Understanding and Combatting COVID-19: Insights from Clinical Characteristics and Management Strategies

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Abstract

In recent years, various emerging diseases of pathogens such as Ebola virus, Zika virus, Nipah virus, and coronavirus have arisen in various geographic zones. The public is threatened with the dissemination of COVID-19 by a new global health epidemic. Data on the clinical characteristics of the patients involved have been expected since December 2019, when the coronavirus disease in 2019 (COVID-19) occurred in Wuhan City and quickly spread throughout China. Data from several research reports, WHO recommendations and other papers were extracted in this study. Readers should be aware that new health features, diagnostic, therapeutic plans and COVID-19 results are revised about every hour. In order to avoid the future spread of the infection to other patients and health care personnel, it is important to classify potential cases as quickly as possible and to separate suspicious persons from the reported COVID-19 cases.

Keywords: COVID-19, Respiratory illness, Diagnosis, Treatment, Prevention, SARS

Significance | Timely analysis is crucial for understanding and combating global health crises like COVID-19 effectively

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Introduction

Coronaviruses are a diverse group of viruses known to cause animal and human diseases. Among them, seven coronaviruses can infect humans globally, with four of them—229E, NL63, OC43, and HKU1—being particularly common. These viruses can lead to various illnesses, from mild common colds to severe respiratory conditions like Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The most recent addition to this list is the novel coronavirus (COVID-19), declared a global public health emergency by the World Health Organization (WHO) in March 2020.

SARS-CoV-2, the virus responsible for COVID-19, is the seventh identified coronavirus capable of infecting humans. It has caused significant mortality rates, with reports indicating a mortality rate of 2.1 percent among cases reported in China and 0.2 percent for cases outside China. Among hospitalized patients, mortality rates have ranged from 11 to 15 percent. By February 2020, over 81,000 laboratory-confirmed cases of COVID-19 had been recorded worldwide. Recent reports have indicated similarities in the magnitude of COVID-19 cases with previous SARS outbreaks, highlighting the urgent need for further research to understand the clinical features and severity of the disease.

This paper aims to reflect on the propagation characteristics of coronaviruses, drawing insights from various authoritative journals and reputable sources, including the study by Murphy et al. (2019). Given its rapid dissemination and evolving nature, it underscores the importance of conducting revised studies to better classify the clinical features and severity of COVID-19, particularly in mainland China.

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Cryo-electron tomography and cryo-electron microscopy studies have shown that coronavirus particles, known as virions, have a spherical shape with a diameter of approximately 125 nanometers (Bárcena et al, 2019). This structure is depicted in Figure 1. One of the most distinguishing features of coronaviruses is their spike projections, which protrude from the outer surface and give the virus a crown-like appearance. These spike projections are crucial in the virus's ability to cause disease. Inside the virion's envelope, there are symmetric nucleocapsids, which are characteristic of positive-sense RNA viruses (Neuman et al, 2016).

The coronavirus genome encodes four structural proteins: membrane (M), spike (S), envelope (E), and nucleocapsid (N). These proteins are located at the 3' end of the genome. The spike (S) protein, weighing approximately 150 kilodaltons, is glycosylated and has an N-terminal signal sequence. Another structural protein found in some beta-coronaviruses is hemagglutinin-esterase (HE). This protein, also known as HE, binds to sialic acids on glycoproteins and possesses acetyl-esterase activity (Deslandes et al, 2020). These activities aid in the virus's entry into cells and facilitate its replication in the body. Additionally, the hemagglutinin-esterase protein increases the neurovirulence of certain coronaviruses, such as the murine hepatitis virus (Huang et al, 2020).

Coronaviruses, characterized as RNA viruses with an envelope, belong to one of five branches of RNA viruses, with coronaviruses mainly falling into branch 2 (Chen et al., 2020). They are classified into animal and human coronaviruses, with the beta-coronavirus being one of the four genera in the coronavirinae family (Wang et al., 2020). Within the beta-coronavirus group, there are four lineages, namely 2a, 2b, 2c, and 2d, with SARS-CoV and SARS-CoV-2 belonging to lineage 2b, and MERS-CoV to lineage 2c (Liya et al., 2020). Although it's uncertain how SARS-CoV, MERS-CoV, and SARS CoV-2 infect humans through animals, bats are considered the natural reservoir for coronaviruses, with a gene similarity of 96.2% between bat genomes and SARS-CoV-2 (Zhou et al., 2020).

SARS-CoV, a spherical enveloped virus with an average diameter of 78 nm, shares a similar assembly process with other coronaviruses. Its genome consists of replicase (rep), spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins, with untranslated regions on both ends. Out of 11 open reading frames (ORFs), ORF1a and ORF1b encode essential non-structural proteins such as RNA-dependent RNA polymerase, helicase/triphosphatase, ribonucleases, and RNA-cap methyltransferases (Rota et al., 2023). Conversely, MERS-CoV encodes sixteen non-structural proteins necessary for transcription and replication through ten ORFs (Skariyachan, 2019).

SARS-CoV-2, another beta coronavirus, shares structural similarities with other coronaviruses. It has spikes measuring 9 to 12 nm in size and a diameter ranging from 60 to 140 nm. The replicase, spike, envelope, membrane, and nucleocapsid proteins are encoded by ORF1a/b from the 5' to the 3' end, with additional ORFs encoding non-structural proteins (Zhu et al., 2020). The spike protein (S) of SARS-CoV-2 has a unique furin-like cleavage site, possibly contributing to its efficient and uncontrolled proliferation compared to other beta-coronaviruses (Rabaan et al., 2020).

COVID-19 spreads mainly when people fail to maintain social distancing from infected individuals, as droplets containing the virus can be emitted when infected individuals cough, sneeze, laugh, or talk. These droplets, whether symptomatic or asymptomatic, can carry the virus. The United States Centers for Disease Control (CDC) recommends a distance of two or six feet for social separation, while the World Health Organization (WHO) suggests one meter, or three feet. It has long been believed that infected individuals can spread the virus without showing symptoms, although the frequency of this occurrence is still unknown. Actions like sneezing and coughing without covering the mouth release droplets into the air, potentially infecting others. Direct contact with infected individuals through touching, embracing, or shaking hands can also spread the virus through these droplets.

Transmission can also occur by touching contaminated surfaces and the face, particularly the lips, eyes, or nose. However, surfaces can be effectively cleaned with common household disinfectants, and hand sanitizer and other antimicrobials can eliminate the virus from hands or surfaces. The virus can remain active on surfaces for varying durations, such as up to four hours on copper, one day on cardboard, and up to three days on stainless steel and plastics. The specific conditions required for the virus to become pathogenic on surfaces are not fully understood. Some animal coronaviruses, like the feline coronavirus, can spread through excrement, although it remains uncertain if this applies to human coronaviruses. Saliva and sputum, rich in viruses, can also facilitate transmission.

While COVID-19 is not considered a sexually transmitted infection, it can spread through personal contact, kissing, and the fecal-oral route. Additionally, few medical procedures pose a higher risk of transmission because they generate aerosols containing the virus.

Literature Review

The literature review method involved analyzing various authoritative publications and credible sources related to coronaviruses, as conducted by Zhu et al. (2020). This analysis encompassed studies from reputable journals sourced through platforms such as PubMed, Google Scholar, ResearchGate, Search Names, CAS 2, SARS CoV, and COVID-19 databases. Additionally, papers relevant to general medicine readership were selected, with a focus on prioritizing controlled experiments, systematic

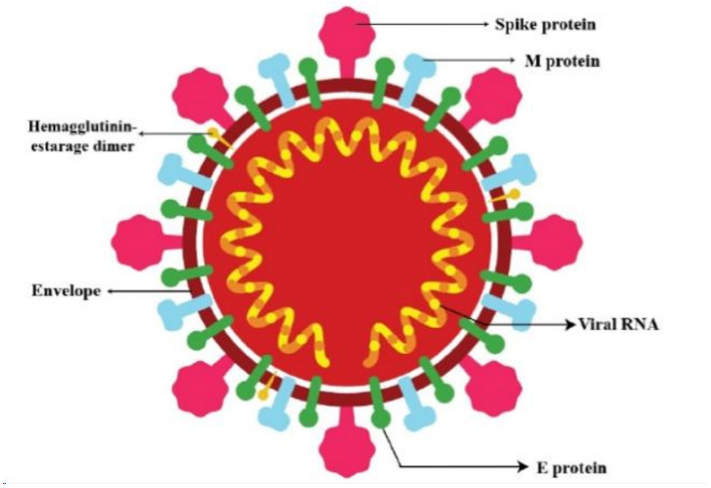

Figure 1. The schematic representation of coronavirus.

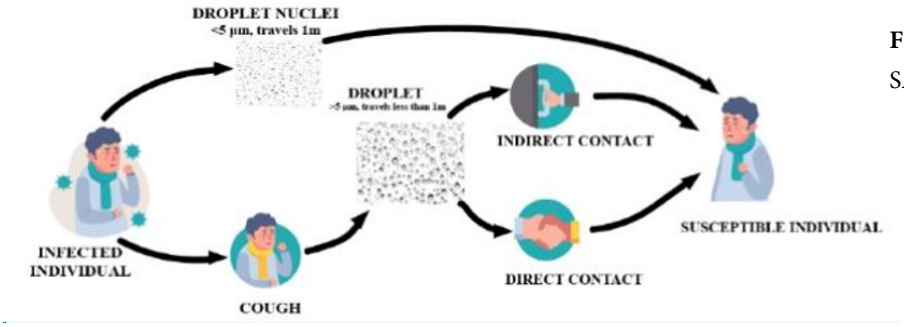

Figure 2. Ways of transmission of SARS-CoV-2.

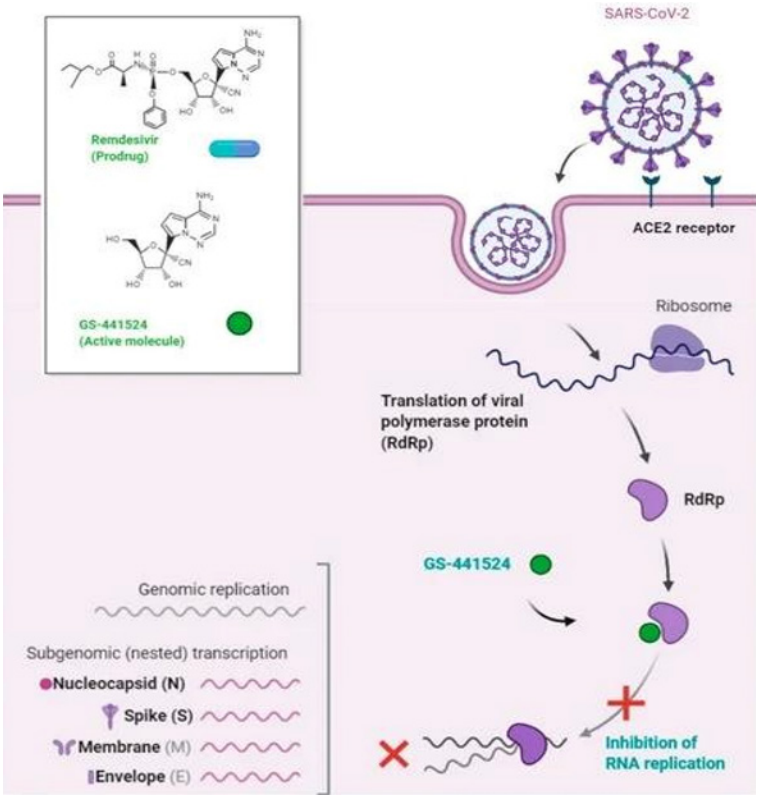

Figure 3. The potential mechanism of action of Remdesivir against coronavirus replication (Reprinted from "Remdesivir: Potential Repurposed Drug Candidate for COVID-19 (Portrait)", by BioRender.com, accessed on 1 April 2020)

Table 1. List of All recommended treatments for COVID-19.

Therapeutics	**Type**
Drug treatment	Remdesivir Favipiravir Lopinavir/ritonavir Ivermectin
Immune-Based Therapy	Blood-derived products Immunomodulatory therapies
Anti-SARS-CoV-2 Antibody Products	Baricitinib Bamlanivimab

evaluations, and recommendations for clinical practice, as outlined by Andersen et al. (2020).

Epidemiology

In December 2019, the outbreak of the novel coronavirus (nCoV) began in Wuhan, China, with the first confirmed case, as validated through laboratory testing (Phan et al., 2020). Initially, the outbreak was linked to the Huanan Seafood Market, where at least 41 individuals were affected (Phan et al., 2020). Local health authorities issued an epidemiological warning in December 2019, leading to the closure of the market in January 2020. Patients exhibiting symptoms such as fever and dry cough were referred to designated hospitals, with 41 cases confirmed using real-time reverse transcription polymerase chain reaction (RT-PCR) testing (Zou et al., 2020).

Outside of China, the illness was first identified in Thailand and Japan on January 13 and 16, respectively, and subsequently spread to other regions across Asia, Europe, North America, South America, Africa, and Oceania, culminating in a global pandemic known as COVID-19 by March 2020 (Huang et al., 2020). As of the submission date, more than 31,103,347 cases of COVID-19 caused by the novel coronavirus SARS-CoV-2 have been reported worldwide, with approximately 397,388 deaths (Zheng et al., 2020). China implemented stringent social distancing measures to contain the outbreak, despite reporting over 80,000 confirmed cases. Italy experienced some of the highest death rates globally (Yi et al., 2020). Initially, cases in affected countries were linked to recent travel to China or close contact with individuals who had traveled there, followed by local person-to-person transmission (Fritterman et al., 2020).

The exact origin of the virus remains uncertain, although the Huanan Seafood Market in Wuhan, China, is considered a potential hotspot for pathogen transmission from wild animals to humans (Futterman et al., 2020). This market reportedly housed various live animals intended for human consumption (Futterman et al., 2020). Bats are believed to be the primary natural reservoirs of SARS-CoV-2 due to genetic similarities with bat coronaviruses, while pangolins are suggested as a transitional animal reservoir in the transmission chain to humans (Gorbalenya et al., 2020).

Diagnose methods

Coronavirus diagnostics primarily rely on nasal swab examination using polymerase chain reaction (PCR) tests. However, due to potential false-negative results, presumptive diagnostics are also employed (Li et al., 2020). Serological testing can aid in diagnosis and assess vaccine reactions, although antibodies may not confer complete immunity as not all antibodies neutralize the infection (Li et al., 2020).

Accurate and timely identification of COVID-19 is crucial to reduce mortality and infections, as clinical features alone are insufficient for diagnosis (To et al., 2020). Several tests are utilized to detect the disease, including reverse-transcription PCR (RT-PCR), real-time RT-PCR (rRT-PCR), and reverse-transcription loop-mediated isothermal amplification (RT-LAMP) (Bhadra et al., 2015). RT-PCR, a nucleic acid-based technique, involves two one-step quantitative tests targeting distinct virus regions using nasopharyngeal or oropharyngeal swabs (Chu et al., 2020).

Additional methods include RNA-dependent RNA polymerase gene detection RT-PCR and the more sensitive SARS-CoV E gene assay when combined with standard RT-PCR (Konrad et al., 2020). Some studies suggest using sputum, BALF, or fecal matter as sampling sources due to their higher viral load (Zhang et al., 2020). RT-LAMP is commonly used for MERS-CoV diagnosis (Lee et al., 2017), while antigen testing and antibody assays offer rapid testing options (Pokhrel et al., 2020).

However, RT-PCR's accuracy varies, with studies reporting identification rates ranging from 38% to 71% due to sample technique flaws and viral load discrepancies (Fang et al., 2020; Shi et al., 2020). RT-PCR typically confirms infection 2-8 days after exposure, with nasopharyngeal swabs showing higher sensitivity than oropharyngeal ones (Pan et al., 2020).

Despite its utility, RT-PCR has limitations such as time-consuming procedures and kit shortages (Zhai et al., 2020). Chest CT scans have been proposed as an adjunct to or alternative for RT-PCR, offering higher sensitivity, especially in detecting ground-glass and consolidative pulmonary opacities with peripheral lung distribution (Ai et al., 2020; Chuang et al., 2020). Notably, CT changes are most prominent around ten days after symptom onset (Pan et al., 2020).

Treatment

Currently, there are no validated therapies specifically for COVID-19, according to the World Health Organization (2020). Treatment mainly focuses on safeguarding vital signs, maintaining oxygen saturation and blood flow, and addressing complications like secondary infections or heart issues. While there isn't a one-size-fits-all treatment for complete recovery, medical professionals are diligently working to manage COVID-19 patients effectively (Zumla et al., 2020).

The choice of COVID-19 therapy depends on the patient's symptoms, with various potential treatments under investigation, including immunosuppressants, monoclonal antibodies, antiviral drugs, and vaccines (Bhavana et al., 2020). Early in the illness, the immune system struggles to halt the SARS-CoV-2 virus's replication, potentially leading to tissue damage due to excessive immune or inflammatory responses later on (Tufan et al., 2020).

Clinical evidence suggests that antiviral treatments are most effective in the early stages of COVID-19, while immunosuppressive and anti-inflammatory therapies may be more beneficial during severe stages of the disease (Wang et al., 2020). Monoclonal antibodies targeting SARS-CoV-2 are particularly effective in the early infection phase, before it progresses to a more acute stage, making them a recommended option by healthcare professionals (Mansourabadi, 2020).

The US Food and Drug Administration (FDA) has approved Remdesivir and Dexamethasone for COVID-19 treatment, especially for hospitalized patients requiring oxygen support (Chorin et al., 2020). Remdesivir, an intravenous nucleotide medication, inhibits virus replication by binding to RNA-dependent RNA polymerase and prematurely terminating RNA transcription (Beigel et al., 2020). Dexamethasone, a corticosteroid, has shown significant impact on patient recovery when administered during the acute phase, especially for those requiring ventilator support (Pasin et al., 2021).

The effectiveness of these treatments and their appropriate timing are critical considerations in COVID-19 management. Table 2 provides an overview of suggested COVID-19 therapies.

Plasma therapy

Passive vaccination, a technique aimed at bolstering immunity against COVID-19, has been explored through various trials including MERS treatment plasma, interferon-beta/ribavirin combination therapy, and lopinavir. However, as highlighted by Holshue et al. (2020), there is currently no expertise in COVID-19 management, and randomized controlled clinical studies are lacking in this area.

Convalescent plasma (CP) has emerged as a potential therapy for critically ill COVID-19 patients (Yiğenoğlu et al., 2020). While the prophylactic use of CP is not recommended by the World Health Organization (WHO) and the FDA (Shen et al., 2020), it can be beneficial for severely ill COVID-19 patients. CP exerts therapeutic effects through various mechanisms facilitated by antibodies, which can directly neutralize infectious pathogens like SARS-CoV-2 and limit pathogenic activity through antibody-dependent cellular cytotoxicity, phagocytosis, and complement activation (Bloch et al., 2020).

Recovered COVID-19 patients can donate plasma after 14 days of complete symptom resolution, provided they have a negative HLA antibody test result and neutralizing antibody titers of at least 1:160. If the required titers are not available, a titer of 1:80 may suffice (Bloch et al., 2020). Linear proportion studies suggest that 3.125 mL/kg of plasma with a titer of >1:64 can provide immunoglobulin levels comparable to 25% of 5 mL/kg of plasma with a titer of 1:160 (Ding et al., 2017). Plasma collection, ranging from 200 to 600 mL, can be facilitated using an apheresis apparatus, with donors' explicit permission required for collections exceeding 750 mL (Shen et al., 2020).

Patients eligible for CP therapy must meet specific criteria, including laboratory-confirmed severe life-threatening COVID-19, respiratory distress with tachypnea, low blood oxygen saturation, lung infiltrates, septic shock, respiratory failure, and multiple organ dysfunction (Khan et al., 2020). Notably, CP therapy has shown no significant adverse effects, with transfusion-related acute lung injury being a rare occurrence but a risk that must be taken seriously in COVID-19 treatment (Thachil et al., 2020).

Antiviral drugs

Lopinavir and ribavirin have shown antiviral activity against coronaviruses in vitro, with concentrations of 4 and 50 μg/mL respectively being effective against SARS-related coronaviruses at 48 hours. However, the impact of anti-HIV medications on the treatment of 2019-nCoV remains uncertain, necessitating further randomized clinical studies in COVID-19 patients (NHS press conference, February 4, 2020).

Remdesivir, initially developed to combat Ebola, has garnered attention for its potential in treating COVID-19. Acting as an antiviral, Remdesivir inhibits viral RNA synthesis and has shown efficacy in treating lung tissue damage. Studies conducted in vitro have demonstrated its effectiveness against SARS-CoV-2, with real human patient trials also showing promise. However, recent meta-analyses have found limited to no impact on hospitalized COVID-19 patients (Hoehl et al., 2020; Sheahan et al., 2020; Grein et al., 2020; Pokhrel et al., 2020; Kumar et al., 2021; Consortium et al., 2020).

Chloroquine and hydroxychloroquine, primarily used to treat malaria, have been investigated for their potential in managing COVID-19. These medications disrupt protease activities and have been found to interact with ACE2 receptors, potentially preventing the entry of SARS-CoV-2. However, while hydroxychloroquine has shown effectiveness against SARS-CoV-2 in vitro, studies have indicated that it only provides symptomatic relief, with high-dose chloroquine posing significant cardiac risks. Improper self-medication with chloroquine can lead to severe adverse effects such as pruritus, hair loss, blindness, and bone marrow suppression (Kumar et al., 2021; Grein et al., 2020; Silver et al., 2013; Cao et al., 2020; Colson et al., 2020; Khan et al., 2020; Margo et al., 2020).

Lopinavir/ritonavir, used together to enhance absorption and function, have been explored for their anti-HIV properties. While lopinavir has been promoted as an anti-HIV medication, its potential anti-SARS-CoV-2 activity has yet to demonstrate clear benefits in clinical trials (Wu et al., 2020; Tang et al., 2020; Cao et al., 2020).

Favipiravir, initially developed to treat influenza, has shown efficacy against several RNA viruses. In vitro research has demonstrated its

anti-SARS-CoV-2 activity, although clinical trials have yet to yield definitive findings. Favipiravir transforms into an active metabolite upon entering infected cells, inhibiting the RNA-dependent RNA polymerase to exert its antiviral action (Wang et al., 2020; Furuta et al., 2013).

Vaccine

Efforts to develop vaccines against COVID-19 are underway globally to curb the spread of SARS-CoV-2. One of the most common targets among vaccine candidates is the S-protein (Thand et al., 2020). Numerous COVID-19 vaccines have been developed, with India recently introducing its first indigenous vaccine. Bharat Biotech, in collaboration with the Indian Council of Medical Research (ICMR) and the National Institute of Virology in Pune, developed Covaxin, which demonstrated 81% effectiveness in preventing symptomatic COVID-19 in late-stage trials (Huang et al., 2020).

Protein Subunit Vaccines

Protein subunit vaccines consist of synthetic peptides or recombinant antigenic proteins that induce a robust immune response, offering long-lasting protection against viruses (Kaur et al., 2020). Since the S-protein is crucial for the virus to enter host cells, it is the primary target for subunit vaccination (Wang et al., 2020). Several vaccines in this category are currently undergoing clinical trials, including the triple antigen vaccine, NVX-CoV2373, Pitt-CoVacc, and a molecular clamp stabilized spike protein vaccine candidate (Coleman et al., 2014).

Viral Vectored Vaccines

Viral vectored vaccines utilize viral vectors devoid of genetic materials to deliver genetic materials to specific cells, triggering a rapid immune response (Kaur et al., 2020). These vaccines are effective in gene transduction and can promote the expression of antigenic proteins, stimulating cytotoxic T cells to eradicate infected cells (Thand et al., 2020). Some viral vector vaccines in development include Ad5-nCoV, ChAdOx1, LV-S-MENP-DC, and Coroflu (Thand et al., 2020).

Live Attenuated Vaccines

Live attenuated vaccines are created by reducing a pathogen's pathogenicity while keeping it viable. These vaccines have lost their ability to cause disease but can still elicit an immune response (Fidel et al., 2020). The DelNS1-SARS-CoV2-RBD vaccine, developed by the University of Hong Kong, uses an influenza-based platform to express the RBD of the S-protein, triggering an immune response (HKU, 2020). Additionally, three SARS-CoV-2 attenuated vaccines, produced using codon deoptimization, are in pre-clinical stages (Jeyanathan et al., 2020).

Efforts to develop COVID-19 vaccines are crucial in combating the pandemic. These vaccines, utilizing various platforms and targeting different components of the virus, offer hope for controlling the spread of SARS-CoV-2 and preventing future outbreaks.

Prevention

To prevent the spread of COVID-19, wash your hands daily with soap, water, or hand sanitizer. According to WHO, handwashing for 40-60 seconds with soap and 20-30 seconds with sanitizer is effective (Ahmed et al, 2020). Hand sanitizers containing alcohol, soap, and water can neutralize the virus due to its lipid envelope (Kabir et al, 2020). Despite women generally being more diligent in handwashing, only 5.3% of people follow proper protocols, suggesting ongoing encouragement and awareness are essential (Borchgrevink et al, 2013).

Avoid close contact with anyone coughing or sneezing and wear a mask to prevent transmission. Refrain from touching your face and cover your mouth and nose when coughing or sneezing with your elbow or tissue. Stay home if you feel unwell and seek medical attention if experiencing symptoms like fever, cough, or difficulty breathing (Chen et al, 2020). While some studies argue that customized masks offer no extra advantage over standard medical masks, it's advisable for individuals, whether symptomatic or not, to wear masks in public settings to prevent asymptomatic transmission (Hoehl et al, 2020; Poon et al, 2020; Adhikari et al, 2020).

Maintaining social distance is crucial in reducing the reproduction number (R) of SARS-CoV-2 below one, thereby slowing the epidemic. Recommendations from WHO and other organizations include avoiding close contact with animals and confirmed or suspected COVID-19 patients. Individuals displaying symptoms should limit interactions, and those with compromised immune systems should avoid social events (Cascella et al, 2020).

Conclusion

In conclusion, COVID-19, caused by the novel coronavirus SARS-CoV-2, has rapidly evolved into a global pandemic with significant public health implications. Characterized by its ability to spread via respiratory droplets and direct contact, the virus has challenged healthcare systems worldwide. Despite extensive research and efforts to combat the disease, effective treatment options remain limited. However, preventive measures such as hand hygiene, wearing masks, practicing social distancing, and staying home when unwell are crucial in mitigating transmission. The development of vaccines offers hope for controlling the spread of the virus and reducing its impact on society. Continued vigilance, public awareness, and adherence to preventive measures are essential in the ongoing battle against COVID-19. Through collaborative efforts and scientific advancements, we can strive to overcome this global health crisis and emerge stronger and more resilient in the face of future challenges.

Author contribution

B.K.A., V.V., T.K.L., M.S.B. conceptualized, reviewed the literature, and wrote the article.

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None declared

Competing financial interests

The authors have no conflict of interest.

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