COVID-19 A Review Article

Pooja Shree Somani[1], Dr. Kumari Manisha[2]
[1]Dept of Zoology
[2]Dept of Agriculture and Botany Science
[1]MJRP University, Jaipur
[2]SBBSU University, Jalandhar, INDIA

Abstract- Coronavirus disease 2019 (COVID-19) *is an infectious disease caused by severe acute respiratory syndrome corona virus 2(SARS-CoV-2). It was first identified in December 2019 in Wuhan, the capital of China's Hubei province, and has since spread globally, resulting in an ongoing pandemic. As of 6 May 2020,more than 3.66 million cases have been reported across 187 countries and territories, resulting in more than 257,000 deaths. More than 1.19 million people have recovered.*
Common symptoms include fever, cough, fatigue, shortness of breath, and loss of smell and taste. While the majority of cases result in mild symptoms, some progress to viral pneumonia, multi-organ failure, or cytokine storm. The time from exposure to onset of symptoms is typically around five days but may range from two to fourteen days.

The virus is primarily spread between people during close contact, often via small droplets produced by coughing, sneezing, and talking. The droplets usually fall to the ground or onto surfaces rather than remaining in the air over long distances. People may also become infected by touching a contaminated surface and then touching their face. On surfaces, the amount of virus declines over time until it is insufficient to remain infectious, but it may be detected for hours or days. It is most contagious during the first three days after the onset of symptoms, although spread may be possible before symptoms appear and in later stages of the disease. The standard method of diagnosis is by real-time reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab.[22] Chest CT imaging may also be helpful for diagnosis in individuals where there is a high suspicion of infection based on symptoms and risk factors; however, guidelines do not recommend using it for routine screening.

I. INTRODUCTION

Recommended measures to prevent infection include frequenth and washing, maintaining physical distance from others(especially from those with symptoms), quarantine, covering coughs, and keeping unwashed hands away from the face. In addition, the use of a face covering is recommended for those who suspect they have the virus and their caregivers. Recommendations for face covering use by the general public vary, with some authorities recommending, some recommending against, and others requiring their use. There is limited evidence for or against the use of masks (medical or other) in healthy individuals in the wider community.

According to the World Health Organization, there are no vailable vaccines nor specific antiviral treatments for COVID-19. On 1 May 2020, the United States gave Emergency Use Authorization to the antiviral remdesivir for people hospitalized with severe COVID-19. Management involves the treatment of symptoms, supportive care, isolation, and experimental measures. The World Health Organization (WHO) declared the COVID-19 outbreak a Public Health Emergency of International Concern (PHEIC) on 30 January 2020 and a pandemic on 11 March 2020. Local transmission of the disease has occurred in most countries across all six WHO regions. (1,2)

II. SIGNS AND SYMPTOMS

Symptoms of COVID-19

Symptom	Range
Fever	83–99%
Cough	59–82%
Loss of appetite	40–84%
Fatigue	44–70%
Shortness of breath	31–40%
Coughing up sputum	28–33%
Muscle aches and pains	11–35%

Fever is the most common symptom, although some older people and those with other health problems experience fever later in the disease. In one study, 44% of people had fever when they presented to the hospital, while 89% went on to develop fever at some point during their hospitalization.
Other common symptoms include cough, loss of appetite, fatigue, shortness of breath, sputum production, and muscle and joint pains. Symptoms such as nausea, vomiting, and diarrhoea have been observed in

varying percentages. Less common symptoms include sneezing, runny nose, or sore throat.

Some cases in China initially presented with only chest tightness and palpitations.

A decreased sense of smell or disturbances in taste may occur. Loss of smell was a presenting symptom in 30% of confirmed cases in South Korea. (2,3)

As is common with infections, there is a delay between the moment a person is first infected and the time he or she develops 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, although 97.5% of people who develop symptoms will do so within 11.5 days of infection.

A minority of cases do not develop noticeable symptoms at any point in time. These asymptomatic carriers tend not to get tested, and their role in transmission is not yet fully known. However, preliminary evidence suggests they may contribute to the spread of the disease. In March 2020, the Korea Centers for Disease Control and Prevention (KCDC) reported that 20% of confirmed cases remained asymptomatic during their hospital stay.

III. COMPLICATIONS

In some, the disease may progress to pneumonia, multi-organ failure, and death. Neurological manifestations includeseizures, stroke, encephalitis, and Guillain–Barré syndrome. Cardiovascular-related complications may include heart failure, irregular electrical activity, blood clots, and heart inflammation.

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. Approximately 20-30% of people who present with COVID-19 demonstrate elevated liver enzymes (transaminases). Liver injury as shown by blood markers of liver damage is frequently seen in severe cases. (3,4)

IV. CAUSE

Transmission

As COVID-19 is a new disease, many aspects as to how it spreads are being researched. The disease is spread during close contact, often by small droplets produced during coughing, sneezing, or talking. During close contact, (1 to 2 metres, 3 to 6 feet), people catch the disease after breathing incontaminated droplets that were exhaled by infected people. However, the droplets are relatively heavy and usually fall to the ground or surfaces, as opposed to being infectious over large distances.

Loud talking releases more droplets than normal talking.

After the droplets fall to floors or surfaces, they still can infect other people, if they touch contaminated surfaces and then their eyes, nose or mouth with unwashed hands. On surfaces the amount of active virus decreases over time until it can no longer cause infection. However, experimentally, the virus can survive on various surfaces for some time, (for example copper or cardboard for a few hours, and plastic or steel for a few days). Surfaces are easily decontaminated with household disinfectants which kill the virus outside the human body or on the hands. Notably, however, disinfectants or bleach should never be swallowed or injected as a treatment or preventative measure, as this is harmful to the body and potentially fatal.

Sputum and saliva carry large amounts of virus. Some medical procedures may result in the virus being transmitted easier than normal for such small droplets, known as airborne transmission.

The virus is most contagious during the first three days after onset of symptoms, although spread is known to occur up to two days before symptoms appear (presymptomatic transmission) and in later stages of the disease. Some people have been infected and recovered without showing symptoms, but uncertainties remain in terms of asymptomatic transmission.

Although COVID-19 is not a sexually transmitted infection, kissing, intimate contact, and faecal oral routes are suspected to transmit the virus.

Virology

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novelsevere acute respiratory syndrome coronavirus, first isolated from three people with pneumonia

connected to the cluster of acute respiratory illness cases in Wuhan. All features of the novel SARS-CoV-2 virus occur in related coronaviruses in nature. Outside the human body, the virus is killed by household soap, which bursts its protective bubble. (4,5)

SARS-CoV-2 is closely related to the original SARS-CoV. It is thought to have a zoonotic origin. Genetic analysis has revealed that the coronavirus genetically clusters with the genus Betacoronavirus, in subgenus Sarbecovirus(lineage B) together with two bat-derived strains. It is 96% identical at the wholegenome level to other bat coronavirus samples (BatCov RaTG13). In February 2020, Chinese researchers found that there is only one amino acid difference in the binding domain of the S protein between the coronaviruses from pangolins and those from humans; however, whole-genome comparison to date found that at most 92% of genetic material was shared between pangolin coronavirus and SARS-CoV-2, which is insufficient to prove pangolins to be the intermediate host.

Pathophysiology

The lungs are the organs most affected by COVID-19 because the virus accesses host cells via the enzymeangiotensin-converting enzyme 2 (ACE2), which is most abundant in type II alveolar cells of the lungs. The virus uses a special surface glycoprotein called a "spike" (peplomer) 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 these hypotheses need to be tested. As the alveolar disease progresses, respiratory failure might develop and death may follow.
SARS-CoV-2 may also cause respiratory failure through affecting the brainstem as other coronaviruses have been found to invade the central nervous system (CNS). While virus has been detected in cerebrospinal fluid of autopsies, the exact mechanism by which it invades the CNS remains unclear and may first involve invasion of peripheral nerves given the low levels of ACE2 in the brain.

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 virus can cause acute myocardial injury and chronic damage to the cardiovascular system. An acute cardiac injury was found in 12% of infected people admitted to the hospital in Wuhan, China, and is more frequent in severe disease. Rates of cardiovascular symptoms are high, owing to the systemic inflammatory response and immune system disorders during disease progression, but acute myocardial injuries may also be related to ACE2 receptors in the heart. ACE2 receptors are highly expressed in the heart and are involved in heart function. A high incidence of thrombosis (31%) and venous thromboembolism (25%) have been found in ICU patients with COVID-19 infections and may be related to poor prognosis. Blood vessel dysfunction and clot formation (as suggested by high D-dimer levels) are thought to play a significant role in mortality, incidences of clots leading to pulmonary embolisms, and ischaemic events within the brain have been noted as complications leading to death in patients infected with SARS-CoV-2. Infection appears to set off a chain of vasoconstrictive responses within the body, constriction of blood vessels within the pulmonary circulation has also been posited as a mechanism in which oxygenation decreases alongside the presentation of viral pneumonia.

Another common cause of death is complications related to the kidneys—SARS-CoV-2 directly infects kidney cells, as confirmed in post-mortem studies. Acute kidney injury is a common complication and cause of death; this is more significant in patients with already compromised kidney function, especially in people with pre-existing chronic conditions such as hypertension and diabetes which specifically cause nephropathy in the long run.

Autopsies of people who died of COVID-19 have found diffuse alveolar damage (DAD), and lymphocyte-containing inflammatory infiltrates within the lung. (5)

Immunopathology

Although SARS-COV-2 has a tropism for ACE2-expressing epithelial cells of the respiratory tract, patients with severe COVID-19 have symptoms of systemic hyperinflammation. Clinical laboratory findings of elevated IL-2, IL-7, IL-6,granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon-γ inducible protein 10 (IP-10), monocyte chemoattractant protein 1 (MCP-1), macrophage inflammatory protein 1-α (MIP-1α), and tumour necrosis factor-α (TNF-α) indicative of cytokine release syndrome (CRS) suggest an underlying immunopathology.

Additionally, people with COVID-19 and acute respiratory distress syndrome (ARDS) have classical serum biomarkers of CRS, including elevated C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer, and ferritin.

Systemic inflammation results in vasodilation, allowing inflammatory lymphocytic and monocytic infiltration of the lung and the heart. In particular, pathogenic GM-CSF-secreting T-cells were shown to correlate with the recruitment of inflammatory IL-6-secreting monocytes and severe lung pathology in COVID-19 patients. Lymphocytic infiltrates have also been reported at autopsy.

V. DIAGNOSIS

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 thegenetic sequence so laboratories across the world could independently developpolymerase chain reaction (PCR) tests to detect infection by the virus. As of 4 April 2020, antibody tests (which may detect active infections and whether a person had been infected in the past) were in development, but not yet widely used. The Chinese experience with testing has shown the accuracy is only 60 to 70%.The FDA in the United States 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 Universitysuggested 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 study asked hospitalised COVID-19 patients to cough into a sterile container, thus producing a saliva sample, and detected the virus in eleven of twelve patients using RT-PCR. This technique has the potential of being quicker than a swab and involving less risk to health care workers (collection at home or in the car).

Along with laboratory testing, chest CT scans may be helpful to diagnose COVID-19 in individuals with a high clinical suspicion of infection but are not recommended for routine screening. Bilateral multilobar ground-glass opacitieswith a peripheral, asymmetric, and posterior distribution are common in early infection. Subpleural dominance, crazy paving (lobular septal thickening with variable alveolar filling), and consolidation may appear as the disease progresses. (6)

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.

Few data are available about microscopic lesions and the pathophysiology of COVID-19.[111][112] The main pathological findings at autopsy are:

- Macroscopy: pleurisy, pericarditis, lung consolidation and pulmonary oedema
- Four types of severity of viral pneumonia can be observed:
  - minor pneumonia: minor serous exudation, minor fibrin exudation
  - mild pneumonia: pulmonary oedema, pneumocyte hyperplasia, large atypical pneumocytes, interstitialinflammation with lymphocytic in filtration and multinucleated giant cell formation
  - severe pneumonia: diffuse alveolar damage (DAD) with diffuse alveolar exudates. DAD is the cause of acute respiratory distress syndrome (ARDS) and severe hypoxemia.
  - healing pneumonia: organisation of exudates in alve olar cavities and pulmonary interstitial fibrosis
  - plasmocytosis in BAL
- Blood: disseminated intravascular coagulation (DIC);[114] leukoerythroblastic reaction[115]
- Liver: microvesicular steatosis

VI. PREVENTION

Preventive measures to reduce the chances of infection include staying at home, avoiding crowded places, keeping distance from others, washing hands with soap and water often and for at least 20 seconds, practising 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. Proper hand hygiene after any cough or sneeze is encouraged. The CDC has recommended the use ofcloth face

coverings in public settings where other social distancing measures are difficult to maintain, in part to limit transmission by asymptomatic individuals. The U.S.National Institutes of Health guidelines do not recommend any medication for prevention of COVID-19, before or after exposure to the SARS-CoV-2 virus, outside of the setting of a clinical trial.

Social distancing strategies aim to reduce contact of infected persons with large groups by closing schools and workplaces, restricting travel, and cancelling large public gatherings. Distancing guidelines also include that people stay at least 6 feet (1.8 m) apart. There is no medication known to be effective at preventing COVID-19.

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