

Review

COVID-19: A brief clinical overview

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Abstract

COVID-19 is an ongoing pandemic that has infected millions and killed hundreds of thousands. This pandemic has led to massive socioeconomic problems across the world, while measures of lockdown were taken to contain the spread of the virus. This is a clinical review paper on COVID-19 to provide a current summary of the illness. The virus causing COVID-19 spreads by droplets between humans during close contact and enters the body through the eyes, nose and mouth. It often presents mildly with fever, loss of smell and taste, a continuous dry cough and shortness of breath; however, it has the potential to be severe, requiring hospital admission including intensive care. At risk groups include the elderly, those with hypertension, diabetes, cardiovascular and lung diseases and other physical comorbidities. Current management is mainly prevention through isolation, and supportive treatment for symptoms. While the vaccines are being developed, the search is on for an effective treatment around the world. Currently, good hand hygiene along with social distancing are the suggested ways to control the spread of the virus and beat the pandemic.

Key words

Coronavirus, COVID-19 virus, Pandemics, Prevention, SARS-CoV-2, Treatment

Introduction

The 2019 coronavirus pandemic is caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). The disease that this virus relates to is known as Coronavirus disease 2019 (COVID-19). This is a novel strain that was newly identified and has genetic similarities to SARS-CoV-1, which was the cause of the SARS outbreak of 2003.¹ This review aims to provide a clinical profile of COVID-19, summarising the current known information about this infection and its management.

Epidemiology

This coronavirus initially affected China, but quickly then spread across the world, where according to the World Health Organisation (WHO), it has infected more than 8.3 million people and has killed over 450,000 by 19 June

2020.² The largest impacted regions include the Americas and Europe, together making up millions of cases. Early studies showed that the majority of cases in China were of people aged between 30 and 79 years.³ In the USA, 65 years and older made up 31% of all cases and 80% of the deaths.⁴

The demographic of people who are most likely to be infected and have severe illness are likely to be elderly, male, and have a comorbidity such as hypertension, cardiovascular disease, diabetes, chronic lung disease, or cancer.⁵ Immunosuppressed patients are also particularly vulnerable. There does not appear to be a greater risk of severe illness in children when compared to adults.⁶

Evidence from USA suggests that COVID-19 affects a disproportionately high number of African Americans.⁷ In the UK, it has been observed that Black, Asian and Minority Ethnic (BAME) groups are at increased risk of infection and death from COVID-19.⁸

Transmission

The virus shows human to human transmission, via droplets produced when an infected person coughs, sneezes or talks. This includes people who are infected but are asymptomatic. In other words, infected persons can be contagious during the pre-symptomatic period that occurs before symptoms appear.

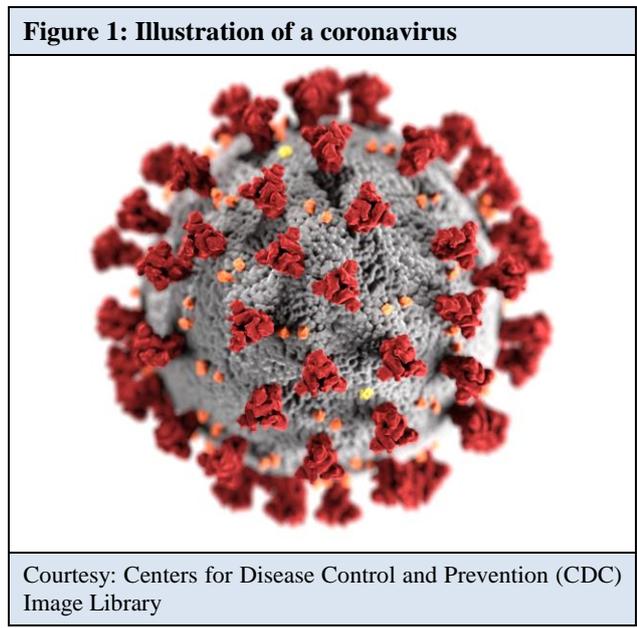
One can also contract the virus from touching contaminated surfaces or objects, then touching their face.⁹ The virus remains potentially infective for different lengths of time on different surfaces such as papers, plastics and metals.¹⁰

The reproductive number (R_0) of a pathogen is the number of people that one infected individual will proceed to infect. Of the coronavirus responsible for COVID-19, the natural R_0 is between 2 and 3, suggesting that without control, the outbreak will continue to spread and grow larger.^{11,12} To decrease and control the outbreak, the R_0 should be brought to a value below 1.

Prevention and protection

Without a vaccine, protecting oneself from the virus is important to reduce the risk of infection. To help do this, it is advised to regularly wash hands with soap and water

or using an alcohol-based hand sanitizer, and use tissues to catch coughs and sneezes.¹⁶ Policies such as self-isolation and social distancing as well as wearing face masks, over both nose and mouth, in public settings will slow the spread of the virus.¹³



Pathophysiology

Coronaviruses are enveloped, positive-sense, single-stranded RNA viruses (Figure 1). The mechanisms that lead to pneumonia and respiratory distress appear to be complex and research is ongoing on this topic. Angiotensin converting enzyme 2 (ACE2) has been recognised as a functional receptor for SARS-CoV-2, which allows the virus to enter the host cell. This receptor is expressed widely throughout the body, and is at higher concentrations in the lung, heart, ilium, kidney and bladder. An infection from this virus, in the severe cases, leads to a large, IL-6 mediated, immune reaction in the host, sometimes called a ‘cytokine storm’. This commonly develops into widespread tissue damage.^{14,15}

Further to this, severe cases have also been associated with thrombosis, pulmonary embolisms strokes. This likely has been caused by the hypercoagulability profile that develops as endothelium is damaged due to the infection.¹⁵ Other complications of the disease include pneumonia, severe acute respiratory syndrome, liver failure and kidney failure and even death.¹⁶

In a considerable proportion of cases COVID-19 results in death. Deaths may be attributed directly to COVID-19 e.g. via terminal organ failure such as respiratory failure or septic shock, or secondary to frailty and age or severe comorbidity, where COVID-19 acted as a secondary factor.^{16,17}

Signs and symptoms

The WHO and the NHS have listed the symptoms associated with COVID-19. These have been summarised in Table 1.^{18,19}

After being infected, the virus has an incubation period of usually four to six days, however this can be stretched up to 14 days. Therefore, infected individuals can be spreading the virus for up to 2 weeks while being asymptomatic.^{20,21} Most infections will be mild, and people will be able to overcome the infection without hospital treatment. Despite this, everyone has the risk of developing COVID-19, becoming seriously ill and needing admission to hospital.^{19,22}

Table 1: Signs and symptoms of COVID-19
<p><i>Common symptoms</i></p> <ul style="list-style-type: none"> • Fever • New, continuous dry cough • Tiredness • Change to or loss of taste or smell
<p><i>Serious symptoms</i></p> <ul style="list-style-type: none"> • Shortness of breath • Chest pain/pressure • Loss of speech or movement
<p><i>Other symptoms</i></p> <ul style="list-style-type: none"> • Aches and pains • Sore throat • Diarrhoea • Conjunctivitis • Headache • A rash on skin • Discolouration of fingers/toes
<p>Sources: WHO Coronavirus Symptoms 2020,¹⁸ National Health Service (NHS) UK, Coronavirus Symptoms 2020.¹⁹</p>

Diagnosis

Diagnosing COVID-19 requires a good background history of exposure along with diagnostic investigations. Key symptoms mentioned above should be present. Important risk factors for contracting the virus include exposure to potentially infected individuals, being older age, and residing in a care facility such as an elderly care home.²³

Diagnostic testing usually requires upper respiratory tract samples; this is done with a viral nose and throat swab. Sputum samples are also beneficial.²⁴ These viral swabs are then polymerase chain reaction (PCR) tested and are used to check for the presence of the virus antigen, not the immune response to the infection. This allows the diagnosing of a current ongoing infection. Early antigen tests allow for faster isolation and treatment, therefore decreasing the spread and improving the prognosis.^{25,26}

Antibody tests are now becoming available to test for the presence of specific antibodies to SARS-CoV-2. This allows the identification of someone who was previously infected; it is not a test to check for current infection. This may suggest that this person has developed some immunity to the virus, however more evidence is needed to say this with certainty.²⁵

Management

The treatment algorithm for COVID-19 can be applied to suspected and confirmed cases. If suspected to have the infection, one should isolate for 14 days (to cover the duration of incubation period) to prevent further infections and they should be monitored in case of deterioration.

People with mild symptoms should isolate and can be treated at home, with medications for symptomatic relief for fever, malaise and cough.

Hospital admission should occur to those who have severe shortness of breath or are developing signs of pneumonia or an influenza like illness.¹³ Patients with risk factors of other comorbidities and frailty should be prioritised during admission.²⁷ Supportive care in hospital includes oxygen, intravenous fluids, and correcting acid/base or electrolyte abnormalities. The use of venous thromboembolism prophylaxis, and inhaled pulmonary vasodilators should be considered. Any causes of anxiety should be minimised.²³

Referral to critical care should be considered for patients who are more frail (clinical frailty scale score of <5) and would benefit from critical organ support.²⁸ In Intensive Care Unit (ICU), patients are constantly monitored for any deteriorating signs and symptoms. In case of respiratory distress, they may require non-invasive ventilation with high flow nasal cannula or intubation. Prone positioning may be used as it improves air entry to lungs and is associated with reduced mortality in acute respiratory distress.²⁹

Many trials are attempting to identify a treatment for coronavirus. One such major trial is the "Randomised Evaluation of COVID-19 Therapy Trial" (RECOVERY trial). This is a trial that is testing many possible treatments and monitoring their effects. Examples of treatments being trialled includes lopinavir-ritonavir (HIV antiretrovirals), low-dose dexamethasone, azithromycin antibiotic, tocilizumab (immunosuppressant) and convalescent plasma donated by COVID-19 survivors (contains anti-COVID-19 antibodies).³⁰ Recent results from this trial show that low dose dexamethasone was able to reduce the number of deaths significantly in those more severely ill (1/3 in those ventilated and 1/5 of those on oxygen only). However, for patients not on respiratory support, this had no significant effect.³¹

Prognosis

Currently there is not a large amount of data detailing the prognosis and future implications of this virus. Roughly 80% of people have mild symptoms only and recover quickly. The case fatality rate increases with age, with most of the death being associated with underlying conditions.²³ WHO reports a roughly 5.8% worldwide mortality from COVID-19, however this does vary from country to country. For example, in Europe, the UK and Italy both have a mortality rate of roughly 14%, whereas Germany and Switzerland's mortality rate is around 5%,

and countries like Austria and Norway have mortality rates at roughly 2-3%.³²

Research is showing that despite there being many strains of SARS-CoV-2 around the world, it has not been associated with increased pathogenicity or transmissibility. Rather, these mutations have been mostly neutral in nature.^{33,34} Further research is needed to identify the reasons for differences in mortality, however, theories propose that the differences may be due to the consequences of early, rigorous testing and lockdown versus not doing so, and the effect of the age structure of a country's population.

Vaccine

There is currently no safe and available vaccine to protect against COVID-19 as vaccine development normally takes a long period of time. There are several clinical trials at different stages where many potential vaccines are being tested. One promising potential vaccine is known as AZD1222, being developed by the University of Oxford and AstraZeneca. It is currently a Phase 2/3 trial, so clinical trials on people is being carried out. It is a recombinant vaccine using chimpanzee adenovirus to carry DNA that codes for the spike protein of SARS-CoV-2. This is the protein that enables the virus to attach to and enter a host cell. It is hoped that exposure to this protein DNA will lead to strong B cell and T cell mediated immune responses, providing immunity to SARS-CoV-2 infection.³⁵

Conclusion

The COVID-19 pandemic hit the world very quickly and is a global health emergency. It is a disease that can affect anyone; spreads easily and has the potential to be fatal. Infection control measures, monitoring and early diagnosis are critically important to prevent its spread and protect the community including those most at risk, the elderly and those with comorbidities. Many who become infected will recover without further support, however for the minority that need admission to hospital, appropriate supportive management will improve their prognosis. Research is ongoing to identify an effective treatment strategy to treat COVID-19, and to develop a vaccine. It is expected that these efforts will lead to containing the pandemic.

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Competing interests: None.

Received: 30 May 2020; **Revised:** 20 June 2020; **Accepted:** 20 June 2020

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Citation: Kar S. COVID-19: A brief clinical overview. *Journal of Geriatric Care and Research* 2020, 7(2): 74-78.

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