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REVIEW ARTICLE: EPIDEMIOLOGY OF COVID'19

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ABSTRACT

Purpose: To carefully review and understand the cause, distribution, progression, determinants and deterrents of COVID-19.

Methodology: Peer reviewed data relevant to study was collected from PubMed, Google Scholar, WHO database, Research gate and Wikipedia based on pre-set inclusion and exclusion criteria.

Findings: Covid-19 is a principally respiratory illness caused by the novel Corona Virus (SARS-CoV2). It started as an epidemic in Wuhan, China in December 2019, became a pandemic in March 2020 and have now infected almost 22 million people over 216 countries causing about three-quarter of a million deaths. It spreads primarily through droplets, aerosols or contact with contaminated surfaces. Illness is usually mild to moderate flu-like symptoms but can be asymptomatic as well as severe especially in patients with underlying co-morbidities. Testing can either be antigen based through polymerase chain reaction or antibody based. Treatment is generally supportive while the efficacy of diverse pharmacological remains controversial. Public education, early diagnosis and isolation, restriction of gatherings and movements have been the main method used worldwide to tackle this outbreak.

Unique contribution to theory, practice and policy: Emphasizes the infectivity of SARS-CoV2 virus and need for health practitioners and general public to adhere strictly to preventive measures in order to avert a global second wave of the pandemic.

Conclusion: COVID-19 is an infectious disease that have rapidly spread from china to the world at large. A lot of efforts and policies have been made to prevent and control its spread. There's need to adhere to guidelines in order to reduce spread and subsequent mortality especially amongst vulnerable groups. As many countries commence protocols to re-open, there's need to do so in line with lessons learnt during this outbreak to avoid a more devastating second wave.

Key Words: *COVID-19, Corona Virus, Coronavirus Pandemic, SARS-CoV2*

INTRODUCTION

Covid-19 is a respiratory illness responsible for the ongoing global pandemic caused by a strain of coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2).¹ On 11 February 2020, the International Committee on Taxonomy of Viruses (ICTV) announced ‘severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2)’ as the name of the new virus causing the ongoing global pandemic. This name was chosen because the virus is genetically related to the coronavirus responsible for the SARS outbreak of 2003, although different from SARS outbreak of 2003. That same day (11, February 2020), WHO announced ‘COVID-19’ as the name of the new disease.² The outbreak was first identified in Wuhan, China, December 2019. On 30 January, 2020, the World Health Organization declared the outbreak a Public Health Emergence of International Concern and a pandemic on 11th March, 2020.^{3,4} By 19th December 2020, almost 75 million cases of COVID-19 have been reported in more than 216 countries and territories, leading to about 1,676,236 deaths with the number of recoveries reaching over 52 million people. The Americas and Europe are the worst hit with over 32 and 23 million cases respectively while Africa and Western Pacific are the least hit with about 1.7 and 1 million cases respectively.⁵

METHODOLOGY

Literature search was carried out in PubMed, Google Scholar, WHO database, Research gate and Wikipedia collating data till December 19th 2020, when this paper was last updated. Key words used for the search includes; “COVID-19”, “coronavirus”, “coronavirus pandemic” and “SARS-CoV2”. Studies with topics relevant to this review were included while studies not significantly related were excluded. Furthermore, only peer-reviewed studies were included in our review.

Viral Structure and Life Cycle

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel virus first isolated from three people who presented with pneumonia connected to the cluster of acute respiratory illness cases in Wuhan.⁶ It’s shown that all features of the novel SARS-CoV-2 virus occur in related coronaviruses in nature.⁷ The virus is a positive sense, single-stranded RNA virus that belong to the subfamily Coronavirinae, family Coronaviridae, order Nidovirales and divided into 4 genera – alpha, beta, delta, gamma.^{8,9} It’s enveloped in a lipid bilayer which fuses with host cell membrane, releasing RNA into cytoplasm and resulting in the translation of various viral proteins. The replicated RNA genome and synthesized viral proteins reassemble into new viruses, which burst out of the cell.¹⁰ The virus contains four structural proteins, namely envelope (E), spike (S), membrane (M) and nucleocapsid (N). The S, M, and E proteins together form the envelope of the virus while the N proteins remain associated with the RNA forming nucleocapsid inside the envelope. Polymers of the S proteins remain embedded in the envelope giving it a crown-like appearance, thus the name coronavirus. The virus enters the cell via binding of two proteins – the S protein with the ACE2 protein. The S – protein is a glycoprotein expressed as a homotrimer on the viral envelope. Each S-protein consists of two subunits - S1 and S2 subunits. The S1 subunit includes a receptor-binding domain that targets receptors on host cells and S2 regulates the membrane fusion. This viral envelope protein, S protein binds with the human protein receptor ACE2 which is abundant in the lung, heart, kidney and adipose tissue. Binding of S-protein with ACE2 allows for membrane fusion and introduction of SARS-CoV-2 RNA into the cell.^{8,9,10,11}

Coronavirus Structure and Protein Visualization

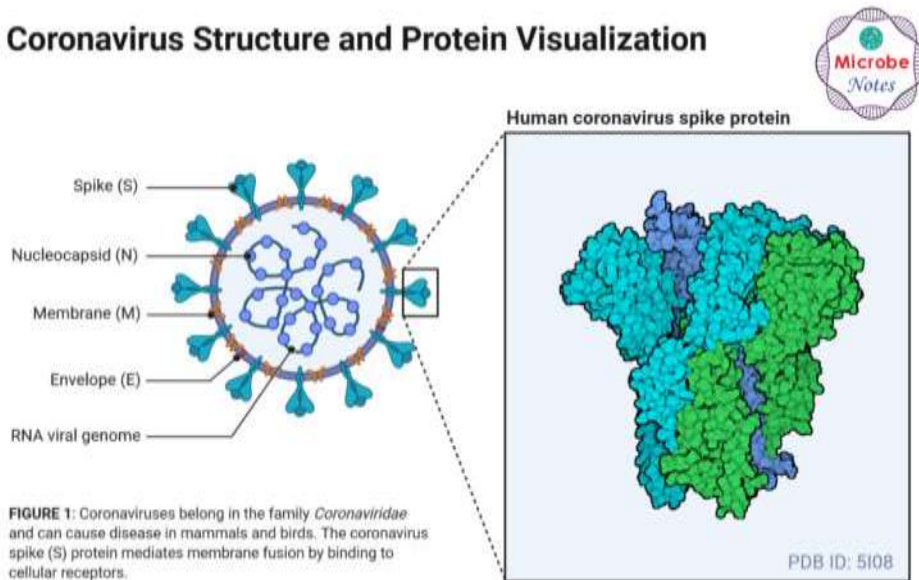


Fig. 1 shows the structure and protein visualization of SARS-COV-2. Adopted from the microbes notes.

Transmission and Infectivity

With regard to COVID-19, early patients were reported to have some link to the Huanan Seafood Market in Wuhan, China, suggesting that these early infections were due to animal-to-human transmission. However, later cases reported among medical staff and others without any history of exposure to the Huanan Seafood Market or visiting Wuhan. This was taken as an indication of human-to-human transmission.²¹

The details of the spread of novel coronavirus are still under investigation.¹² The spread of COVID-19 is rapid contributing to its ascension from an epidemic in December to a Pandemic in March.¹⁰ People are most infectious when they show symptoms (symptomatic transmission) but may be infectious for up to two days before symptoms appear (pre-symptomatic transmission). People can also transmit the virus without showing any symptom (asymptomatic transmission) but it's still unclear how often this happens. A recent review done in June 2020 revealed that 40-45% of infected people are asymptomatic.¹² The potential of asymptomatic patients infecting others is justifiable by multiple studies. Younger patients tend to remain asymptomatic while the elder usually show symptoms.¹⁰

Transmission usually occurs from close contacts and droplets produced by an infected person during coughing, sneezing, talking or singing. Transmission may also occur through aerosols.^{10,12,14} However, there is scarce evidence to suggest airborne transfer. Very minimal to RNA concentration is found in airborne samples. Urine or serum samples of positive patients that have been investigated showed no RNA detected. Viral RNA can also be detected on fomites including cardboard, copper and plastics. On fomites, the amount of viable active virus decreases over time until it can no longer cause infection. It is not known what viral load is required to cause infection

via this method but it can be detected for up to four hours on copper, up to one day on cardboard and up to three days on plastic (polypropylene) and stainless steel.^{10,12,13,14} Sputum and saliva carry large amounts of virus. Although COVID-19 is not a sexually transmitted infection, direct contact such as kissing, intimate contact and fecal-oral routes are suspected to transmit the virus. The virus may occur in breast milk but it's not known whether it is infectious and transmittable to the baby.^{15,16,17,18,19} In addition, in a small study conducted on women in their third trimester who were confirmed to be infected with the coronavirus there was no evidence that there is transmission from mother to child. However, all pregnant mothers underwent caesarean sections, so it remains unclear whether transmission can occur during vagina birth.²²

The WHO's initial estimate of the basic reproduction number, R_0 were 1.4-2.5 with an average of 1.95. However, an early April 2020 review found the R_0 (without control measures) to be higher at 3.28 and the median R_0 to be 2.79.²⁰

The mean incubation period is about 5 days with a range between 1-14 days. The period from the onset of COVID-19 symptoms to death ranged from 6-41 days with a median of 14 days. This period is said to be dependent on some factors including the age and immune status of the patient. It was observed to be shorter among elderly patients.²²

Symptoms tend resolve after 10 days. However, viral shedding is said to continue despite symptoms disappearing. Studies have shown that COVID-19 RNA viral shedding persists for about 18 days (by nasopharyngeal swab) or 19 days (via feces).¹⁰ While mild and asymptomatic cases tend to shed 10 days (between 8-15 days) after symptom resolution, with 90% resolving after 10 days and nearly all cases resolving after 15 days, severe cases continue to shed up until 25 days after initial symptoms arise. Furthermore, severe cases also have 60 times more viral load than mild cases.¹⁰ Due to these findings, the Chinese Municipal Health Commission has recommended against discharging patients until the patient has remained afebrile for three days and RT-PCR becomes negative.¹⁰ Similarly, WHO revised the criteria for discharging patients from isolation without requiring testing which was published on 27th May 2020.²³ According to WHO, for symptomatic patients, discharge should be considered 10 days after symptom onset, plus at least 3 additional days without symptoms (including without fever and without respiratory symptoms).^{24,25} For asymptomatic cases, 10 days after positive test for SARS-CoV-2.²⁶

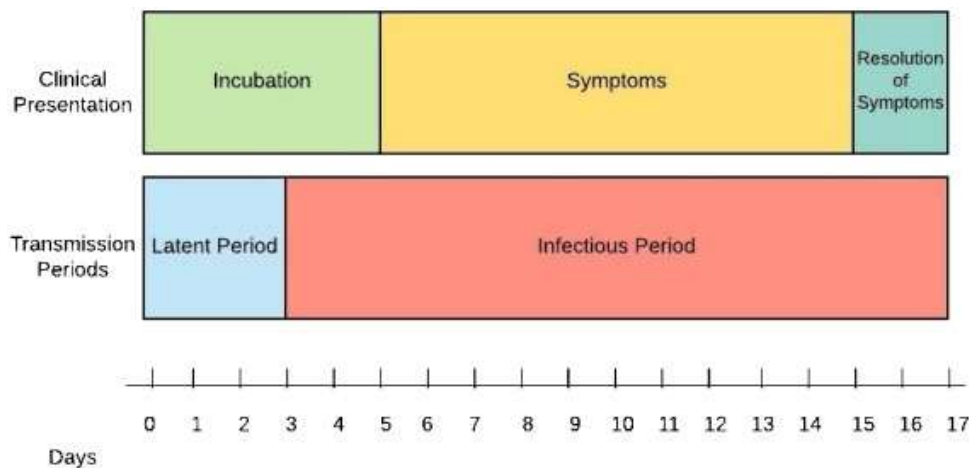


Fig. 2 illustrates COVID-19 Clinical and Transmission Periods.

Clinical Features

The complete clinical manifestation is not clear yet, as the reported symptoms range from mild to severe, with some cases even resulting in death.²¹ Moreover, symptoms are relatively non-specific. The most commonly reported symptoms are fever and dry cough. Less common symptoms include fatigue, phlegm, dyspnea, anosmia, myalgia, sore throat, chills, vomiting, diarrhea, hemoptysis and rash.^{27,28,29} complications include acute respiratory distress syndrome, myocardial injury, co-infection and acute kidney injury.¹⁰

Pathogenesis

Patients infected with COVID-19 showed high leucocytes numbers and abnormal respiratory findings and increased levels of plasma pro-inflammatory cytokines. The main pathogenesis of COVID-19 infection as a respiratory system targeting virus was severe pneumonia, RNAemia, combined with the incidence of ground-glass opacities and acute cardiac injury. In patients with COVID-19, significantly high blood levels of cytokines and chemokines were noted. These included IL1 β , IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFN γ , IP10, MCP1, MIP1 α , MIP1 β , PDGFB, TNF α , and VEGFA.²²

Laboratory Findings

Laboratory values that suggest COVID-19 infection include lymphopenia, prolonged prothrombin time, elevated lactate dehydrogenase, elevated alanine aminotransferase, elevated neutrophils, eosinopenia, elevated C-reactive protein and elevated troponin. The most common findings are eosinopenia and lymphopenia.¹⁰

Diagnosis

COVID-19 can be provisionally diagnosed on the basis of symptoms and confirmed using the reverse transcription polymerase chain reaction (RT-PCR) testing of infected secretions or CT imaging of the chest.^{30,31}

Viral testing

This test involves the use of real time rRT-PCR which detects the presence of viral RNA fragments in nasopharyngeal swab samples.³²

Imaging

The characteristic features of symptomatic COVID-19 patients on chest radiographs and computed tomography include asymmetric peripheral ground-glass, opacities without pleural effusions.³³ Due to overlap with other infections such as adenovirus, imaging without confirmation by rRT-PCR is of limited specificity in identifying COVID-19, however it has been demonstrated to be faster and more sensitive than PCR according to a large study conducted in China.^{33,31} Chest CT scans of COVID-19 reveal bilateral ground glass opacification or consolidation. Ground-glass opacification is dominant during early stages and consolidation presents at later stages.¹⁰

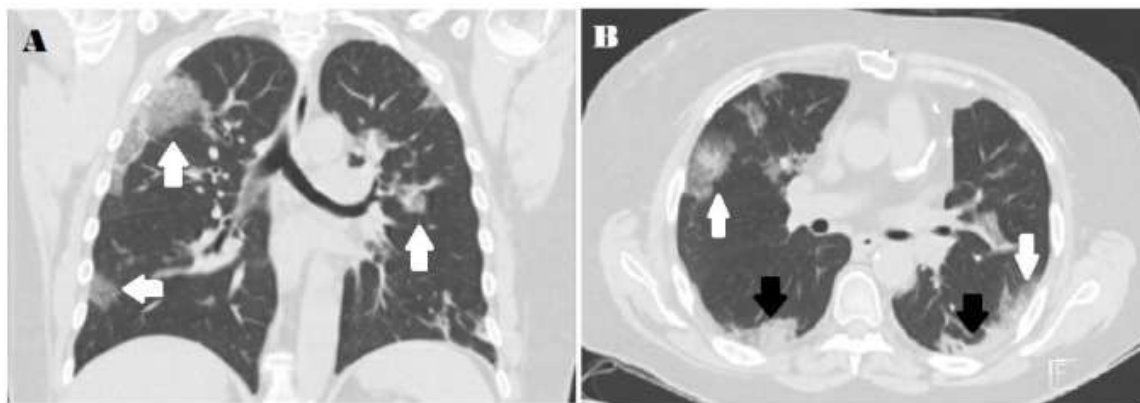


Fig. 3A shows Coronal thin-section unenhanced CT image showing ground-glass opacities with a rounded morphology

Fig. 3B shows axial thin-section unenhanced CT scan showing diffuse bilateral confluent and patchy ground-glass (white arrows) and consolidative (black arrows) pulmonary opacities.

Adapted from Siordia JA Jr. Epidemiology and clinical features of COVID-19: A review of current literature. *J Clin Virol.* 2020;127:104357. doi:10.1016/j.jcv.2020.104357

Prevention and Control

A pivotal part of managing COVID-19 is trying to decrease and delay the epidemic peak, known as ‘flattening the curve’.³⁴ Preventive measures advocated to reduce the chances of infection include the stay-home order, social distancing, use of face mask in public, avoiding crowded places, observing good personal hygiene such as hand washing with soap and water, use of hand-sanitizers, practicing good respiratory hygiene, and avoiding touching eyes, nose or mouth with unwashed hands.^{35,36,37}

The WHO, the Chinese National Health Commission and the United States’ National Institutes of Health have published recommendations for treating hospitalized COVID-19 patients.^{38,3,40}

General supportive treatments, personal hygiene and a healthy lifestyle are recommended for those with mild symptoms.^{41,42}

Like for many disease outbreaks, different nations have adopted the 3 level model of prevention for COVID-19. Firstly, by ensuring public education through the diverse media outlets there is increase in public awareness on public measures like use of alcohol based hand sanitizers, frequent hand washing, use of protective tools like facemasks, common symptoms of illness, protocols for testing and protocol for presentation to healthcare facilities. Studies have shown that increased awareness and adherence to these policies have helped reduce spread of COVID-19.⁴³ This have been augmented with government policies restricting movements and non-essential gatherings to curtail the spread of the disease.⁴⁴ Also diverse studies are ongoing to develop an effective vaccine that will help build acquired immunity against the disease.⁴⁵ The RNA vaccine BNT162b2 funded by Pfizer and BioNTech showed a 95% efficacy in preventing Covid-19 in a randomized study which had 43,548 participants.⁴⁶ This brings a lot of hope in the global fight against SAR-CoV2.

Early detection, isolation and treatment of cases have been shown to prevent further spread to vulnerable population with overall reduction in cases and mortality. Different nations have spent billions world over to obtain effective testing kits and set up centers for treatment of COVID-19 patients. The WHO emphasizes on general supportive treatment while different countries have developed their own personal management protocols including different pharmaceutical agents regardless like Hydroxychloroquine, Remdesivir, Lopinavir/Ritonavir, etc.⁴⁷

Lastly many countries have developed and instituted protocols in place to prevent a second wave as they gradually relieve restrictions previously set to curtail the spread of COVID-19. This encompasses changes in the nature of operation cutting through different sectors. Such measures includes distancing at schools and public places, incorporation of hand-washing equipment into public places, use of protective face masks, home rapid test kits for high risk groups (e.g health workers) and national vaccination programmes.

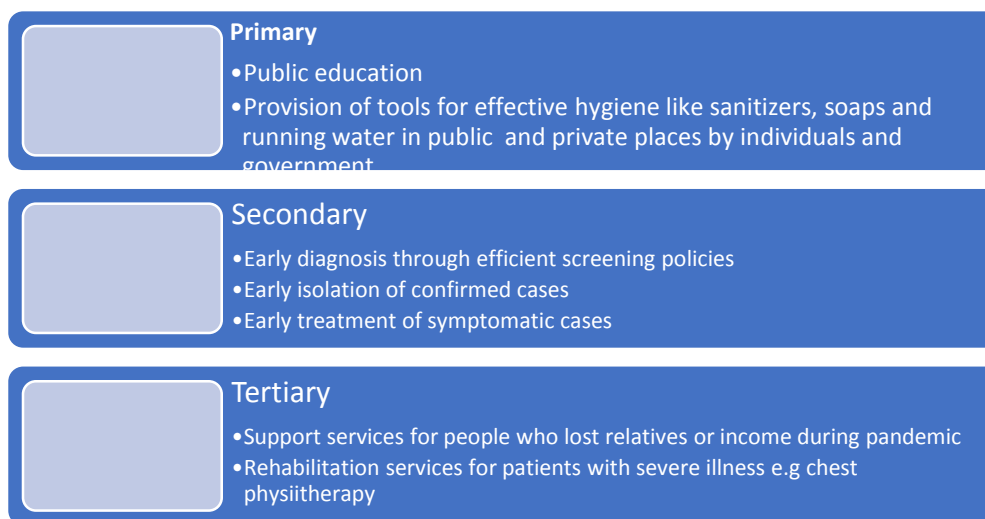


Fig. 4 illustrating Prevention and Control of COVID-19

Conclusion

COVID-19, caused by the SARS-CoV2 which started as “pneumonia of unknown cause” in Wuhan, China has now taken the world unawares within the period of one year. It has varying presentations like fever, generalised body pain, loss of smell, loss of taste and dry cough. It is spread through droplets produced when coughing, sneezing, talking and singing, and can also be transmitted through fomites. With a mean incubation period of 5 days, the infection can progress from mild to severe conditions, with the outcome determined by factors such as age and immune status of the patient. So far, the management is mostly preventive, through public education on social distancing, use of face coverings in public, practice of good personal and respiratory hygiene and the just recently developed RNA vaccine. General supportive treatment and trial of pharmacotherapy have also been useful.

Recommendation

The hope that the world is nearing the end of this ravaging pandemic has no doubt been upheld by the development of vaccines. However, mass production and worldwide distribution would take some time. Hence, it is imperative we continue practices such as maintaining good hygiene, prompt public health response, quick and efficient information sharing and close synergism between nations, as these have helped slow down the highly infectious COVID-19 disease. It has become very imperative to strictly follow public health guidelines in order to avert a second global wave of the pandemic.

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