



**CORONAVIRUSES- REVIEW ARTICLE**

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**ABSTRACT**

Coronaviruses (CoV) are a great family of viruses that cause ailment ranging from the common cold to more severe sicknesses such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). 2-14 days represents the current official estimated range for the novel coronavirus COVID-19. The World Health Organization (WHO) declared the 2019–20 coronavirus outbreak a pandemic and a Public Health Emergency of International Concern (PHEIC).

**KEYWORDS:** Coronaviruses (Covid-19), Infection, Pandemic.

**INTRODUCTION**

Coronavirus disease (COVID-19) is a new strain that was discovered in 2019 and has not been formerly acknowledged in humans. Coronaviruses are zoonotic, meaning they are transmitted between animals and people. Thorough investigations found that SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to Human beings. Several known coronaviruses are socializing in animals that have not yet infected humans.

Common signs of contamination include respiratory symptoms, temperature, cough, shortness of breath and breathing problems. In more severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death.

Standard recommendations to stop contamination blowout consist of regular hand washing, masking the mouth and nose once coughing and sneezing, thoroughly cooking meat and eggs. Avoid close connection with anybody showing symptoms of respiratory complaint such as coughing and sneezing.

Coronavirus disease spreads primarily through contact with an infected person when they cough or sneeze. It also spreads when a person touches a surface or object that has the virus on it, then touches their eyes, nose, or mouth.

**COVID-19 Incubation Period**

The incubation period (time from exposure towards the development of symptoms) of the virus is estimated to be between 2 and 14 days based on the following sources.

- The World Health Organization (WHO) reported an incubation period for COVID-19 between 2 and 10 days.
- China's National Health Commission (NHC) had initially estimated an incubation period from 10 to 14 days
- The United States' CDC estimates the incubation period for COVID-19 to be between 2 and 14 days
- DXY.cn, a leading Chinese online community for physicians and health care professionals, is reporting an incubation period of "3 to 7 days, up to 14 days".

The incubation period has been found to be as long as 24 days (range: 0-24 days; median: 3.0 days) in a study published on February 9. The WHO said a very long incubation period could reflect a double exposure. 24 days represented an outlier observation that must be taken into consideration in the context of the main finding of the study. WHO is not considering changing recommendations regarding incubation periods.

More recently, however, a case with an incubation period of 19 days was observed in a JAMA study published on Feb. 21, and another case with an incubation period of 27 days was reported by Hubei Province on Feb. 22. Incubation period of 5.2 days on average.

A Chinese study published in the *New England Journal of Medicine* on Jan. 30<sup>[7]</sup>, has found the incubation period to be 5.2 days on average, but it varies greatly among patients. The Chinese team conducting the study said their findings support a 14-day medical observation period for people exposed to the pathogen.

### 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.<sup>[3]</sup> 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  $\beta$  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<sup>4</sup>. 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%).<sup>[5]</sup>

### Epidemiology and Pathogenesis

All ages are susceptible. Infection is transmitted through large droplets generated during coughing and sneezing by symptomatic patients but can also occur from asymptomatic people and before onset of symptoms.<sup>9</sup> Studies have shown higher viral loads in the nasal cavity as compared to the throat with no difference in viral burden between symptomatic and asymptomatic people.<sup>12</sup> Patients can be infectious for as long as the symptoms last and even on clinical recovery. Some people may act as super spreaders; a UK citizen who attended a conference in Singapore infected 11 other people while staying in a resort in the French Alps and upon return to the UK.<sup>[6]</sup> These infected droplets can spread 1–2 m and deposit on surfaces. The virus can remain viable on surfaces for days in favourable atmospheric conditions but are destroyed in less than a minute by common disinfectants like sodium hypochlorite, hydrogen peroxide etc.<sup>[13]</sup> Infection is acquired either by inhalation of these droplets or touching surfaces contaminated by them and then touching the nose, mouth and eyes.

The virus is also present in the stool and contamination of the water supply and subsequent transmission via aerosolization/feco oral route is also hypothesized.<sup>[6]</sup> As per current information, transplacental transmission from pregnant women to their fetus has not been described.

However, neonatal disease due to post natal transmission is described. The incubation period varies from 2 to 14 d [median 5 d]. Studies have identified angiotensin receptor 2 (ACE<sub>2</sub>) as the receptor through which the virus enters the respiratory mucosa.<sup>[7]</sup>

The basic case reproduction rate (BCR) is estimated to range from 2 to 6.47 in various modelling studies. In comparison, the BCR of SARS was 2 and 1.3 for pandemic flu H1N1 2009.<sup>[5]</sup>

### Clinical Features<sup>[3,5]</sup>

The clinical features of COVID-19 are varied, ranging from asymptomatic state to acute respiratory distress syndrome and multi organ dysfunction. The common clinical features include fever (not in all), cough, sore throat, headache, fatigue, headache, myalgia and breathlessness. Conjunctivitis has also been described. Thus, they are indistinguishable from other respiratory infections. In a subset of patients, by the end of the first week the disease can progress to pneumonia, respiratory failure and death. This progression is associated with extreme rise in inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNF $\alpha$ .

The median time from onset of symptoms to dyspnea was 5 d, hospitalization 7 d and acute respiratory distress syndrome (ARDS) 8 d. The need for intensive care admission was in 25–30% of affected patients in published series. Complications witnessed included acute lung injury, ARDS, shock and acute kidney injury. Recovery started in the 2nd or 3rd wk.

The median duration of hospital stay in those who recovered was 10 d. Adverse outcomes and death are more common in the elderly and those with underlying co-morbidities (50–75% of fatal cases). Fatality rate in hospitalized adult patients ranged from 4 to 11%. The overall case fatality rate is estimated to range between 2 and 3%.

Interestingly, disease in patients outside Hubei province has been reported to be milder than those from Wuhan. Similarly, the severity and case fatality rate in patients outside China has been reported to be milder. This may either be due to selection bias wherein the cases reporting from Wuhan included only the severe cases or due to predisposition of the Asian population to the virus due to higher expression of ACE<sub>2</sub> receptors on the respiratory mucosa.

Disease in neonates, infants and children has been also reported to be significantly milder than their adult counterparts. In a series of 34 children admitted to a hospital in Shenzhen, China between January 19th and February 7th, there were 14 males and 20 females. The median age was 8 y 11 mo and in 28 children the infection was linked to a family member and 26 children had history of travel/residence to Hubei province in China. All the patients were either asymptomatic (9%) or

had mild disease. No severe or critical cases were seen. The most common symptoms were fever (50%) and cough (38%). All patients recovered with symptomatic therapy and there were no deaths. One case of severe pneumonia and multiorgan dysfunction in a child has also been reported. Similarly the neonatal cases that have been reported have been mild.

### DIAGNOSIS<sup>[6]</sup>

A suspect case is defined as one with fever, sore throat and cough who has history of travel to China or other areas of persistent local transmission or contact with patients with similar travel history or those with confirmed COVID-19 infection. However cases may be asymptomatic or even without fever. A confirmed case is a suspect case with a positive molecular test.

Specific diagnosis is by specific molecular tests on respiratory samples (throat swab/ nasopharyngeal swab/ sputum/ endotracheal aspirates and bronchoalveolar lavage). Virus may also be detected in the stool and in severe cases, the blood. It must be remembered that the multiplex PCR panels currently available do not include the COVID-19. Commercial tests are also not available at present. In a suspect case in India, the appropriate sample has to be sent to designated reference labs in India or the National Institute of Virology in Pune. As the epidemic progresses, commercial tests will become available.

Other laboratory investigations are usually non specific. The white cell count is usually normal or low. There may be lymphopenia; a lymphocyte count <1000 has been associated with severe disease. The platelet count is usually normal or mildly low. The CRP and ESR are generally elevated but procalcitonin levels are usually normal. A high procalcitonin level may indicate a bacterial co-infection. The ALT/AST, prothrombin time, creatinine, D-dimer, CPK and LDH may be elevated and high levels are associated with severe disease.

The chest X-ray (CXR) usually shows bilateral infiltrates but may be normal in early disease. The CT is more sensitive and specific. CT imaging generally shows infiltrates, ground glass opacities and sub segmental consolidation. It is also abnormal in asymptomatic patients/ patients with no clinical evidence of lower respiratory tract involvement. In fact, abnormal CT scans have been used to diagnose COVID-19 in suspect cases with negative molecular diagnosis; many of these patients had positive molecular tests on repeat testing.

### DIFFERENTIAL DIAGNOSIS<sup>[7]</sup>

The differential diagnosis includes all types of respiratory viral infections [influenza, parainfluenza, respiratory syncytial virus (RSV), adenovirus, human metapneumovirus, non COVID-19 coronavirus], atypical organisms (mycoplasma, chlamydia) and bacterial infections. It is not possible to differentiate COVID-19 from these infections clinically or through routine lab

tests. Therefore travel history becomes important. However, as the epidemic spreads, the travel history will become irrelevant.

### TREATMENT<sup>[7,8]</sup>

Treatment is essentially supportive and symptomatic. The first step is to ensure adequate isolation (discussed later) to prevent transmission to other contacts, patients and healthcare workers. Mild illness should be managed at home with counseling about danger signs. The usual principles are maintaining hydration and nutrition and controlling fever and cough. Routine use of antibiotics and antivirals such as oseltamivir should be avoided in confirmed cases. In hypoxic patients, provision of oxygen through nasal prongs, face mask, high flow nasal cannula (HFNC) or non-invasive ventilation is indicated. Mechanical ventilation and even extra corporeal membrane oxygen support may be needed. Renal replacement therapy may be needed in some. Antibiotics and antifungals are required if co-infections are suspected or proven.

The role of corticosteroids is unproven; while current international consensus and WHO advocate against their use, Chinese guidelines do recommend short term therapy with low-to-moderate dose corticosteroids in COVID-19 ARDS. Detailed guidelines for critical care management for COVID-19 have been published by the WHO. There is, as of now, no approved treatment for COVID-19. Antiviral drugs such as ribavirin, lopinavir-ritonavir have been used based on the experience with SARS and MERS. In a historical control study in patients with SARS, patients treated with lopinavir-ritonavir with ribavirin had better outcomes as compared to those given ribavirin alone.

In the case series of 99 hospitalized patients with COVID-19 infection from Wuhan, oxygen was given to 76%, non-invasive ventilation in 13%, mechanical ventilation in 4%, extracorporeal membrane oxygenation (ECMO) in 3%, continuous renal replacement therapy (CRRT) in 9%, antibiotics in 71%, antifungals in 15%, glucocorticoids in 19% and intravenous immunoglobulin therapy in 27%. Antiviral therapy consisting of oseltamivir, ganciclovir and lopinavir-ritonavir was given to 75% of the patients. The duration of non-invasive ventilation was 4–22 d [median 9 d] and mechanical ventilation for 3–20 d [median 17 d]. In the case series of children discussed earlier, all children recovered with basic treatment and did not need intensive care.

There is anecdotal experience with use of remdesvir, a broad spectrum anti RNA drug developed for Ebola in management of COVID-19. More evidence is needed before these drugs are recommended. Other drugs proposed for therapy are arbidol (an antiviral drug available in Russia and China), intravenous immunoglobulin, interferons, chloroquine and plasma of patients recovered from COVID-19.

## PRACTICE SAFE INFECTION CONTROL PROTOCOLS<sup>[9,10]</sup>

- **Use preprocedural rinse of peroxide.**<sup>[2]</sup> The concentration of any rinse used should be at least 5%. Over-the-counter peroxide is typically 2%, so it would need to be diluted. However, in the dental industry, we have two products, Colgate Proxyl and Listerine Whitening Mouthrinse, that are 1.5%. Utilize what you may already have in office or can get through your dental suppliers. Rinse at the beginning of the appointment for 60 seconds and again after the appointment. Over-the-counter peroxide is not currently available in most stores, as the CDC is recommending cleaning surfaces in the home with peroxide.
- At this time, the ADA and CDC are **only recommending peroxide** to destroy the virus. While chlorine dioxide and chlorhexidine have been shown to kill some viruses, at this time, the American Dental Association and the Centers for Disease Control and Prevention have not endorsed their use for destroying COVID-19. In some other countries, public health authorities have advised to continue to use the recommended standard of a chlorhexidine rinse *followed* by peroxide rinse.
- **ALWAYS** wear appropriate personal protective equipment (PPE) when working directly with patients. This includes safety glasses, gowns, lab jackets, face shields, gloves, and a mask appropriate for the task.
- Consider alternating levels of mask protection when performing activities to address mask shortage. The layering of lower level mask does not increase your protection.
  - **Level 1 mask** (particulate filtration  $\geq 95\%$ ): Use when minimal risk of exposure exists. Ideal for procedures where there is a low amount of aerosols (e.g., patient exams, cleaning operatories, taking impressions, trimming/finishing/polishing temporaries, taking radiographs).
  - **Level 2 mask** (particulate filtration 98%): Use when procedures create light to moderate amounts of aerosols. This includes limited oral surgery, endodontics, prophylaxis, restorative/composite, and sealants.
  - **Level 3 mask** (particulate filtration 98%): Use when procedures create moderate to heavy amounts of aerosols. This includes complex oral surgeries, crown preparations, implant placement, periodontal surgery, use of ultrasonic scalers, and laser-based procedures
- **What about N95 masks?**<sup>[11]</sup> N95 mask or respirators can reduce the dental provider's exposure to all airborne particles from large droplets to small aerosols. They must be custom fitted to each wearer and employees must have annual training for the N95. If a dental office elects to use N95 mask, they must have a written OSHA Respiratory Standard. Wearers of an N95 must have medical clearance to evaluate their ability to wear a respirator safely.

They are not recommended for persons with facial hair, or some medical conditions. The CDC recommends that in times of shortage, as with the COVID-19 pandemic, only health-care professionals who work in a sterile field or may be exposed to high-velocity splash, spray, or splatter of blood, such as those in an operative or procedural setting, wear N95 respirators.

### Patient screening<sup>[12]</sup>

- Front desk staff should call and screen patients prior to their scheduled appointments. Additionally, staff should screen patients when arriving for their appointments.
- Reschedule any patient who discloses they have had flu-like symptoms that include a high fever, dry cough, or difficulty breathing. Or if they have been in contact with anyone who has tested positive for COVID-19 within the last three weeks or 21 days.

### General housekeeping

- Avoid direct handshaking, hugging, or greetings that require direct contact.
- Provide hand-sanitizer in all operatories, at the front desk, and in all bathrooms.
- Disinfect common areas including entry doors, reception chairs, and front desk counters throughout the day. Diluted household bleach will kill the virus.
- Wash hands often and refrain from touching your face—eyes, nose, and mouth.

### Prevention<sup>[12]</sup>

Preventive measures must focus on optimizing infection control protocols, self-isolation, and patient isolation during the provision of clinical care. The WHO has advised against close contact with patients, farm animals, and wild animals.<sup>[4]</sup> Patients and the general public must cover coughs and sneezes to help prevent aerosol transmission. Frequent handwashing with soap and water is also required. As an alternative measure, hand sanitizers can also be used. Immunocompromised individuals are advised to avoid public gatherings. Emergency medicine departments must apply strict hygiene measures for the control of infections. Healthcare personnel must use personal protective equipment such as N95 masks, FFP3 masks, gowns, eye protection, gloves, and gowns.

### CONCLUSIONS

The COVID-19 pandemic is spreading across the globe at an alarming rate. It has caused more infections and deaths as compared with SARS or MERS. Based on R0 values, it is deemed that SARS-CoV-2 is more infectious than SARS or MERS. Elderly and immunocompromised patients are at the greatest risk of fatality. The rapid spread of disease warrants intense surveillance and isolation protocols to prevent further transmission. No confirmed medication or vaccine has been developed. Current treatment strategies are aimed at symptomatic care and oxygen therapy. Prophylactic vaccination is

required for the future prevention of COV-related epidemic or pandemic.

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