediates virus entry into host cells. Among the structural proteins, the spike forms large protrusions from the virus surface, giving corona viruses the appearance of having crowns (hence their name; *corona* in Latin means crown). In addition to mediating virus entry, the spike is a critical determinant of viral host range and tissue tropism and a major inducer of host immune responses. ^[1] Corona viruses usually affect mammals and birds, causing a variety of lethal diseases. In general, corona viruses cause widespread respiratory, gastrointestinal and central nervous system diseases in humans and other animals, threatening human health and causing economic loss from mild upper to lower respiratory tract infections. ^[1] Corona viruses are capable of adapting to new environments through mutation and recombination with relative ease. As such, they can affect new hosts and tissues. For this reason, although rarely, certain corona viruses that usually affect only certain animal species can generate new strains that can cross over to human hosts and then be transmitted between humans. Since humans had not been exposed to such viruses before and cannot be protected by previous vaccines or natural immunity, these mutations can rapidly lead to disease outbreaks and, eventually, pandemics.

IS COVID-19 PANDEMIC?

The SARS-CoV-2 is a novel strain of coronavirus that was first detected in the city of Wuhan, in the province of Hubei, in the People's Republic of China – a city with a population of 11 million. The outbreak started as pneumonia of unknown causal agent at the end of December 2019.

Phylogenetics analyses undertaken with available full genome sequences suggest that bats appear to be the reservoir of COVID-19 virus, but the intermediate host(s) has not yet been identified. ^[2] On 30 January 2020, the World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern. On 11 February 2020, the International Committee on Taxonomy of Viruses (ICTV) decided to name the virus as **severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)**, and the WHO finally decided to name the disease caused by this virus as **COVID-19** (for **Coronavirus** disease identified in 2019). Following large outbreaks of the disease in multiple countries, with thousands of deaths around the world, on 11 March 2020 the WHO declared the outbreak to be a pandemic. The virus seems to have mutated already after its original transmission from the animal host or reservoir to humans, leading to at least two different strains. Population genetic analyses of 103 SARS-CoV-2 genomes indicated that these viruses evolved into two major types (designated L and S). Although the L type (~70%) is more prevalent than the S type (~30%), the S type was found to be the ancestral version. ^[3] While both types play a part in the current outbreak, the higher prevalence of the L-type suggests that it is more aggressive. It is important to keep in mind that viruses mutate all the time and that not all mutations are indicative of increased disease severity or transmission rates. In fact, differences between the two types of the novel coronavirus are so small that researchers are reluctant to even classify them as separate strains. Given that multiple groups around the world are working on a vaccine, knowing the exact number of strains (or types) of the virus is crucial because, in order to be effective, the eventual vaccine will have to target features present in all known strains (or types).

MODES OF TRANSMISSION:

The transmission of SARS-CoV-2 occurs by the following mechanisms:

- Most often, spread from person to person among close contacts (about 6 feet/1.8 meters).
- Person-to-person spread is thought to occur mainly via respiratory droplets produced when an infected person coughs or sneezes (land in mouth, nose or eyes of nearby people or inhaled into the lungs) similar to how influenza and other respiratory pathogens spread.

- It may be possible that a person can get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose or possibly their eyes, but this is not thought to be the main way the virus spreads. ^[4] There is evidence that corona viruses can remain infectious on inanimate surfaces for several hours or even days. ^[5]
- Typically, with most respiratory viruses, people are thought to be most contagious when they are most symptomatic (the sickest). With COVID-19, however, there have been reports of spread from an asymptomatic infected patient to a close contact. Recent studies suggest that asymptomatic (or pre-symptomatic) patients may indeed be driving the rapid expansion of the disease. ^[6]
- Also, patients may remain contagious up to two weeks after the remission of symptoms mostly waned by the end of the first week, viral RNA remained detectable in throat swabs well into the second week. Stool and sputum samples remained RNA-positive over even longer periods, in spite of full resolution of symptoms. ^[7]
- Minimal information is available regarding COVID-19 during pregnancy. Intrauterine or perinatal transmission has not been identified. In two reports including a total of 18 pregnant women with suspected or confirmed COVID-19 pneumonia, there was no laboratory evidence of transmission of the virus to the neonate. Two neonatal cases of infection have been documented. In one case, the diagnosis was made at day 17 of life after close contact with the infant's mother and a maternity matron who were both infected with the virus. The other case was diagnosed 36 hours after birth; the source and time of transmission in that case were unclear. ^[8]
- In limited studies on women with COVID-19 and another coronavirus infection, Severe Acute Respiratory Syndrome (SARS-CoV), the virus has not been detected in breast milk. The CDC recommends that a mother with flu continue breastfeeding or feeding expressed breast milk to her infant while taking precautions to avoid spreading the virus to her infant.

EPIDEMIC STAGES:

STAGE 1: In the first stage of a pandemic, the disease doesn't spread locally- cases reported are usually people who have had travel history to an already affected country.

STAGE 2: This is the stage of local transmission – when people who have brought the virus into the country transmit it to people they come in contact with, usually friends and family. At this stage, it is easy to trace spread and quarantine people.

STAGE 3: The third stage is when the source of the infection is untraceable; this stage is identified by people who haven't had travel history getting affected by the virus – once here spread is extremely contagious and difficult to control.

STAGE 4: china has been the only country to experience stage 4, where spread is practically uncontrollable and there are many major clusters of infection all over the country.

INCUBATION PERIOD: The time between catching the virus and beginning to have the symptoms of the disease is called incubation period. It ranges from 1-14 days, most commonly around five days.

DURATION OF TREATMENT: Mild case it usually takes 2 weeks in case of severe case it takes 3-6 weeks.

DISEASE PREVENTION:

- Frequently clean hands by using alcohol-based hand rub or soap and water;
- When coughing and sneezing cover the mouth and nose with a flexed elbow or tissue – throw the tissue away immediately and wash hands;
- Avoid close contact with anyone who has fever and cough;
- If you have fever, cough and difficulty breathing seek medical care early and share previous travel history with your healthcare provider;

- When visiting live markets in areas currently experiencing cases of novel coronavirus, avoid direct unprotected contact with live animals and surfaces in contact with animals;
- The consumption of raw or undercooked animal products should be avoided. Raw meat, milk or animal organs should be handled with care, to avoid cross-contamination with uncooked foods, as per good food safety practices.
- The median incubation period is estimated at 5.1 days. This suggests that the 14-day quarantine period recommended by the WHO is reasonable. 97.5% of people who develop symptoms will do so within 11.5 days of exposure.
- Self-isolation means avoiding situations where you could infect other people. This means all situations where you may come in contact with others, such as social & faith based gatherings, workplaces, schools, health care facilities, prisons, sports gatherings, all public gatherings.^[9]

DIAGNOSTIC TESTING FOR COVID-19:

There are currently several tests available in the market or under development for diagnosing COVID-19 (SARS-COV-2 infection). They are mostly based on molecular diagnosis (complex polymerase chain reaction (PCR) or reverse transcription polymerase chain reaction (RT-PCR) techniques) targeting different parts of the viral genome. Some serological assays are also in development, but currently they cannot compete in accuracy with molecular diagnosis particularly in the early phase of infection. This is particularly true for patients who are immuno compromised, and in the elderly. This lack of equivalency is also true in terms of analytical performance.

SYMPTOMS:

For confirmed COVID-19 cases, reported illnesses have ranged from people with little to no symptoms to people being severely ill and dying. Symptoms can include (on admission to hospital):

- Fever (>80% of the patients)
- Dry Cough (>80%)
- Shortness of breath (31%)
- Muscle ache (11%)

The disease may also occur with mild symptoms only, including: low-grade fever, cough, malaise, rhinorrhoea, sore throat without any warning signs, such as shortness of breath or difficulty in breathing, increased respiratory secretions (i.e. sputum or hemoptysis), gastrointestinal symptoms such as nausea, vomiting, and/or diarrhoea and without changes in mental status (i.e. confusion, lethargy).^[2]

Preliminary data report 11% lethality among hospitalized patients.

Complications occurred in 33% of the patients, and included: acute respiratory distress syndrome (ARDS) (17%), acute renal injury, acute respiratory injury, septic shock and ventilator-associated pneumonia.

Risk factors for severe illness are not yet clear, older patients or patients with underlying medical comorbidities (diabetes, hypertension, cardiovascular disease, cancer) may be at higher risk. In the most severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death. Disease in children appears to be relatively rare and mild with approximately 2.4% of the total reported cases reported among individuals aged under 19 years.

TREATMENT GUIDELINES

Currently, there is no specific medicine or vaccine for COVID-19 and no medicines or vaccines have been fully tested for safety and efficacy.

At present, antiviral therapy is mainly used, as well as symptomatic and supportive treatment based on the clinical condition of the patient. Supportive treatments include oxygen therapy, hydration, fever/pain control, and antibiotics in the presence of bacterial co-infection.

According to the diagnosis and treatment plan recommended by the Chinese health authorities, the antiviral drugs that can be tested for treatment mainly include α -Interferon (aerosol inhalation therapy), lopinavir/ritonavir,

, chloroquine phosphate, umifenovir and others. With regards to immunotherapy, for patients with extensive lung disease and severe disease, and laboratory testing of elevated IL-6 levels, tocilizumab can be tried. It is not recommended to use three or more antiviral drugs at the same time .^[10] In the report of the first case of COVID-19 patients in the United States published in NEJM, the patient's symptoms improved significantly after receiving Remdesivir. The antiviral effects of the triple combination (umifenovir + recombinant interferon α -2b + lopinavir/ritonavir) and the dual combination (recombinant interferon α -2b + lopinavir/ritonavir) were compared. The results of the study showed that the triple combination including umifenovir can significantly shorten the negative nucleic acid time of respiratory virus and the average hospitalization time. Also, Professor Li Lan-juan team evaluated the effect of low and medium doses of glucocorticoids on virus clearance. The results of the study showed that low and medium doses of glucocorticoids did not significantly shorten the median time to negative nucleic acid conversion of respiratory virus and median time to improve lung imaging. Corticosteroids are not routinely recommended for viral pneumonia or acute respiratory distress syndrome (ARDS) and should be avoided because of the potential for prolonging viral replication as observed in MERS-CoV patients, unless indicated for other reasons (e.g., COPD exacerbation, refractory septic shock following surviving Sepsis, progressive deterioration of oxygenation indicators and excessive activation of the body's inflammatory response, consider using glucocorticoids for a short period of time (3-5 days). The recommended dose of methylprednisolone should not exceed 1 -2mg / kg / day

CONVALESCENT PLASMA THERAPY:

For COVID-19 patients with rapid disease progression, severe and critical illness, convalescent plasma therapy (CPT) can be tried. CPT utilizes a certain titre of virus-specific antibodies in the plasma of the convalescent individual to enable the patient receiving the infusion to obtain passive immunity and remove pathogens from the blood circulation. This method has been successfully used in the treatment of SARS and H1N1 influenza, and is an effective treatment.

The use of CPT treatment can follow the following principles (National Health Commission of the People's Republic of China, 2020):

- In principle, the course of disease does not exceed three weeks. Also, the patient should have a positive viral nucleic acid test or viraemia certified by clinical experts.
- Patients with severe disease with rapid disease progression, or critically ill early stage patients, or patients comprehensively evaluated by clinical experts as requiring plasma therapy. The infusion dose is determined according to the clinical situation and the weight of the patient, usually the infusion dose is 200-500 ml (4-5 ml/kg).

Before, during, and after the infusion, detailed records and clinical observation should be made to assess the adverse effects of plasma infusion. The main types of adverse transfusion reactions include transfusion-related circulation overload, transfusion-related acute lung injury, transfusion-related dyspnea, allergic reactions, transfusion-associated hypotension reactions, non-hemolytic febrile reactions, acute hemolytic transfusion reactions, and delayed hemolytic transfusion reaction, infectious transfusion reaction, other/unknown, etc.

The most clinical trials of antiviral medicines are anti-HIV medicines (14 items, such as lopinavir/ritonavir, darunavir/cobistat, zidovudine), followed by anti-influenza viruses medicines (13, such as umifenovir, favipiravir), and five clinical trials of remdesivir, which are considered to have potential efficacy against COVID-19.