

Covid-19 (Pandemic): A Review Article

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ABSTRACT

Coronaviruses are a group of enveloped viruses with nonsegmented, single-stranded, and positive-sense RNA genomes. Coronaviruses belong to the "Coronaviridae family", which causes various diseases, from the common cold to SARS and MERS. In March 2020 the World Health Organization declared the SARS-Cov-2 virus a global pandemic. We performed a review to describe existing literature about Corona Virus Disease 2019 (COVID-19) history, Symptoms, Epidemiology, Clinical features, Clinical manifestations, Diagnosis, Treatment, Prevention.

Key words: COVID-19, Symptoms, Epidemiology, Clinical features, Clinical manifestations, Diagnosis, Treatment, Prevention

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INTRODUCTION

The human body is exposed to a variety of infectious microorganisms, such as viruses, bacteria, fungi, protozoa, and helminths, which cause tissue damage through different mechanisms. Viruses are unique among these five types of infectious organisms in that they can manipulate the host-cell machinery in a unique way and continuously evolve to survive and prosper in all species [1].

COVID-19 is the disease caused by a new coronavirus called SARS-CoV-2. WHO first learned of this new virus on 31 December 2019, following a report of a cluster of cases of 'viral pneumonia' in Wuhan, People's Republic of China [2].

Since December 2019, a novel coronavirus disease had rapidly spread throughout China, leading to a global outbreak, and causing considerable public health concern. World Health Organisation (WHO) announced the outbreak of COVID-19 as a global public health emergency on 30 January 2020. In India, the first case of COVID-19 was reported on January 27, 2020, in Kerala district. Since then, there is a wide variation in the reporting of cases across the country. The case reporting is based on the SARS-CoV-2 antigen testing by Real-Time Reverse

Transcription Polymerase Chain Reaction (RT-qPCR) or by Rapid Antigen Test (RAT) [3].

Coronavirus (CoV) is clustered under the viral family group that causes disease in mammals and birds. A pandemic novel coronavirus was named as "Corona Virus Disease 2019" (2019-nCoV) by World Health Organization (WHO) in Geneva, Switzerland. As its RNA pattern is closer to SARS, the 2019 Coronavirus is renamed as SARSCoV-2 pandemic. It belongs to the subfamily Orthocoronavirinae inside the family Coronaviridae, order Nidovirales, and the realm Riboviria [4]. A two-dimensional view of Corona beneath a transmission electron microscopy reveals a characteristic look of "paying homage to a crown" around the virions. This led to naming the virus "Corona", meaning "crown" or "halo" in Latin

This is the deadly third-generation virus in Corona family preceded by severe acute respiratory syndrome (SARS) in 2003, killed almost 10% of total affected patients (8429) across 29 international locations and Middle East Respiratory Syndrome (MERS) in 2012, even more lethal with a mortality rate of 30% of the infected patients [4].

HISTORY

Coronaviruses are enveloped positive sense RNA viruses ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving it a crown like appearance under the electron microscope; hence the name coronavirus [3]. Four corona viruses namely HKU1, NL63,

229E and OC43 have been in circulation in humans, and generally cause mild respiratory disease.

There have been two events in the past two decades wherein crossover of animal betacoronaviruses to humans has resulted in severe disease. The first such instance was in 2002–2003 when a new coronavirus of the β genera and with origin in bats crossed over to humans via the intermediary host of palm civet cats in the Guangdong province of China. This virus, designated as severe acute respiratory syndrome coronavirus affected 8422 people mostly in China and Hong Kong and caused 916 deaths (mortality rate 11%) before being contained. Almost a decade later in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV), also of bat origin, emerged in Saudi Arabia with dromedary camels as the intermediate host and affected 2494 people and caused 858 deaths (fatality rate 34%) [5].

SYMPTOMS

A wide range of symptoms are found in COVID-19 patients, ranging from mild/moderate to severe, rapidly progressive, and fulminant disease. Symptoms of COVID-19 are non-specific and disease presentation can range from asymptomatic to severe pneumonia. Incidence of asymptomatic cases ranges from 1.6% to 51.7% and these people do not present typical clinical symptoms or signs and do not present apparent abnormalities in lung computed tomography. The most common symptoms of COVID-19 are fever, cough, myalgia, or fatigue and atypical symptoms include sputum, headache, haemoptysis, vomiting, and diarrhoea. Some patients may present with sore throat, rhinorrhoea, headache, and confusion a few days before the onset of fever, indicating that fever is a critical symptom, but not the initial manifestation of infection. Furthermore, some patients experience loss of smell (hyposmia) or taste (hypogeusia), which are now being considered early warning signs and indications for self-isolation [6].

The most common symptoms of COVID-19 are

- Fever.
- Dry cough.
- Fatigue.

Other symptoms that are less common and may affect some patients include

- Loss of taste or smell.
- Nasal congestion.
- Conjunctivitis (also known as red eyes).
- Sore throat.
- Headache.
- Muscle or joint pain.
- Different types of skin rash.
- Nausea or vomiting.
- Diarrhea.
- Chills or dizziness.

Symptoms of severe COVID-19 disease include:

- Shortness of breath.

- Loss of appetite.
- Confusion.
- Persistent pain or pressure in the chest.
- High temperature (above 38 °C).

Other less common symptoms are

- Irritability.
- Confusion.
- Reduced consciousness (sometimes associated with seizures).
- Anxiety.
- Depression.
- Sleep disorders.
- More severe and rare neurological complications such as strokes, brain inflammation, delirium and nerve damage.

People of all ages who experience fever and/or cough associated with difficulty breathing or shortness of breath, chest pain or pressure, or loss of speech or movement should seek medical care immediately. If possible, call your health care provider, hotline or health facility first, so you can be directed to the right clinic [1].

EPIDEMIOLOGY

All ages are at risk of getting the illness. This is because the ailment is transmitted through large droplets that result from coughing and sneezing by symptomatic individuals. In some instances, the infection can happen from asymptomatic individuals and before the beginning of symptoms. As of March 2020, the WHO announced that there are about 87,317 cases of COVID-19 globally as well as confirmed cases of deaths is 2,977. This implies that the disease symptoms are mild as only 3.42 per cent of patients with it have died because of the virus. At the same time, the high number of incidences and deaths have been identified in China. It is that 92 per cent of the total number of occurrences have been reported in Asia, mainly China. Importantly, the confirmed incidences are clinically identified and laboratory-confirmed. Further, outside Asia, the number of cases and deaths differs due to the on-going nature of the disease, population density, degree of testing and reporting, and timing of reducing strategies. The features of COVID-19 are categorized into the host of the virus, transmission mode and incubation period. In the first place, the Chinese horseshoe bat is the natural hosts and the terminal hosts are humans. Also, the transmission is from individual to individual through aerosol droplets. Lastly, the incubation period varies from two to fourteen days. Therefore, COVID-19 cumulative incidence differs depending on the country and incidences have been confirmed in almost all continents [7].

GEOGRAPHIC DISTRIBUTION

Since the initial report from China, the disease spread rapidly, and the number of cases increased exponentially. On January 11, the first case was reported outside mainland China in Thailand,⁷ and within months, the disease spread to all the continents except Antarctica.

India reported its first case of COVID-19 on January 30, 2020. This rose to three cases by February 3, 2020. No further cases were reported in February 2020. However, by mid-March, the number of infected cases started to increase, and many cases were reported from all over India. The first COVID-19 related death in India was reported on March 12, 2020. By the second week of April, the disease spread to all states in India except Sikkim. At the time of writing this manuscript, there have been 2,170,265 cases and 135,163 deaths globally and 15,712 cases and 507 deaths in India [8,9].

TRANSMISSION

Zoonotic transmission initially appeared to be a plausible cause as majority of early cases had a history of exposure to wet markets [10]. However, by the end of January 2020, the number of people who developed the disease without exposure to the market or another person with respiratory symptoms increased. The spread of the disease among persons who did not visit Wuhan and among healthcare workers suggested a person-to-person spread of the virus [11,12]. The exact mode of transmission of this virus is unknown. But, as with other respiratory viruses, droplet borne infection, either directly or indirectly, through fomites is probably the predominant mode of transmission. At present, there is no evidence for airborne transmission of the virus. [12, 13] Although virus particles have been detected in stool samples of both symptomatic and convalescing patients, the risk of feco-oral transmission is unclear [13].

Period of Infectivity

The duration for which a patient with COVID-19 remains infective is unclear. Viral load in the oropharyngeal secretions is highest during the early symptomatic stage of the disease [13,14]. The patient can continue to shed the virus even after symptom resolution [13]. In a study from China, the median duration of virus shedding was 20 days (interquartile range [IQR] 17.0–24.0) amongst the survivors [15]. A study of viral dynamics in mild and severe cases revealed that mild cases tend to clear the viruses early, while severe cases can have prolonged viral shedding [16]. Data from studies using twin respiratory and fecal sampling have shown viral shedding can persist in stools for more than 4 weeks even when respiratory samples are negative [17]. Xu et al identified male sex, delayed hospitalization after illness, and invasive mechanical ventilation as risk factors for prolonged viral shedding [13]. Transmission during the asymptomatic phase has also been reported. In a study from Singapore, 6.4% of the 157 locally acquired cases of COVID-19 were attributed to transmission during the asymptomatic phase of the disease [18].

CLINICAL FEATURES

The clinical features of this ailment vary, extending from an asymptomatic state to acute respiratory distress syndrome to septic shock and multi-organ dysfunction. Ideally, this ailment is categorized depending on its severity and this include mild, moderate, severe, and

critical. The shared symptoms of individuals with the disease include fever (98.6 per cent), tiredness (69.6 per cent), dry cough, and looseness of the bowels.

Asymptomatic infections

Asymptomatic infections have been well documented [19-27]. One review estimated that 33 percent of people with SARS-CoV-2 infection never develop symptoms [28]. This estimate was based on four large population-based, cross-sectional surveys, among which the median proportion of individuals who had no symptoms at the time of a positive test was 46 percent (range 43 to 77 percent), and on 14 longitudinal studies, among which a median of 73 percent of initially asymptomatic individuals remained so on follow-up. However, there is still uncertainty around the proportion of asymptomatic infections, with a wide range reported across studies. Additionally, the definition of "asymptomatic" may vary across studies, depending on which specific symptoms were assessed. The range of findings in studies evaluating asymptomatic infections is reflected in the following examples:

- In a COVID-19 outbreak on a cruise ship where nearly all passengers and staff were screened for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), approximately 19 percent of the population on board tested positive; 58 percent of the 712 confirmed COVID-19 cases were asymptomatic at the time of diagnosis [29,30]. In studies of subsets of those asymptomatic individuals, who were hospitalized and monitored, approximately 77 to 89 percent remained asymptomatic over time [30,31].
- In a smaller COVID-19 outbreak within a skilled nursing facility, 27 of the 48 residents (56 percent) who had a positive screening test were asymptomatic at the time of diagnosis, but 24 of them developed symptoms over the next seven days [32].
- Other studies, particularly those conducted among younger populations, have reported even higher proportions of infections that are asymptomatic [33-37]. As an example, in an outbreak on an aircraft carrier, a quarter of the crew, among whom the mean age was 27 years, tested positive for SARS-CoV-2 [36]. Among the 1271 cases, only 22 percent were symptomatic at the time of testing and 43 percent remained asymptomatic throughout the observation period. High rates of asymptomatic infection have also been reported among pregnant women presenting for delivery [2,34].

Patients with asymptomatic infection may have objective clinical abnormalities [24,38]. As an example, in a study of 24 patients with asymptomatic infection who all underwent chest computed tomography (CT), 50 percent had typical ground-glass opacities or patchy shadowing, and another 20 percent had atypical imaging abnormalities [38]. Five patients developed low-grade fever, with or without other typical symptoms, a few days after diagnosis. In another study of 55 patients with asymptomatic infection identified through contact tracing, 67 percent had CT evidence of pneumonia on

admission; only two patients developed hypoxia, and all recovered [24].

As above, some individuals who are asymptomatic at the time of diagnosis go on to develop symptoms (ie, they were actually presymptomatic). In one study, symptom onset occurred a median of four days (range of three to seven) after the initial positive RT-PCR test [30].

SEVERITY OF SYMPTOMATIC INFECTION

Spectrum of infection severity

The spectrum of symptomatic infection ranges from mild to critical; most infections are not severe [19,39-44]. Specifically, in a report from the Chinese Centre for Disease Control and Prevention that included approximately 44,500 confirmed infections with an estimation of disease severity [45]:

- Mild disease (no or mild pneumonia) was reported in 81 percent.
- Severe disease (eg, with dyspnea, hypoxia, or >50 percent lung involvement on imaging within 24 to 48 hours) was reported in 14 percent.
- Critical disease (eg, with respiratory failure, shock, or multiorgan dysfunction) was reported in 5 percent.
- The overall case fatality rate was 2.3 percent; no deaths were reported among noncritical cases.

Similarly, in a report of 1.3 million cases reported to the United States Centers for Disease Control and Prevention (CDC) through the end of May 2020, 14 percent were hospitalized, 2 percent were admitted to the intensive care unit (ICU), and 5 percent died [46]. The risk of severe illness varied by age and underlying comorbidities.

Infection fatality rates

The case fatality rate only indicates the mortality rate among documented cases. Since many severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections are asymptomatic and many mild infections do not get diagnosed, the infection fatality rate (i.e., the estimated mortality rate among all individuals with infection) is considerably lower and has been estimated in some analyses to be between 0.15 and 1 percent, with substantial heterogeneity by location and across risk groups [47-50].

Fatality rates among hospitalized patients

Among hospitalized patients, the risk of critical or fatal disease is high [51-57]. In a study from early in the pandemic that included 2741 patients who were hospitalized for COVID-19 in a New York City health care system, 665 patients (24 percent) died or were discharged to hospice [54]. Of the 647 patients who received invasive mechanical ventilation, 60 percent died, 13 percent were still ventilated, and 16 percent were discharged by the end of the study. The in-hospital fatality rate associated with COVID-19 has been higher than that for influenza [58-60]. As an example, in an

analysis of hospital data from the United States Veterans Health Administration, patients with COVID-19 were five times more likely to die during the hospitalization than patients with influenza (21 versus 3.8 percent) [44].

Over the course of the pandemic, declining in-hospital fatality rates have been reported [61-64]. As an example, in a retrospective study of a national surveillance database in England that included over 21,000 critical care patients with COVID-19, ICU survival improved from 58 percent in late March 2020 to 80 percent by June 2020 [61]. The reasons for this observation are uncertain, but potential explanations include improvements in hospital care of COVID-19 and better allocation of resources when hospitals were not overburdened.

In resource-limited settings, in-hospital mortality rates may be higher than those reported elsewhere. As an example, in a study from 10 countries in Africa, where there was a median of two intensive care specialists in each hospital and a minority of facilities did not have pulse oximetry, the in-hospital 30-day mortality rate following critical care admission was 48 percent [65]. Mortality was associated with underlying comorbidities as well as resource shortages.

Excess deaths during the pandemic

Neither the case fatality rate nor the infection fatality rate account for the full burden of the pandemic, which includes excess mortality from other conditions because of delayed care, overburdened health care systems, and social determinants of health [66-68].

Incubation period and serial interval

The mean or median incubation period of the disease ranges from 5 to 6 days [69,70]. Lauer et al estimated that 2.5% of the patients will develop symptoms within 2.2 days (95% CI, 1.8 to 2.9 days) and 97.5% of patients will develop symptoms within 11.5 days (95% CI, 8.2-15.6 days).

Serial interval refers to the time interval between the onset of symptoms in the primary case and the secondary case. The mean serial interval is estimated to be approximately 4 to 5 days [71,72]. By analysing data from 468 infector-infectee pairs, Du et al noted that 59 secondary cases had symptoms earlier than their primary case. This suggested that there is a possibility that the transmission of the disease occurred during the asymptomatic phase of illness in this group of patients [73].

Period of Infectivity

The duration for which a patient with COVID-19 remains infective is unclear. Viral load in the oropharyngeal secretions is highest during the early symptomatic stage of the disease [74]. The patient can continue to shed the virus even after symptom resolution. In a study from China, the median duration of virus shedding was 20 days (interquartile range [IQR] 17.0-24.0) amongst the

survivors [75]. A study of viral dynamics in mild and severe cases revealed that mild cases tend to clear the viruses early, while severe cases can have prolonged viral shedding [76]. Data from studies using twin respiratory and fecal sampling have shown viral shedding can persist in stools for more than 4 weeks even when respiratory samples are negative [77]. Transmission during the asymptomatic phase has also been reported. In a study from Singapore, 6.4% of the 157 locally acquired cases of COVID-19 were attributed to transmission during the asymptomatic phase of the disease [78].

DIAGNOSIS

When is a COVID 19 diagnostic test required?

Diagnostic testing for COVID-19 is conducted to find out whether a person is infected with the SARS-CoV-2 virus, responsible for COVID-19 infection. Your healthcare practitioner may recommend you the same if:

- You are experiencing symptoms of COVID 19 such as high fever, cough, shortness of breath, excessive fatigue, etc.
- You have long-term health conditions such as asthma, heart diseases, etc. and experience a sudden worsening of symptoms.
- You have come in contact with someone tested positive for COVID 19 recently.
- You are a healthcare worker working in a hospital environment.
- You require hospitalization for treatment or surgery of existing medical conditions.

What are the different laboratory tests available to diagnosis COVID 19?

In general, there are two types of tests for diagnosing COVID-19 namely, Antigen or rapid testing and Molecular

or PCR testing. The antigen test is often used as a point-of-care test, less expensive and yields quicker results within minutes. However, there is a higher chance of false-negative results as compared to molecular testing. Molecular testing yields more accurate results but are time-consuming [79].

TREATMENT

Initially, early in the pandemic, the understanding of COVID-19 and its therapeutic management was limited, creating an urgency to mitigate this new viral illness with experimental therapies and drug repurposing. Since then, due to the intense efforts of clinical researchers globally, significant progress has been made which has led to a better understanding of not only COVID-19 and its management but also has resulted in the development of novel therapeutics and vaccine development at an unprecedented speed [80].

PREVENTION

Preventive measures are the current strategy to limit the spread of cases. Early screening, diagnosis, isolation, and treatment are necessary to prevent further spread. Preventive strategies are focused on the isolation of patients and careful infection control, including appropriate measures to be adopted during the diagnosis and the provision of clinical care to an infected patient [81]. Important COVID-19 prevention and control measures in community are summarized in Table 1.

Table 1: COVID-19 prevention and control measures in community.

Quarantine	Other Measures
Voluntary quarantine (self-quarantine)	Avoiding crowding
Mandatory quarantine	Hand hygiene
Private residence	Isolation
Hospital	Personal protective equipment
Public institution	School measures/closures
Others (cruise ships, etc)	Social distancing
	Workplace measures/closures

CONCLUSION

As everyone across the globe is aware that there is no accurate medicine for Covid-19 till date, hence it is very important to prevent the spread in the society. Notably, COVID-19 is an RNA virus that poses a threat to public health. Currently, the disease has caused thousands of infections and deaths. The main points in preventing the spread in society are hand hygiene, social distancing and quarantine.

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