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The penetration, possibility of protection and treatment of COVID-19

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Abstract

The COVID-19 pandemic, caused by the novel SARS-CoV-2 coronavirus, has had an unprecedented global impact, highlighting the urgent need to understand the virus's penetration mechanisms, prevention methods, and the most effective treatment strategies. This review aims to provide a comprehensive overview of the current knowledge and emerging developments in these areas. Firstly, the review examines the intricate pathways through which SARS-CoV-2 penetrates host cells. It explores the viral entry receptors, including angiotensin-converting enzyme 2 (ACE2), and highlights the potential involvement of other receptors. Additionally, the review delves into the processes of viral replication, shedding light on the viral kinetics and factors influencing transmissibility. Secondly, the review presents an in-depth analysis of the various measures employed to protect individuals and communities from SARS-CoV-2 infection. It discusses the effectiveness of non-pharmaceutical interventions, such as physical distancing, mask-wearing, and hand hygiene, in reducing transmission. Furthermore, the review explores the development and deployment of vaccines, including traditional approaches and novel vaccine platforms, examining their efficacy, safety, and the challenges posed by emerging variants. Lastly, the review provides an overview of the current treatment strategies for COVID-19. It evaluates the effectiveness of antiviral drugs, immunomodulatory therapies, and supportive care approaches in managing the disease. By gaining a deeper understanding of these aspects, we can contribute to the development of evidence-based interventions and improve global health outcomes in the face of COVID-19 and future pandemics.

Keywords: COVID-19, SARS-CoV-2, Penetration Mechanisms, Viral Entry Receptors, Viral Replication, Treatment Strategies

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Background

The COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 has dramatically altered the global landscape, challenging our societies, economies, and healthcare systems [1, 2]. As the world continues to grapple with the repercussions of this unprecedented crisis, it becomes increasingly crucial to delve deeper into the intricacies of COVID-19, including its penetration mechanisms, potential protective measures, and innovative treatment strategies. By exploring these facets, we can foster a deeper understanding of the virus and pave the way for groundbreaking solutions to mitigate its impact [2]. At its core, the penetration of SARS-CoV-2 is a complex interplay between viral factors and the host's physiological processes. Unraveling the mysteries of how the virus infiltrates host cells and establishes infection is vital for developing effective interventions [3]. Recent advancements in virology and molecular biology have shed light on the viral entry receptors, particularly the role of angiotensin-converting enzyme 2 (ACE2), as well as the intricate mechanisms of membrane fusion and viral replication. Understanding these processes can aid in the development of targeted therapies and preventive strategies to halt viral transmission [4]. In the quest for protecting individuals and communities from COVID-19, non-pharmaceutical interventions have played a pivotal role. Measures such as physical distancing, mask-wearing, and hand hygiene have proven effective in reducing viral spread. However, the ever-evolving nature of the virus, with the emergence of new variants, demands continuous adaptation of protective measures [5]. Vaccination campaigns have also played a central role in curbing the pandemic, with remarkable strides made in developing and deploying vaccines. Novel vaccine platforms, such as mRNA technology, have demonstrated unprecedented speed and efficacy. However, challenges remain, necessitating ongoing research to enhance vaccine effectiveness and address vaccine hesitancy [6]. Treating COVID-19 patients presents unique challenges due to the diverse clinical manifestations and severity of the disease [7]. The development and optimization of

treatment strategies have been crucial in saving lives and minimizing the burden on healthcare systems. Antiviral drugs, immunomodulatory therapies, and supportive care approaches have demonstrated varying degrees of effectiveness. However, the landscape of COVID-19 treatment continues to evolve as researchers investigate repurposed drugs, such as antimalarials and antivirals, alongside novel therapeutics like monoclonal antibodies and convalescent plasma [8]. Moreover, innovative approaches, such as RNA-based vaccines and gene-editing technologies, hold significant promise in transforming the treatment landscape. In this context, this paper aims to delve into the intricacies of COVID-19, offering a comprehensive exploration of its penetration mechanisms, potential protective measures, and innovative treatment strategies. By synthesizing the latest research and emerging concepts, this paper aims to illuminate the path forward in combating the pandemic. Through interdisciplinary collaboration and cutting-edge advancements in science and technology, we can aspire toward a future where the impact of COVID-19 is significantly minimized, ultimately safeguarding the health and well-being of individuals and societies worldwide.

Corona SARS, Middle East Respiratory Syndrome (MERS-CoV), and COVID-19

Corona Middle East was first identified in Saudi Arabia on September 24, 2012. Corona is the sixth virus of the coronavirus family; the incubation period of this virus is ten days or more [9]. Coronavirus is unlikely to cause a pandemic due to its inability to survive in the environment for extended periods [10]. Its presence in the environment alive does not exceed several hours, ranging from 8 to 48 hours at a temperature of 20 oC, and relative humidity 40%. As for Corona SARS, which continues in the environment for 5 days at a temperature ranging from 22-25 oC, and a relative humidity of 40-50% [11]. This indicates that SARS-CoV is more prevalent than MERS-CoV. However, MERS-CoV has caused significantly higher mortality, with a death rate of approximately 60% [12]. This considerable percentage is higher than that caused by Corona SARS about 10%. MERS virus was isolated from a man who died of severe shortness of breathing and kidney failure. It may be one of the coronaviruses that infect a person who has had a mutation. Thus, this strain has become able to infect the kidneys, a characteristic that is not present in other coronaviruses. MERS virus may be one of the coronaviruses that originally infects the animal. As a result of the mutation, the virus became able to infect humans and the ability to infect kidney cells [13]. Bats were initially thought to be the primary source of the virus, but this hypothesis has not been definitively proven [14]. MERS-CoV is a beta virus, and a detailed analysis of the evolution of strains has revealed a close relationship with European bat species of the Vespertilionidae family [15]. The result of the animal survey was to examine and test about 1,100 specimens of bats in the cities of Bisha and Unaizah, and Riyadh, Saudi Arabia, using the technique of chain reaction, the detection of coronavirus at a high rate in the bats of the types Pipistrellus and Rhinopoma [16]. A study further determined that single-humped camels, used for meat, dairy production, and racing, could be a source of the MERS virus [17]. Blood samples were collected (349) from a variety of livestock such as camels, cows, sheep, and goats from Oman, Holland, Spain, and Chile. Then the tests showed the presence of antibodies to the MERS virus in all 50 samples taken from camels in Oman, while not found in the other animals. It has been proven from vaccines taken from camels in the Canary Islands and Oman that they are positive vaccines that contain protein antibodies to the MERS virus [17]. These vaccines were collected from camels from mid-2012 to mid-2013: a test of sera taken from 50 Omani camels from the racing camel, and about 14.3% of Spanish camels showed that they contained 1% of the protein-stranded antibodies to the MERS virus. This study indicates that coronavirus or related viruses have infected camel groups, and may have spread widely between Omani camels [18]. Air travel plays a significant role in the potential spread of emerging diseases. This is evident by the rapid spread of the SARS virus in 2003 when the infection was spread from China to at least 17 countries in no less than 7 days. Carefully looking at what happened in 2003, Hufnagel has designed a mathematical model that accurately mimics the spread of SARS to countries that have experienced four or more cases [19]. The benefit of having a model means that once the raw data is available, it can be expected which the areas will be most vulnerable to the virus. Moreover, the study shows how difficult it is to contain the infection outbreaks by vaccination alone. A global pandemic caused by SARS-CoV-2, known as COVID-19, began in December 2019 in Wuhan, central China. Virus 2 associated with the severe acute respiratory syndrome (SARS-CoV-2). The disease was discovered in December 2019 in Wuhan, central China, and the World Health Organization classified it on March 11, 2020, as a pandemic, and declared a state of emergency. The virus can spread directly between people, and the infection rate appears to have risen in mid-January 2020. Several countries in Europe, North America and Asia, and the Pacific have reported infections reaching their lands (Figure 1).

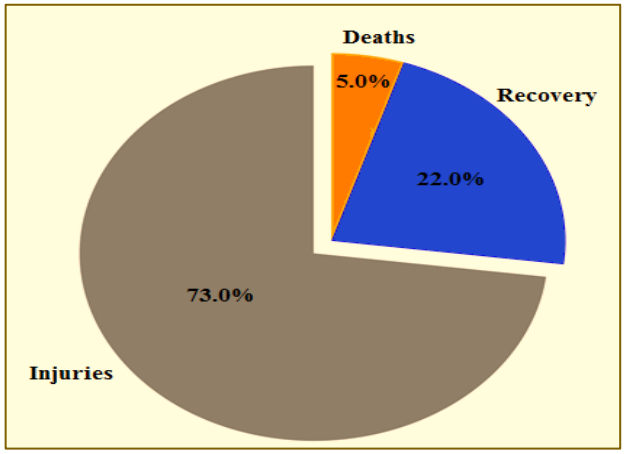

Figure 1: COVID-19: Proportion of injury, recovery and mortality (April 28, 2020).

The incubation period for SARS-CoV-2 is approximately 5 days or more, with initial evidence suggesting that it can be infectious before symptoms appear. Through a comparison of data related to the MERS virus reported by the Kingdom of Saudi Arabia, and SARS cases in Canada, China, Taiwan, and Singapore. The considerable proportion of men among patients with MERS virus is higher, and their ages are greater than SARS cases [20]. Besides, the mortalities are also much higher in MERS than when compared to the number of deaths caused by SARS (Figure 2).

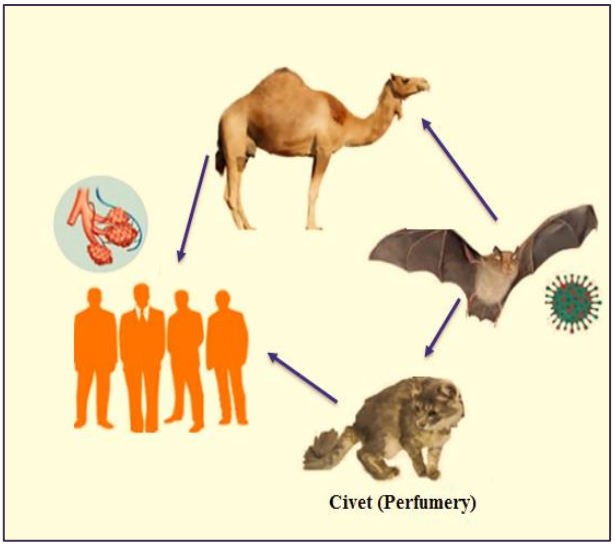

Figure 2: A mechanism for transmission of SARS and MERS viruses.

An abundance of conserved acidic residues in the two consecutive fragments of the FP termed FP1 and FP2 (residues 816-835 and 835-854 in SARS-CoV-2, respectively) and the LLF hydrophobic motif (L821/L822/F823 in SARS-CoV-2 (Figure 3) have provided important insights into the functional significance of specific regions of the FP.

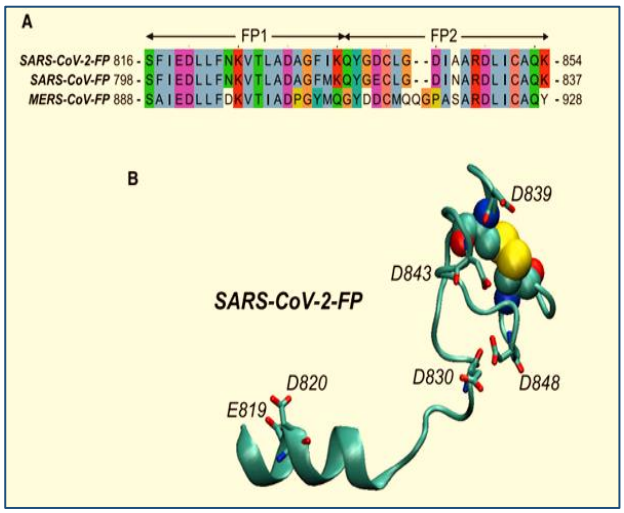

Figure 3: (A) Sequence alignment of the fusion peptide (FP) segments from the spike proteins of SARS-CoV-2 (top), SARS-CoV (middle), and MERS-CoV (bottom) CoVs. The sequences are coloured according to ClustalX scheme. The conserved acidic residues are shown in purple, and the conserved Cys residues, forming a disulfide bond (C840 and C851 in SARS-CoV-2-FP numbering), are highlight in orange. FP1 and FP2 fragments of the peptide are marked and labelled. (B) Structural model of SARS-CoV-2-FP used in this study. The acidic residues are shown in licorice and labelled.[24] License Number 5565460034391.

However, isothermal titration calorimetry (ITC) tests with the MERS-CoV FP revealed that it binds to a single Ca2+ ion, unlike the SARS-CoV FP and the SARS-CoV-2 FP. Importantly, the findings from similar tests performed with the SARS-CoV-2 FP seem to be in great accord with, and replicate, the structural and functional conclusions drawn from these investigations. Mutagenesis studies showed that the conserved LLF motif in the FP1 portion of SARS-CoV FP is essential for membrane insertion and peptide fusogenicity. Electron spin resonance experiments demonstrated that Ca2+-dependent FP-membrane interactions disrupt the lipid bilayer by rearranging lipid headgroup and backbone atoms at the interaction site. However, they do not affect the hydrophobic core of the membrane. Ca2+ binding sites on CoV FPs and their potential roles in specific (yet undiscovered) FP-membrane interactions remain unclear. This has complicated the analysis of the impact of viral interactions with the membrane, and therefore, the development of strategies to reduce infectiousness by targeting this crucial area. Based on their studies, researchers hypothesized a wide variety of Ca2+ ion engagement patterns with the FP's acidic residues. Two favored mechanisms of membrane penetration were identified by extensive simulations of spontaneous membrane binding of all possible forms of Ca2-bound SARS-CoV-2-FP. The peptide residues F833/I834, located in the FP2 region near the S2 domain in the spike context, are inserted hydrophobically in one of these mechanisms. Second, the N-terminal part of the F1 segment, which is uncoupled following the S20 cleavage, is a common entry point. Ca2+ ions bind to pairs of acidic residues D830 and D839, and E819 and D820, to cause the hydrophobic insertion of the highly conserved residues L822 and F823 (LLF motif). Ca2+ binding plays a significant part in the mechanism, and their comprehensive control simulations indicated that membrane binding/insertion of the SARS-CoV-2 FP is significantly reduced without Ca2+ ions. Furthermore, the peptide's binding caused it to effect structural alterations on the lipid bilayer, the type and extent of which depended on the quantity of the peptide in the immediate area. Taken together, our results provide light on the structural dynamics behind the crucial function of Ca2 binding in the membrane penetration of SARS-CoV-2-FP and give novel mechanistic insights into this process. Table (1) displays the relative distribution of Coronavirus infections and deaths in the world from 2012 to 2014. The COVID comes again in 2019 to exceed the total number of infections to 92 million, while the number of deaths resulting from the virus approached two million deaths.

Table 1: The relative distribution of injuries and deaths of coronavirus cases in the world from 2012 to 2014 [22, 23].

Country	Infected (%)	Deaths (%)
Saudi Arabia	449 (86.0)	121(81.2)
The United Arab Emirates	33(6.3)	9(6.0)
Jordan	9(1.7)	5(3.4)
Qatar	7(1.3)	4(2.7)
United Kingdom	4(0.8)	3(2.0)
Kuwait	3(0.6)	1(0.6)
Tunisia	3(0.6)	1(0.6)
Oman	2(0.4)	2(1.3)
France	2(0.4)	1(0.6)
Germany	2(0.4)	1(0.6)
Netherlands	2(0.4)	0(0.0)
Italia	1(0.2)	0(0.0)
Philippines	1(0.2)	0(0.0)
Spain	1(0.2)	0(0.0)
Greece	1(0.2)	0(0.0)
Egypt	1(0.2)	0(0.0)
Malaysia	1(0.2)	1(0.6)

Penetration Mechanisms of SARS-CoV-2

Viruses are significantly smaller than bacteria, most of which range between 10 and 300 nanometers in diameter [25]. Some filoviruses have a total length of 1,400 nm; its diameters are about 80 nanometers. The whole virus molecule, known as the virion, is made up of nucleic acid surrounded by a protein protective coating called a capsid. The latter is made up of identical protein units called capsules. Viruses can have a greasy "coating" derived from the host cell membrane [26]. The caps are made of proteins encoded by the viral genome and is used as a basis for the morphological distinction between viruses. The genome comprises the genes of the virus, which carry the code to manufacture new viruses and transfer the inherited characteristics to the next generation. Viruses usually carry between 2 to 200 genes, also the enormous simulator virus has an estimated sixty to a thousand genes, it is more than what many bacteria species carry [27]. Cells of non-host organisms contain various organisms, which are essential for life such as proteins that make proteins, mitochondria or other energy-generating organisms, and the complex membranes involved in the transport of cellular molecules [28]. As for viruses, since they are not cells, and they do not have any of these structures, they remain inactive until they infect a living cell with infection. Finding suitable soil. However, viruses, unlike seeds, do not carry the genes that carry the code of all proteins they need to complete their life cycle [29]. Therefore, it abducts the cell's organelles to use what it needs from them, and often the cell itself kills during this. This method in life means that viruses are forced to obtain the necessary components of their life cycle from other organisms, and from here, they are called emergency parasites. Even the simulated virus, which infects amoeba, is forced to borrow organelles from the amoeba cell in order to be able to synthesize its proteins in order to collect new viral components of the same kind. Viruses that infect animals infect cells by combining with specific receptor particles on the surface of the cell. The molecules of the receptor differ from one virus to another according to its type, and although some are located above most cells, there are particles that are limited to specific types of cells [30]. A popular example is HIV, which holds the entry key to the CD4 lock, and thus only those cells that carry the CD4 molecules above their surface are the only ones that can be infected with this virus [31]. This particular reaction determines the outcome of the transmission of infection, which in the case of HIV leads to the destruction of helper T cells, which leads to CD4, which are very important for immune response [31]. This leads to a failure of the immune system, with a very serious opportunistic infection, and if the patient is not treated, his death is inevitable. Once a virus is bound to the appropriate cellular receiver, its envelope penetrates the cell; its genome is released within the cell cytoplasm. Once a virus is bound to the appropriate cellular receiver, its envelope penetrates the cell, its genome is released and released within the cell cytoplasm [32]. The main goal of the virus is to reproduce successfully; its genetic material must download the information carries onto the host cell. In most cases, this occurs within the cell nucleus, where the virus has access to the molecules, it requires starting making its proteins. However, some large viruses, such as smallpox, carry genes with the enzymes they need to manufacture their proteins. DNA viruses disintegrate as they enter the cell in the form of pieces of cellular DNA. Viral DNA code is transcribed into RNA messages translated into viral proteins by cell ribosomes. New viruses leave the cell by budding method, through cell membranes. In this case, the cell may be spared death and perform a storage function for viral infection. As for RNA viruses, they precede DNA by actually owning their genetic code in the RNA form. Also, because it carries with it the enzymes that its RNA can clone and translate into proteins, it is for this reason that it is not very dependent on cellular enzymes, and is often able to complete its life cycle within the cytoplasm without disrupting the cells [33]. Once the virus penetrates the host cell through a specific receptor on the cell surface, replication and translation occur (Figure 4).

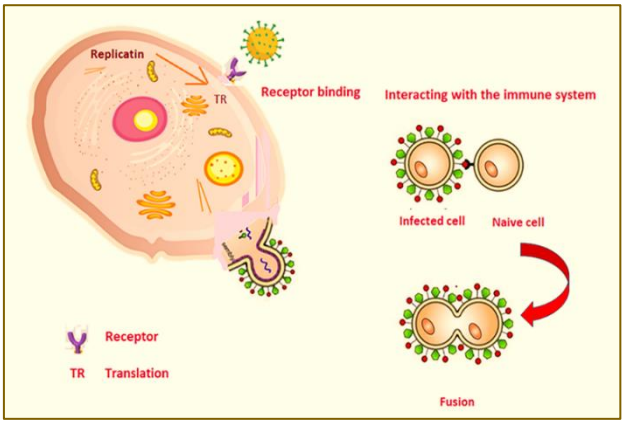

Figure 4: Virus penetration to the host cell modified from [34]

This process allows the production of viral proteins, which are processed within the cell using the endoplasmic reticulum and Golgi apparatus [35]. Viral proteins and RNA are packed into new viruses, which are then released from the host cell. These viruses interact with the host's immune system, often triggering immune responses. Infected cells can display viral proteins on their membranes, which interact with adjacent cell receptors, leading to cellular fusion [36]. Coronaviruses primarily cause respiratory and digestive infections and are genetically classified into four main genera: alpha-coronavirus, beta-coronavirus, gamma-coronavirus, and delta-coronavirus [36]. The coronavirus genome, which ranges in size from approximately 26,000 to 32,000 bases, contains a variable number (6 to 11) of open reading frames (ORFs). Characterization and sequence of the virus responsible for COVID-19 (display SARS-CoV-2 protein sequence) determined that it was a new COV that participated in the identity of the 88% sequence with a COV similar to a SARS striker, indicating that it originated in bats [37]. Additionally, studies have shown that this virus, designated as 2019-nCoV or SARS-CoV-2, shares a 79.5% sequence identity with SARS-CoV [38]. The coronary genome encodes four main structural proteins: the spike (S) protein, nucleocapsid (N), membrane protein (M) and casing protein (E). Protein S is responsible for facilitating COV entry into the target cell. It consists of a short intracellular tail, anchored across the membrane, and a large external domain consisting of a subunit bound to S1 and a subunit S2 that fuses with a membrane. The virus enters the body through the nose, mouth, or eyes. Using its S protein, it binds to respiratory cells that express a protein called ACE2. For the first time, scientists have analyzed the structure of the S protein at the atomic level [39]. S1 that contains an area that identifies the ACE2 receptors present on the surface of the

affected cell (the target cell, the host), and then adheres to it, and S2 that contains an area that helps the virus enter the cell by merging the surrounding membrane with Affected cell membrane. After S1 attaches to the ACE2 receptor, the Spike protein is cleaved. Therefore, the S2 region, which merges the virus membrane with the affected cell membrane, is exposed [40]. The SARS-CoV-2 S protein genomic sequence analysis confirmed that it was only 75% identical to the SARS-CoV S protein. Nevertheless, the S-binding stimulus for the receptor in protein S showed that most of the essential amino acid residues for binding to the receptor were saved between SARS-CoV Also, SARS-CoV-2, indicating that 2 CoV strains use the same host entering the cell. The entrance receptor used by SARS-CoV is the angiotensin-converting enzyme 2 (ACE II) [41]. It is an external peptidase that catalyzes the conversion of angiotensin I to the angiotensin nucleopeptide [42], or the conversion of angiotensin II to the heptagonal peptide angiotensin [43]. Angiotensin-converting enzymes have a direct effect on the function of the heart and are commonly expressed in the cells of the membranous endothelium of the heart and kidneys. ACE2 is a type I membrane protein that acts as a carboxypeptidase and also participates in the renin-angiotensin system [44]. This enzyme is mainly produced by the lungs, and its primary function is to regulate blood pressure by converting angiotensin 1 to angiotensin 2, which shrinks blood vessels and liberates aldosterone from the adrenal gland [45]. The rate of this enzyme rises in many lung diseases, especially in Sarcoidosis, a chronic inflammatory disease that leads to the development of granulomas in the lungs, liver, and spleen. Some individuals, who suffer from high blood pressure or diabetes, are forced to take drugs to increase the amount of ACE2 in their cells, to control the conditions [46]. A study was carried out on patients with Coronavirus, who suffer from some critical diseases. Therefore, they found that the most common diseases are: high blood pressure (23.7%), diabetes (16.2%), and heart disease (5.8%) [47]. Besides, the study also raised the hypothesis that COVID-19 relates to cells inside the body easier with the presence of blood pressure drugs that can make this process easier for these viruses. Additionally, the study suggested that people with diabetes and high blood pressure may be more at risk because of changes in their genes, which causes them to produce more ACE2 naturally [48]. These data indicate that the expression of ACE2 increments in diabetes, and treatment with ACE inhibitors and ARBs increase the expression of ACE2 [47]. Consequently, increasing expression of ACE2 will facilitate COVID-19 infection. So, it is considered that treating diabetes and high blood pressure with ACE2 drugs raises the risk of developing severe and fatal corona disease. If this hypothesis is confirmed, it may lead to a struggle over treatment. Nevertheless, doctors have warned that the results are not evidence of a direct link, and patients should continue to take their medications. It simply raises a possible question about whether a type of blood pressure drug and heart disease drug called angiotensin-converting enzyme (ACE) inhibitor may increase the chances of a severe COVID-19 infection [49]. ACE inhibitors interfere with angiotensin II (Ang II), a hormone that causes arteries to contract and raises blood pressure [50]. As for angiotensin receptor blockers, they block Ang II and prevent it from adhering to blood vessels and organs to prevent its effect on them. The use of ACE inhibitors causes a marked decrease in Ang II production, which leads to low blood pressure. Epidemiological and clinical studies have shown that ACE inhibitors decrease the progress of nephropathy associated with diabetes independently of the effect of dropping their blood pressure. This technique is used to block kidney failure in diabetics. ACE inhibitors are effective for indications other than high blood pressure, even in patients with normal blood pressure [51]. The viral genome contains fewer than 30,000 genetic bases and a limited number of genes. Once the virus enters the cell, it releases a portion of its genetic material in the form of RNA. After the virus enters the cell, it uses its resources as a plant to replicate and multiply the viral RNA [52]. The infected cell reads the viral RNA and produces proteins according to the instructions inside it. The proteins that are produced are used to make new copies of the virus later. As infection and inflammation progress, cell mechanisms begin to produce more RNA and virus proteins at a faster rate, to make full copies of it [53]. The last stage of replicating the virus is to release new copies of the virus that were produced in the host cell. Each infected cell can release millions of copies of viruses before eventually decomposing and dying. At the last stage of replicating the virus, it releases new copies that were generated in the host cell. Each infected cell can liberate millions of copies of viruses before ultimately decaying and dying. After the virus exits the infected cell, it can infect neighboring cells and begin its reproduction cycle again. It can come out, through coughing and sneezing, and a mine with viruses from the respiratory tract to infect people and located on nearby surfaces, and the virus can remain infectious there for a few hours up to days [54]. COVID-19 induces fever as the immune system attempts to combat the virus. In severe cases, the immune system may overreact and attack pulmonary cells. The lungs begin to fill with fluid, and the cells that are dying, which makes breathing a difficult task [55]. A small proportion of the infection can lead to acute respiratory distress syndrome and even death [55].

Diagnosis and possible treatments

The specific diagnosis is by specific molecular tests on respiratory specimens (throat swab/nasopharynx/sputum / endotracheal aspiration and bronchial wash) [55]. The clinical features of COVID-19 vary widely, with an incubation period ranging from 2 to 14 days. It ranges from an asymptomatic condition to acute respiratory distress syndrome (ARDS) and multi-organ failure. Common clinical symptoms include fever (though not in all cases), cough, sore throat, fatigue, headache, muscle pain, and shortness of breath (dyspnea) [56]. Conjunctivitis has also been reported, making it 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 significantly elevated inflammatory cytokines, including interleukin-2 (IL-2), interleukin-10 (IL-10), granulocyte colony-stimulating factor (G-CSF), IFN-γ-inducible protein 10 (IP-10, CXCL10), macrophage inflammatory protein-1 alpha (CCL3), and tumor necrosis factor-alpha (TNF-α) [57]. A recent study found that the average time from the onset of the disease to the development of dyspnea was 5 days, and 25-30% of affected patients required intensive care. The complications seen include acute lung and acute kidney injuries, and the recovery had started in the second or third week [56]. Poor

outcomes and mortality are more common in the elderly and those with underlying conditions, accounting for approximately 50-75% of fatal cases [58]. Interestingly, the disease in patients outside Wuhan is more moderate, this may be either, because of selection bias as the cases reported from Wuhan included only severe cases, or the Asian population's preparedness for the virus, due to the high expression of ACE2 receptors on the respiratory mucosa. Clinical studies have also shown that the disease in infants and children is remarkably decreasing than in their adult counterparts [59]. Platelet counts are typically normal or slightly reduced. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels are generally elevated, whereas procalcitonin levels are usually normal. A high level of procalcitonin may indicate infection with a common bacterial infection. ALT / AST, prothrombin time, creatinine, D-dimer, CPK, and LDH may be high and high levels are associated with severe illness [56]. Chest X-rays usually show bilateral infiltration, but they may be normal in early disease [60]. CT scans are more sensitive and specific, often revealing ground-glass opacities, consolidation, and subpleural involvement It is also abnormal in asymptomatic patients/patients without clinical evidence of lower respiratory tract infection. Abnormal CT scans were used to diagnose COVID-19 in suspected cases with negative molecular diagnostics. Many of these patients had positive molecular tests on repeated testing [61]. Antivirals are a class of drugs specifically designed to treat viral infections. Antiviral drugs are used to treat specific viruses, as are the antibiotics used to kill bacteria. However, it varies from most antibiotics; it does not damage the target pathogen, but rather restricts its growth from the start. Bacteria differ from the virus, being mostly single-celled organisms [62]. They live free and can invade the body and multiply inside it, causing disease. The bacteria also have strong exogenous cell walls and are essential for their survival. Penicillin and its derivatives can target these unique structures and leave the cells of the host untouched. However, viruses are not cells and take advantage of the reproductive mechanism of the cells have infected, so it has been proven how difficult it is to find drugs that prevent the virus from multiplying without harm to the host cells [63]. Nevertheless, there are now approximately 40 pharmacologically valid drug compounds, but most of them are active only against one virus or one group of viruses. All antimicrobials, including antivirals, may be exposed to drug resistance, because the pathogens mutate over time, which reduces their response to treatment. Many anti-retroviral compounds operate like the acyclovir action by inhibiting the essential viral enzymes for the reproduction of the virus. In the case of HIV, these compounds target reverse transcription, protease, or viral fusion enzymes. Other drugs block the entry of HIV into the cell [64]. However, the resistance to a specific remedy is often generated due to the rapid mutation of HIV. It is now evident that combining at least three drugs from different classes, a method known as highly active antiretroviral therapy (HAART), is preferred over monotherapy [64]. Another type of infection that can be treated with a variety of anti-viral drugs is influenza. The influenza virus is a negative encapsulated RNA that contains a virus with a segmented genome, and its genetic material is encoded with eight parts of RNA [65]. RNA segments are loaded in nucleocapsids protein, and a complex set of polymerase proteins is attached to each of the genomic parts. The RNA protein complexes are arranged into the lining of a lipoprotein fixed internally with matrix protein, with hemagglutinin, neuraminidase, and M2 proteins on the outside surface of viral particles [66]. These drugs rely on two modes of action: one that inhibits the action of the viral enzyme neuraminidase, and the other that prevents the virus from entering the host cells. During the short treatment period required to recover from the flu, drug resistance is not a problem in general, but in the event of a pandemic or pandemic, it may also be the case. A recent study confirmed the urgent need to increase the stockpile of oseltamivir (Tamiflu), in addition to more anti-viral drugs, including zanamivir (Relenza), after an evaluation of the effect of these drugs in the case of swine flu H1N1 virus (swine flu). NA) and its resistance against Tamiflu (His274Tyr) is now widespread in H1N1 seasonal strains [67]. Monoclonal antibodies were discovered in the 1970s with specialized reagents for the proteins of each of the viruses so that these reagents could be used within diseased tissues. Likewise, antibodies to specific viruses can be identified within blood samples [68]. The merging of B lymphocytes into the spleen with myeloma cells leads to the emergence of a hybridoma cell line by multiplication either in vitro or in vivo (mouse) can produce relatively identical antibodies. The hybridoma cells inherit the nonspecific growth properties of myeloma cells and the secretory capabilities of B-lymphocyte antibodies. Monoclonal antibodies generated by the unique hybridoma cell line are homogeneous and identify a single epitope of an antigen (Figure 5).

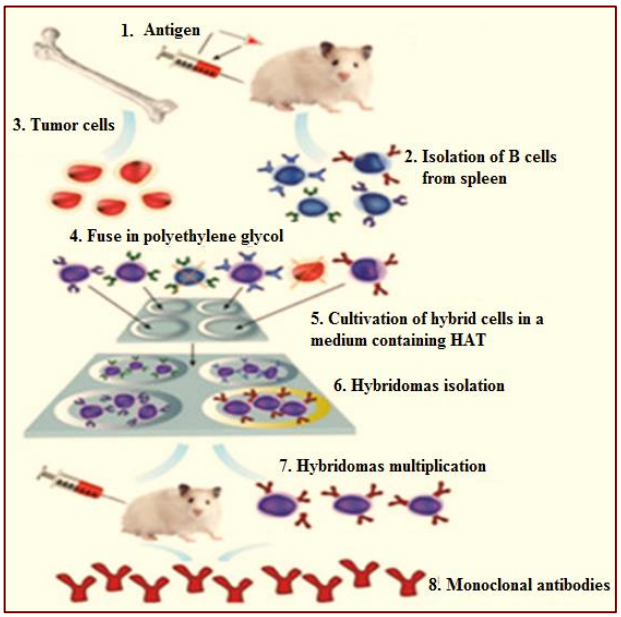

Figure 5: Hybridoma technique concerns the production of monoclonal antibodies specific to an antigen.

Monoclonal is used to frustrate the activity of some molecules, stimulate the manner of cellular apoptosis, and regulate the pathway of some signals inside the cells according to its purpose [69]. There is a study that confirmed that injecting monkeys of the type "rhesus macaque" with a single dose of a mixture antibodies like, PGT121, and PGDM1400, protected them from HIV for about six months [70]. In the recent past, when SARS and MERS spread, patients were treated with a set of FDA-licensed antivirals for use against similar off-label antivirals that included drugs such as lopinavir, ritonavir, and interferon beta, along with some immune stimulants, but the results were not at

the desired level [71]. Patients were randomly selected, to receive either lopinavir-ritonavir (400 mg and 100 mg) orally twice daily plus standard care, or standard care alone for 14 days [72]. Standard care, as necessary, was supplemental oxygen, non-invasive, and internal ventilation, antibiotic agents, vascular support, renal replacement therapy, and extracorporeal oxygen. Studies have shown that SARS-CoV-2 viral pneumonia patients have progressed in the second week of the disease, and with the temporal effects of treatment observed in previous SARS antiviral studies [73]. Investigations also revealed that the number of lopinavir-ritonavir recipients who had severe complications such as acute kidney injuries and secondary infections or who needed mechanical non-surgical ventilation was lower than those who were not receiving treatment. These observations generate hypotheses and require additional studies to determine whether the treatment of lopinavir-ritonavir given at a particular stage of the disease can reduce some complications in COVID-19. The study did not find that adding lopinavir-ritonavir treatment reduced viral RNA loads or the duration of viral RNA detection, compared to standard supportive care alone. SARS CoV-2 RNA was detected in 40.7% of patients in the lopinavir-ritonavir group at the end of the experiment (day 28). A recent report showed that the average duration of viral shedding in COVID-19 was 20 days in patients with severe disease and could reach 37 days. These data should be useful in future studies to assess the combination of lopinavir-ritonavir and other antiviral agents that may enhance antiviral effects and improve clinical outcomes [74]. Viral load is the total amount of the virus present within the human body. Usually, this term refers to the measurable amount of virus in a particular substance, such as blood or plasma. For example, a patient who responds well to some types of remedy may have a diminished percentage of viruses in his body. Viral load in patients, who are having COVID 19, is at its peak in the onset of the disease, which explains why the epidemic is rapidly spreading. So, many have in mind the question of how to reduce and prevent the viral load in the body? To date, no drug or vaccine has been recognized for COVID 19, as is the effect of drugs in case of infection with other viruses such as influenza [75]. Recently, the scientists indicated that people who are exposed to a greater viral load might experience symptoms that are more critical when they contract Coronavirus. For influenza, the initial exposure to more viruses - or a higher dose of infection - can raise the possibility of infection and disease [76]. In 2009, a new form of influenza appeared in Mexico, resulting in a pandemic that gave researchers one of the best opportunities to study the formation of an immune fingerprint using modern methods of immunology [77]. A series of studies indicates that the virus-induced a strong immune response, to the point that it stimulated in people who had had significant immunity. Many individuals have been produced antibodies, which not only attack the new strain but also their broader faction [78]. There are no antiviral agents known to be effective in treating SARS, and no antiviral agents are known to be effective against metapneumovirus or coronavirus in humans or animals [56]. The human coronavirus is a member of the Coronaviridae family. Various strains of the human coronavirus have been isolated from mild human respiratory infections for many years, and it is common knowledge that these viruses are part of a variety of "cold" viruses [79]. There was a little direct characterization of human CoV and the specific aspects of molecular and cell biology. However, a large amount of literature on the cortical mouse virus known as the mouse hepatitis virus (MHV) has been written, which is much more severe in the mouse than the human CoV virus so far in humans [80]. Coronaviruses have long been regarded as unique and very far from viruses that contain the supergroup of glycoproteins. The genome structure and replication approach of Coronavirus differ significantly, and the entry proteins themselves are more complex and have a different overall structure [81]. The usage of peptides to restrain membrane fusion and infection with the virus that causes human infection and the human coronavirus in preventing SARS or other acute respiratory diseases caused by these factors [65]. An appendage is usually arbitrated by a viral peripheral glycoprotein, and membrane fusion or entry is usually mediated by a viral transmembrane glycoprotein. In several cases, the viral glycoproteins responsible for binding and merging are synthesized as a complex compound, which is subsequently divided by a polypeptide split event into two functional subunits, and this occurs with influenza and HIV, for example [82]. In other cases, such as measles, the binding and fusion functions are always separated into two different glycoproteins. Remdesivir is an approved drug originally designed to treat Ebola, which prevents viral replication. Previous trials of this drug showed the possibility of liver toxicity [83]. Remdesivir has been used in the treatment of MERS virus in laboratory cultured cells as well as in mice [72]. The results showed that the preventive and curative use of the drug led to improved lung function and reduced vulnerability to the virus. Remdesivir suppresses the replication of the virus within the host cell by reducing the production of RNA, and it can succeed in killing the virus [84]. On February 25, 2020, NIH announced the start of randomized clinical trials to investigate the safety and efficacy of the use of experimental drug Remdesivir in patients (COVID-19). Besides, Remdesivir, medicines for HIV (AIDS), stem cells, and some traditional Chinese treatments are competing to prove their effectiveness in treatment. There are more than 80 treatment trials launched to find a cure for the virus [85]. The stages of improvement or worsening of the patient's condition should be measured, regardless of the type of treatment being tested. It is noteworthy that two of the drugs used in these experiments are drugs to treat AIDS and work to stop some of the enzymes that the virus needs to double, and it has shown achievement in the improvement of laboratory animals infected with SARS and MERS viruses. It is necessary to use therapeutic substances that are not harmful to human health, and I recommend here to the nanomaterials of polysaccharide, which may be extracted from mushrooms or bacteria. Polysaccharides from the bacteria Bacillus subtilis (BSEPS) were examined to create nanomaterials using microwave heat. This substance had remarkable results on cirrhosis and improvement of cytokines, notably interferon. Therefore, the interferon is needed to prevent the spread of the virus, and initiate the chain of events of immune resistance [86].

Challenges and Innovations in Vaccine Development

Clinical trials are typically conducted in three phases. The first phase involves a small group of healthy volunteers to test the vaccine's safety and monitor for adverse effects. The second phase includes several hundred participants to evaluate the vaccine's effectiveness during advanced testing. In the third

phase, the vaccine is tested on thousands of participants. The annual flu vaccine, for instance, is updated annually to account for new viral strains. Many of the technologies used to produce vaccines are relatively new; for instance, no vaccine based on genetic material such as RNA or DNA has been approved to date [87]. Therefore, the COVID-19 vaccine should be considered entirely new. It was subsequently modified and reused for SARS-CoV-2, undergoing stringent safety tests to mitigate the risk of adverse effects [88]. A similar effect was observed in animals injected with an early experimental vaccine from SARS. It was subsequently modified, but after being reused for SARS Cove-2 and subjected to particularly stringent safety tests to exclude the risk of the disease [88]. For these reasons, it may take some time to experiment with the vaccine and the regulatory approval it requires. This process could ultimately cost hundreds of millions of dollars, a sum not readily available to the National Institutes of Health, startups, or universities. It also does not have production and technology facilities to manufacture and distribute the vaccine widely [89]. None of the pharmaceutical companies can guarantee their profits, because the new product could mean heavy losses, especially if the demand for it fades. Vaccine development involves several stages, beginning with understanding the virus's characteristics and behavior in the host (which is not possible on the level of the "Coronavirus" due to the difficulty of knowing the pattern of its spread between cases and countries), then it is tested on animals, then it is performed on humans to test the immune responses in numbers. If it is found that the vaccine is safe and effective, the necessary regulatory approvals must be passed [90]. An efficient way to manufacture it is also required before it is ready for delivery. In general, developing new vaccines requires a long period between one and several years. According to the World Health Organization, it may take considerable time before a vaccine for the coronavirus becomes widely available. Besides, some pharmaceutical companies prefer to invest their resources in economically profitable drugs, such as pain relievers [90]. Some of them have been reluctant to search for a vaccine to treat the Coronavirus for several reasons, foremost among which is the possibility of lifting the state of emergency before the vaccine is developed. The coronavirus may mutate before a treatment is discovered, with variations potentially differing by region. A study by several Chinese researchers indicated that the virus developed into two strains, one of which is fiercer [91]. In contrast, some experts question this study because it was conducted on a limited scale, in addition to the lack of evidence by the World Health Organization on this development. In times of low disease and epidemic prevalence, there are no drivers for the development of vaccines for viral diseases [92]. Research and development are limited to medical research centers with limited financial resources compared to the huge budgets of drug companies. The financial allocations for making vaccines are declining. Therefore, some experts have suggested setting up a global vaccine development fund to fund research related to Ebola and Corona, other than when they are both spreading [84]. In this context, some analyzes have argued that the response to the Coronavirus was supposed to have started since the spread of SARS over the past decade. The discontinuation of the SARS vaccine research program has greatly contributed to the spread of the Coronavirus. As with Ebola, government funding has stopped and the pharmaceutical industry has stopped as soon as the emergency is lifted, with some advanced research ending before it begins [93]. The infrastructure for transporting and distributing the vaccine remains insufficient, even with efforts to accelerate its development. As it requires a partnership between biotechnology companies, government agencies, and universities, intending to produce a large amount of it [94]. A particular institution - regardless of its capacity - cannot develop the vaccine alone. It is certain that the new vaccine will require millions, if not billions, of doses in the coming years. The possibility of side effects, which is one of the main reasons why vaccines often do not obtain regulatory approval for several years, was that to fight the swine flu epidemic in 2009, six million people were given the Pandemrix vaccine. It is the vaccine that was later withdrawn after discovering its negative effect on some people's narcolepsy [95]. It is worth noting that vaccine development is an industry with increased risks. In the 1980s, when pharmaceutical companies began to bear the legal costs of vaccine damage, many chose to leave simply that industry and work in the pharmaceutical industry. In conclusion; despite the rapid technological developments, scientific progress, and the intensity of global investments in medical technology, there are still many restrictions that slow the emergence of a suitable vaccine, with the growing concern of major companies working in medical products about spending on producing a vaccine to counteract a corona that appears after a decline The virus is universal and then exposes them to major losses.

There is empirical evidence from both animal and human studies that the BCG vaccine has unspecified effects on the immune system. These effects were not well recognized, and their clinical significance is unknown. There is no evidence that Bacille Calmette-Guérin (BCG) vaccine protects people from infection with COVID-19 [96] . Two clinical trials are being conducted on this question, and the WHO will assess evidence when available. In the absence of evidence, the WHO does not recommend BCG vaccination to prevent COVID-19 [97]. The World Health Organization continues to recommend newborn BCG vaccination in countries or places where TB cases are high [98]. A recent study suggested a link between the tuberculosis vaccine and the prevalence of COVID-19, which found that countries that have mandatory policies forcing their citizens to vaccinate against tuberculosis have lower numbers of cases and death rates following the new epidemic that the world is currently experiencing [99]. However, BCG vaccine is a vaccination administered to children under five years of age to reduce their chances of contracting tuberculosis, it does not provide them with full protection, as it works to progress the immunity against germs and bacteria that cause the disease by no more than 70%. Also, a large percentage the vaccine loses its effect when some individuals over time, and vaccination is only one dose, and it is not recommended to take additional doses [100]. The vaccine works to stimulate the body's immune system and raise its efficiency significantly so that it can combat the germs and bacteria that cause the disease, which reduces the chances of being able to be in the body if exposed to infection it out. BCG often causes blisters at the injection site that may last for months, usually resulting in a scar [101]. The development and deployment of effective vaccines against SARS-CoV-2 have been instrumental in the global response to the COVID-19 pandemic. However, vaccine development is a complex process that faces various challenges. Developing a safe and effective

vaccine against SARS-CoV-2 within an accelerated timeframe has been a significant challenge in the global response to the COVID-19 pandemic. Vaccine development typically involves a series of rigorous preclinical and clinical testing phases that can span several years [102, 103]. However, the urgent need to curb the spread of the virus and save lives necessitated unprecedented efforts to expedite the vaccine development process. In this section, we will delve into the challenges and innovative strategies employed to enhance speed and efficiency in COVID-19 vaccine development [104]. The preclinical stage of vaccine development involves laboratory and animal testing to assess the vaccine's safety and immunogenicity before proceeding to human trials [105]. In the context of COVID-19, researchers faced the challenge of rapidly moving from the identification of the SARS-CoV-2 genome to the development of vaccine candidates. Advances in genomics, structural biology, and immunology played a crucial role in expediting this stage [106]. Researchers swiftly identified key viral targets, such as the spike (S) protein, and employed innovative approaches to vaccine design, leveraging existing knowledge from previous coronavirus outbreaks (e.g., SARS and MERS) [107]. Clinical trials are essential for evaluating vaccine safety, efficacy, and dosage. Traditional vaccine development typically follows a stepwise approach with distinct phases (Phase 1, 2, and 3) involving progressively larger cohorts of volunteers [108]. However, to expedite COVID-19 vaccine development, these phases were partially overlapping, enabling the collection of safety and efficacy data in parallel. Additionally, the recruitment of large and diverse study populations was facilitated through international collaborations and global partnerships [109]. The utilization of innovative vaccine platforms has been instrumental in accelerating vaccine development. One notable example is the use of mRNA-based vaccines, such as the Pfizer-BioNTech and Moderna vaccines. mRNA vaccines utilize a novel approach that involves introducing the viral genetic material (mRNA) encoding the SARS-CoV-2 spike protein into the body [110]. This technology offers several advantages, including rapid design and production, scalability, and flexibility in targeting different variants. The platform's plug-and-play nature allowed for a quick pivot to the development of specific COVID-19 mRNA vaccines [107]. Regulatory processes play a crucial role in ensuring the safety and efficacy of vaccines. Regulatory authorities, such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), have implemented expedited review and approval processes to address the urgency of the pandemic while maintaining rigorous standards. Regulatory agencies collaborated closely with vaccine developers to streamline the evaluation process, accelerate review timelines, and prioritize resources for COVID-19 vaccines [111]. Rapidly scaling up vaccine manufacturing and establishing efficient distribution networks were key challenges. To meet the global demand for COVID-19 vaccines, manufacturers utilized various strategies, such as partnering with contract manufacturers, expanding production facilities, and leveraging established vaccine manufacturing platforms [112]. Furthermore, parallel planning for distribution, including cold chain logistics and equitable allocation strategies, allowed for a prompt and efficient rollout of vaccines to different regions. The remarkable speed and efficiency achieved in COVID-19 vaccine development have showcased the power of scientific collaboration, technological advancements, and the determination of global stakeholders [113]. However, it is essential to note that the accelerated timeline did not compromise on safety and efficacy evaluations. Rigorous monitoring of vaccine safety and ongoing post-approval surveillance are critical to ensure the long-term benefits and address any potential adverse events. The efficacy and durability of vaccines are crucial factors in determining their effectiveness in preventing SARS-CoV-2 infection and reducing the severity of COVID-19 [114]. Vaccine efficacy refers to the ability of a vaccine to protect individuals from developing the disease, while durability refers to the duration of protection provided by the vaccine [115]. Understanding and optimizing both efficacy and durability are essential for the successful control of the COVID-19 pandemic [114]. Vaccine efficacy is a measure of how well a vaccine prevents infection or reduces the severity of the disease. In the context of COVID-19, vaccine efficacy has been determined through large-scale clinical trials, comparing the rates of infection and disease severity between vaccinated and placebo groups. Achieving high vaccine efficacy is crucial for reducing the transmission of the virus and achieving herd immunity. However, several factors can influence vaccine efficacy: The emergence of new variants of SARS-CoV-2 has raised concerns about potential reductions in vaccine efficacy. Some variants exhibit mutations in the spike protein, which may impact the binding of neutralizing antibodies generated by the vaccine [116]. Ongoing surveillance and research are crucial to monitor the effectiveness of vaccines against different variants and to inform the development of updated vaccine formulations that target specific variants [117]. Vaccine efficacy may vary among different age groups and individuals with underlying medical conditions. Older adults and those with compromised immune systems may have a reduced immune response to vaccination, necessitating tailored vaccination strategies to ensure optimal protection [118]. While COVID-19 vaccines have demonstrated high efficacy in preventing severe disease, breakthrough infections can still occur, leading to asymptomatic or mild cases. However, even in these cases, vaccinated individuals are often protected from severe illness and hospitalization. Vaccine effectiveness in reducing transmission and asymptomatic infections continues to be a subject of ongoing research [119]. The durability of vaccine-induced immunity refers to the length of time that a vaccine provides protection against SARS-CoV-2 infection. Determining the durability of COVID-19 vaccines is an ongoing process as the vaccines are relatively new [120]. The magnitude and quality of the immune response elicited by the vaccine play a role in determining its durability. Vaccines that generate robust and long-lasting immune responses, including the production of neutralizing antibodies and the activation of T-cells, are more likely to provide durable protection. Ongoing research is being conducted to assess the persistence of vaccine-induced immune responses and the potential need for booster doses [121]. Variants of SARS-CoV-2 that evade vaccine-induced immunity can potentially impact the durability of protection. Monitoring the emergence and spread of variants is crucial to understand their potential impact on vaccine durability and inform the development of updated vaccines targeting specific variants [122]. The establishment of immune memory, including the generation of long-lived B-cells and memory T-cells, is a critical aspect of durable immunity. These memory cells can recognize and mount

a rapid and effective immune response upon re-exposure to the virus, potentially providing long-term protection. Ongoing research aims to understand the dynamics of immune memory following vaccination and natural infection. The emergence of new variants has prompted the development of updated vaccine formulations targeting specific variants or incorporating multiple variant strains. Variant-specific booster doses may also be considered to enhance protection against emerging variants [123]. Heterologous vaccination, also known as mix-and-match or prime-boost strategies, involves administering different types of vaccines for the initial and booster doses. This approach aims to enhance immune responses and potentially provide broader protection against different variants [124]. For example, combining an adenovirus vector-based vaccine with an mRNA-based vaccine has shown promising results in terms of boosting immune responses. While neutralizing antibodies play a crucial role in preventing infection, T-cell responses are important for controlling and clearing the virus. Research is underway to explore the role of T-cell responses in vaccine efficacy and durability. Innovative vaccine designs that specifically target T-cell responses, such as viral vector vaccines encoding multiple viral proteins, are being investigated [125]. Adjuvants are substances that can enhance the immune response to vaccines. Their use in COVID-19 vaccine development aims to improve vaccine efficacy and potentially extend durability. Adjuvants can stimulate a stronger and longer-lasting immune response, leading to enhanced protection. Various adjuvants are being tested in clinical trials to optimize COVID-19 vaccine effectiveness [126]. Long-term monitoring of vaccinated individuals is crucial to assess vaccine durability and evaluate the need for booster doses. Real-world data on vaccine effectiveness, breakthrough infections, and the impact of variants are continually collected and analyzed to inform vaccination strategies and potential modifications. Adaptive vaccine design involves flexible and responsive approaches to vaccine development that can quickly adapt to the changing landscape of the pandemic. This includes the ability to rapidly design and produce updated vaccines to address [127] emerging variants and to target vulnerable populations based on evolving epidemiological data. Immune profiling techniques, such as analyzing antibody levels, T-cell responses, and other immune markers, are employed to assess vaccine efficacy and durability. These approaches provide insights into the immune responses induced by vaccines, identify correlates of protection, and guide vaccine development strategies [128]. The emergence of new variants of SARS-CoV-2 has posed significant challenges to vaccine development. Some variants exhibit mutations in the spike protein, the target of most vaccines, which may affect vaccine effectiveness [129]. Vaccines developed based on the original virus strain may have reduced efficacy against certain variants. To address this challenge, vaccine manufacturers are exploring strategies such as updating vaccine formulations to target specific variants or developing multivalent vaccines that provide broad protection against multiple strains [130]. Vaccine hesitancy and misinformation have presented obstacles in achieving widespread vaccine uptake. Building trust and confidence in COVID-19 vaccines among the population is essential. Communication campaigns, community engagement, and education about vaccine safety and efficacy have been employed to address vaccine hesitancy [131]. Additionally, real-world data on vaccine effectiveness and safety have played a crucial role in reassuring the public and countering vaccine misinformation [131]. Ensuring equitable access to vaccines across countries and populations has been a significant challenge. Limited vaccine supplies, distribution bottlenecks, and vaccine nationalism have resulted in disparities in vaccine coverage between high-income and low-income countries. International collaborations, initiatives such as COVAX, and technology transfer agreements are being implemented to enhance global vaccine equity and facilitate access to vaccines for all. Despite these challenges, vaccine development has witnessed remarkable innovations and advancements. The use of novel vaccine platforms, such as mRNA and viral vector-based technologies, has demonstrated the potential for rapid vaccine development and scalability. Additionally, advancements in vaccine delivery systems, including needle-free administration methods, are being explored to enhance vaccine accessibility and acceptability. Furthermore, research continues on next-generation vaccines that offer improved efficacy, durability, and broader protection against emerging variants. These include the development of multivalent vaccines, the use of conserved viral targets, and the exploration of novel vaccine platforms, such as protein subunit vaccines and virus-like particles.

Treatment Strategies for COVID-19

Effective treatment strategies play a critical role in managing COVID-19 and reducing the severity of illness, particularly for individuals who develop severe symptoms or complications. Over the course of the pandemic, various treatment approaches have been explored and refined to improve patient outcomes [132]. Supportive care is the cornerstone of COVID-19 treatment, focusing on symptom management and providing essential medical support to patients. This includes monitoring vital signs, ensuring adequate oxygenation, maintaining hydration, and managing complications such as secondary infections [133]. Supportive care also involves providing psychological support and addressing the mental health impact of the disease on patients and healthcare workers. COVID-19 can lead to respiratory distress and low oxygen levels in severe cases [133]. Oxygen therapy is crucial for maintaining adequate oxygenation and supporting respiratory function. This may include supplemental oxygen delivered via nasal cannula, face mask, or high-flow nasal oxygen systems. In critical cases, mechanical ventilation or extracorporeal membrane oxygenation (ECMO) is often necessary. Antiviral medications target the replication of SARS-CoV-2, aiming to reduce viral load in infected individuals [134]. Remdesivir, an antiviral drug, has received emergency use authorization or approval in multiple countries for treating COVID-19. It has shown modest benefits in reducing the time to recovery in hospitalized patients [135]. Other antiviral drugs, such as molnupiravir and favipiravir, are also being investigated for their efficacy against SARS-CoV-2. COVID-19 increases the risk of blood clot formation and thrombosis. Anticoagulant medications, such as low molecular weight heparin or direct oral anticoagulants, are frequently administered to hospitalized patients to prevent or treat blood clots and reduce the risk of complications [136]. Risk assessment and individualized treatment decisions are tailored to the patient's condition and bleeding risk. Several drugs have been repurposed or developed specifically for the treatment of COVID-19. These

drugs target different aspects of the disease, including viral replication, the immune response, and the prevention of complications such as blood clotting. Remdesivir is an antiviral drug that works by inhibiting the replication of the SARS-CoV-2 virus. It was originally developed for the treatment of Ebola virus disease and has shown promise in shortening the recovery time for hospitalized patients with severe COVID-19. Remdesivir has received emergency use authorization or approval in several countries and is typically administered intravenously [137].

Dexamethasone is a corticosteroid that has anti-inflammatory properties. It has been shown to reduce mortality in critically ill COVID-19 patients requiring supplemental oxygen or mechanical ventilation. Dexamethasone mitigates excessive immune responses and inflammation in severe COVID-19 cases [138]. Tocilizumab is an immune modulator that targets the interleukin-6 (IL-6) pathway, which plays a role in the inflammatory response. It is used in the treatment of severe COVID-19 cases with evidence of systemic inflammation [139]. Tocilizumab has demonstrated effectiveness in reducing the risk of mechanical ventilation and improving outcomes in some patients [140]. Baricitinib is a Janus kinase (JAK) inhibitor that modulates the immune response. It has shown benefits when used in combination with remdesivir for the treatment of hospitalized patients with COVID-19, especially those requiring supplemental oxygen or non-invasive ventilation. Baricitinib helps reduce inflammation and may prevent disease progression [141]. Convalescent plasma is obtained from individuals who have recovered from COVID-19 and contains antibodies against the virus. It is used as a passive immunization therapy to provide temporary protection and boost the immune response in patients with severe or life-threatening COVID-19. The efficacy of convalescent plasma is still being studied, and its use may vary based on local guidelines [142]. Monoclonal antibody therapies use laboratory-engineered antibodies to target specific viral proteins. These antibodies neutralize the virus and reduce the severity of illness. Monoclonal antibody treatments such as casirivimab/imdevimab and bamlanivimab/etesevimab have been authorized for emergency use in certain high-risk populations, particularly for individuals with mild to moderate COVID-19 [143]. COVID-19 is associated with an increased risk of blood clotting and thrombosis. Anticoagulant medications, such as low molecular weight heparin or direct oral anticoagulants, are frequently administered to hospitalized patients to prevent or treat blood clots and reduce the risk of complications [144]. It's important to note that the use of these drugs may vary based on factors such as disease severity, patient characteristics, and local treatment guidelines. The safety and efficacy of these drugs are being continuously evaluated through clinical trials and real-world data analysis. Treatment decisions should be made in consultation with healthcare professionals based on individual patient needs and the latest available evidence. As the horrific epidemic of COVID- 19 infection spreads, the number of patients grows, necessitating standard treatment for the virus, which repairs tissue damage caused by viruses and boosts patients' immunity [145]. Treatment protocols have appeared for Coronavirus patients that rely mainly on herbs to speed up the healing processes for patients and raise their immunity to face the virus when infected with it. Researchers have created sprays from a group of herbs that include black seed oil mixed with mushrooms and honey and have also been used as a topical treatment for pneumonia or bronchial pneumonia that affects severe cases of Corona [146]. Some physicians have confirmed that honey, chamomile, and nigella help in potentiating the immune system, along with watercress, which increases the acidity level that helps in fighting the virus. Clinical trials also confirmed that COVID-19 positive patients who were given Ayurveda treatment showed 20 to 60% better improvement in various tests such as C-reactive protein, Procalcitonin, D Dimer, and RT-PCR, compared to conventional treatment. About 86.66% of the patients in the traditional protocol tested negative for Corona on the fifth day compared to 60% of the patients undergoing conventional treatments, and on the tenth-day test, all patients were tested negative. Moreover, none of the patients who underwent physiotherapy had progressed to ventilators. Moderate or need respirators or have experienced any negative-effects. In a recent study, Egyptian samples for propolis were analyzed and studied using molecular docking for their anti-COVID-19 activity. Another study looked into pollen grain analysis and found that the Cyperaceae family was dominant in Alexandria propolis samples; the Asteraceae family was dominant in Tanta and Menoufia propolis samples. The analysis of propolis samples by scanning electron microscopes shows that all propolis samples have a putative gel such as morphology [147]. Concerning reference antiviral drugs, Remdesivir, Lopinavir, and Umifenovir have been shown for the most part to achieve promising binding results. The modes of binding and orientation were examined concerning their antiviral activity during an analysis of the binding interactions of the tested fractions. Moreover, H-arene interactions with Tyr505 within RNA-dependent RNA polymerase, spike protein S1, and main protease enzymes pockets, Octatriacontyl Penta-fluoropropionate had interactions of hydrogen bonds with Lys798, Asp42, and Met49. Standard patient care plus propolis for seven days or standard patient treatment alone (n=42) has been received with an oral dose of 400mg/day or 800 mg/day (n=42). The attending physician determined that the standard care included all the necessary interventions. Acute kidney damage and the need for intensive care or vasoactive drugs were secondary outcomes. In both propolis groups, the hospital period was reduced compared to controls after the intervention; median seven days at 400mg/day and six days at 800mg/day compared to 12 days at standard care alone [148]. Although "COVID-19" is seen as a disease that affects mainly the lungs, it also can damage many other body organs. The risk of long-lasting health problems can increase damage to organs. Imaging tests taken months after recovering from Corona, for example, revealed long-term damage to the heart muscle, even in people who had only mild symptoms, and this may increase the risk of heart failure or other heart complications in the future [149]. The type of pneumonia usually associated with "COVID- 19" can cause long-term damage to the alveoli in the lung, and the resulting scar tissue can lead to long-term respiratory problems [150]. The brain may be affected adolescents may develop several brain conditions, including strokes, convulsions, and "Guillain-Barré" syndrome. It can also increase the risk of developing Parkinson's disease and Alzheimer's disease. COVID-19 can increase the likelihood of blood cells clumping and forming clots cause heart attacks and strokes [151]. Other organs affected by blood clots include the lungs, legs, liver, and kidneys, and the virus can

weaken blood vessels and cause them to leak, which may contribute to long-term problems in the liver and kidneys. It is also a symptom of post-corona syndrome, general weakness, and exacerbation of chronic diseases. A person may suffer in such a case from muscle aches and headaches. A study revealed that two-thirds of patients who showed mild or moderate symptoms reported at least one long-term symptom after sixty days of recovery [152]. The study included a sample of 150 non-critical coronavirus patients, between March and June. In a similar study, 87% of patients suffered from at least one long-term symptom, especially fatigue and shortness of breath. That study included elderly patients who had suffered severe complications from the infection. These disorders that accompany patients after recovering from viruses are not surprising, according to the researchers, because they are recorded after recovery from several viral infections such as hepatitis B, what is known as the " Epstein-Barr" virus, and sometimes even the common flu. The Epstein-Barr virus is known as, herpes which affects most people and can cause many diseases, including mononucleosis [152]. Many studies have monitored COVID-19 recovery patients, revealing persistent symptoms beyond the lungs, including diabetes and venous thromboembolic diseases. The angiotensin converting enzyme-enriched in the proximal tubule renal can mediate SARS-CoV-2 entry into the epithelial cells to accumulate and cause cytotoxicity and inflammatory cell infiltration. A previous study reported persistent impairment of kidney function with the potential for progression to end-stage kidney disease requiring dialysis [153]. A study showed that 13% of patients without acute kidney injury and with normal glomerular filtration rate in the acute stage had decreased eGFR upon follow-up [154].

Corona's impact on the environment

The Coronavirus pandemic has profoundly impacted the environment and climate in several ways. For instance, the sharp decline in individual travel, along with reduced social and commercial activities, has significantly decreased air pollution in many regions [155]. According to an Earth-system scientist, China's lockdowns and related initiatives led to a 25% reduction in carbon emissions over two months, potentially saving at least 77,000 species. However, the outbreak disrupted environmental diplomacy efforts, including the postponement of the 2020 United Nations Climate Change Conference. Additionally, the economic fallout is expected to slow investments in green energy technologies. In January and February, satellite images from the US Space Agency (NASA) and the European Space Agency revealed a decrease in China's nitrogen dioxide emissions, which are caused by the use of fossil fuels [156]. This was attributed to the country's economic slowdown during the quarantine. In Italy, satellite data showed a significant decrease in nitrogen dioxide emissions in the north. Additionally, waterways in Venice became clearer as tourist boat activity dropped dramatically. In India, according to the Energy and Clean Air Research Centre, the national curfew imposed on 22 March brought nitrogen dioxide pollution to its lowest level in the spring [157]. In North America, one of the most polluting regions globally, similar developments are expected to coincide with a large-scale economic downturn in various areas. Of course, this does not imply that the world is experiencing a health crisis comparable to its current efforts to combat greenhouse gas emissions. But what is happening now should give us reason to think carefully about the impact of human activities - including mobility, travel, and trekking - on the condition on our planet's surface [158]. The imposition of restrictions on unnecessary travel and movement has led airlines to keep their planes on the ground, which has led to these companies drastically reducing the number of their flights or halting them completely. A study published in 2018 showed that eight percent of the world's greenhouse gas emissions are caused by tourism activity and that air travel has a large share in this regard [158]. According to a study published in May 2020, the global daily carbon emissions decreased by 17% during the April lockdown process and could result in an annual decrease in carbon emissions of up to 7%. This decrease was mainly due to a reduction in transport use and industrial activities. However, the dropping rapidly resulting from the limited industrial production was observed to return to normal [159]. However, social changes caused by the epidemic and lockdowns such as telecommuting and digital conferencing may have a more sustainable impact than a short-term limitation of transportation use. Despite all of this, the concentration of carbon dioxide in the atmosphere reached its highest level in human history ever in May 2020. A pandemic is the worst possible method for reducing emissions; technological, behavioral, and structural changes are far more effective. Global demand for fossil fuels has decreased by nearly 10% in the coronavirus measures, and many energy economists are said to believe this will not return to normal before the crisis [160]. The Coronavirus pandemic may have pushed the fossil fuel industry into a definitive decline as demand for oil and gas declines and governments rush to switch to clean energy. It is expected that the annual decline in demand for fossil fuels by 2% will lead to the collapse of future profits of oil, gas, and coal companies from 39 trillion dollars to 14 trillion dollars. Yet, according to Bloomberg New Energy Finance, more than half a trillion dollars worldwide are currently pumped into carbon-intensive industries [160]. The International Energy Agency warned that the economic disruption caused by the coronavirus outbreak could delay or hinder investments in green energy, despite the temporary reduction in global carbon emissions. Long quarantine periods, however, strengthened the dependence on remote work policies. The widespread use of disposable face masks has resulted in a significant amount of plastic waste being dumped into the environment, exacerbating the global plastic waste crisis [161].

Future Directions and Implications

Future directions and implications in the context of COVID-19 are multifaceted and encompass various aspects of the disease, including prevention, treatment, public health strategies, and research [162]. The primary goal of COVID-19 vaccination is to achieve widespread immunization within populations. Vaccination programs aim to reach as many eligible individuals as possible, providing them with protection against the virus. The implication of widespread immunization is a significant reduction in the number of COVID-19 cases, hospitalizations, and deaths. Herd immunity, also known as population immunity, occurs when a sufficient proportion of the population becomes immune to a disease, either through vaccination or prior infection. Successful vaccine development and high vaccination coverage can contribute to achieving herd immunity against

COVID-19 [162]. The implications of reaching herd immunity include an additional layer of protection for vulnerable individuals who cannot be vaccinated, such as those with compromised immune systems or certain medical conditions [163]. Vaccines have shown efficacy in reducing the severity of COVID-19 symptoms and complications among vaccinated individuals who still contract the virus [164]. Even if breakthrough infections occur, vaccinated individuals are generally less likely to experience severe illness, require hospitalization, or die from COVID-19. The implication is that successful vaccine development can alleviate the burden on healthcare systems, minimize the strain on medical resources, and save lives. Vaccinated individuals who contract the virus are less likely to transmit it to others compared to unvaccinated individuals. Vaccination can reduce the viral load and duration of shedding, thereby decreasing the overall transmission of SARS-CoV-2 in communities. The implication is that successful vaccine development can contribute to the reduction of community transmission, helping to control the spread of the virus and bring the pandemic under control [165]. Successful vaccine deployment plays a crucial role in restoring societal and economic activities that have been disrupted by the pandemic. As vaccination rates increase and the risk of severe illness decreases, public health measures such as lockdowns, travel restrictions, and physical distancing can be gradually eased [166]. The implication is that widespread immunization can pave the way for the reopening of businesses, schools, and other public spaces, allowing for a return to a more normal way of life. The global implications of successful vaccine development extend beyond individual countries. Global collaboration in vaccine distribution and access is critical for controlling the pandemic on a global scale. Successful vaccine development can enable countries to contribute to global vaccination efforts, particularly in low-income and resource-constrained regions. The implication is that by ensuring equitable access to vaccines worldwide, the global impact of COVID-19 can be reduced, preventing the emergence of new variants and supporting global health security [165]. The development of broad-spectrum antivirals or novel therapeutic approaches may also be explored to address future viral outbreaks. The availability of effective antiviral treatments would significantly impact the management of COVID-19, providing options for early intervention and reducing the severity of the disease [167]. Effective antiviral treatments would enable early intervention in COVID-19 cases, potentially reducing the severity of the disease and its associated complications. By targeting the virus directly, these treatments could help inhibit viral replication, limit viral spread within the body, and prevent the progression of the infection to severe stages. Early intervention can lead to better patient outcomes, shorter hospital stays, and reduced strain on healthcare systems [168]. The availability of effective antiviral treatments would expand the range of treatment options for COVID-19. Currently, treatment mainly focuses on supportive care and management of symptoms. Antivirals could provide a specific and targeted approach to combat the virus, complementing existing therapies and potentially improving the overall effectiveness of treatment strategies [169]. This could lead to better control of the disease and improved recovery rates. Antiviral treatments that effectively inhibit viral replication can significantly reduce viral shedding, the release of the virus from an infected individual. By limiting viral shedding, the risk of transmission to others can be significantly reduced. This would have important implications for controlling the spread of COVID-19, especially in high-risk settings such as healthcare facilities, long-term care facilities, and community outbreaks. Broad-spectrum antivirals or novel therapeutic approaches would be particularly valuable for high-risk groups, such as the elderly, immunocompromised individuals, and those with underlying health conditions [170]. These populations are more susceptible to severe illness and complications from viral infections. Effective antiviral treatments could provide an added layer of protection and enhance the management of COVID-19 in these vulnerable populations. The development of broad-spectrum antivirals and novel therapeutic approaches has implications beyond COVID-19. It contributes to overall pandemic preparedness by expanding the arsenal of tools available to combat emerging viral infections. The knowledge gained from the development of antiviral treatments for COVID-19 can be applied to future viral outbreaks, facilitating a more rapid and effective response [171]. The availability of effective antiviral treatments for COVID-19 would have a significant global health impact. Access to these treatments in low-income and resource-limited settings could help reduce the burden of the disease and improve outcomes in regions with limited healthcare infrastructure. By providing options for treatment and reducing the severity of COVID-19, these advancements can contribute to global health equity and support efforts to mitigate the impact of future viral outbreaks worldwide [172]. As the COVID-19 pandemic continues, there is increasing recognition of the long-term health effects experienced by individuals who have recovered from the illness. Referred to as "long COVID" or "post-acute sequelae of SARS-CoV-2 infection" (PASC), these long-term effects can persist for weeks or months after the initial infection, even in individuals with mild or asymptomatic cases [173]. Understanding and addressing these long-term effects are crucial for effective healthcare planning and providing appropriate support to COVID-19 survivors. Future research will focus on unraveling the underlying mechanisms of long COVID and identifying the risk factors that contribute to its development. This includes investigating the immune response, potential viral persistence or organ damage, and individual factors such as age, pre-existing conditions, and genetic predisposition. Understanding these mechanisms and risk factors will enable healthcare providers to better predict, prevent, and manage long-term effects in COVID-19 survivors [174]. Long COVID can impact various bodily systems, including respiratory, cardiovascular, neurological, and psychological functions. Future research will explore effective rehabilitation strategies tailored to address these specific areas of impairment [175]. This may involve multidisciplinary approaches, including physical therapy, respiratory therapy, cognitive rehabilitation, mental health support, and occupational therapy. Developing evidence-based rehabilitation programs will be crucial for restoring functional abilities and improving the quality of life for individuals with long COVID [175]. Given the potential for prolonged symptoms and complications, long-term monitoring and follow-up care for COVID-19 survivors will be essential. Future healthcare planning will involve establishing specialized clinics or programs dedicated to assessing and managing long COVID cases. Regular medical check-ups, diagnostic tests, and comprehensive evaluations can help identify

and address any evolving health issues, enabling timely interventions and appropriate support for long-term recovery [176]. Psychological implications, including anxiety, depression, post-traumatic stress disorder (PTSD), and cognitive difficulties, have been reported in individuals with long COVID. Future research will focus on understanding the mental health impact of COVID-19 and developing targeted interventions to support mental well-being [177]. This may involve access to mental health services, counseling, cognitive-behavioral therapy, and support groups to address the psychological effects of the illness. The recognition and understanding of long COVID have implications for public health planning and policy development. Healthcare systems need to allocate resources to address the long-term healthcare needs of COVID-19 survivors [178]. This includes considering the potential impact on healthcare utilization, workforce planning, disability support systems, and insurance coverage for long-term complications. Incorporating long COVID into public health strategies will ensure comprehensive care and support for affected individuals. The COVID-19 pandemic has underscored the critical need for robust pandemic preparedness plans at both national and global levels [179].

Future pandemic preparedness plans will involve strengthening surveillance systems to facilitate early detection and monitoring of infectious diseases. This includes improving the capacity for rapid reporting, data sharing, and analysis of disease trends. Enhanced surveillance systems enable timely identification of outbreaks, prompt response measures, and effective containment strategies [172]. The development and deployment of rapid and accurate diagnostic tests are crucial for effective pandemic response. Future efforts will focus on advancing diagnostic technologies, such as point-of-care tests, high-throughput screening methods, and molecular diagnostics. Rapid diagnostics enable early identification of infected individuals, enabling prompt isolation, contact tracing, and targeted interventions. The COVID-19 pandemic exposed vulnerabilities in global supply chains for essential medical resources, including personal protective equipment (PPE), ventilators, and pharmaceuticals. Future pandemic preparedness plans will involve diversifying and strengthening supply chains to ensure the availability of critical resources during times of crisis [180]. This includes increasing domestic production capacity, establishing strategic stockpiles, and improving coordination among manufacturers, distributors, and healthcare providers. The pandemic has highlighted the need for resilient and adaptable healthcare infrastructure. Future efforts will involve investing in healthcare systems to enhance capacity, expand healthcare facilities, and strengthen the healthcare workforce. This includes bolstering hospital infrastructure, ensuring adequate staffing levels, and improving surge capacity to handle increased patient volumes during pandemics. A coordinated and collaborative global response is essential for effective pandemic preparedness. Future efforts will involve strengthening international cooperation, information sharing, and resource mobilization. This includes improving communication channels among countries, sharing best practices, and establishing frameworks for rapid response and resource allocation during global health emergencies. Continuous investment in research and development is vital for pandemic preparedness. Future efforts will involve supporting basic and applied research to advance our understanding of emerging pathogens, develop new therapeutics and vaccines, and identify innovative approaches for disease prevention and control. Robust research infrastructure and funding mechanisms will be necessary to accelerate the development and deployment of novel interventions. The implications of these future efforts in pandemic preparedness include more effective containment measures, early detection and response to emerging pathogens, and a coordinated and resilient global response [181]. By enhancing surveillance systems, improving diagnostics, strengthening supply chains, and investing in healthcare infrastructure, nations can be better equipped to prevent, detect, and mitigate the impact of future pandemics. The lessons learned from the COVID-19 experience provide valuable insights and underscore the urgency of building a more prepared and resilient world [182]. The COVID-19 pandemic has had a profound impact on mental health and social well-being globally. As we look towards the future, it is crucial to address the mental health consequences and rebuild societal systems that have been affected by the pandemic. Future efforts will involve allocating resources and investing in mental health services to meet the growing demand for support [183]. This includes ensuring access to affordable and accessible mental health care, expanding the availability of mental health professionals, and integrating mental health services into primary care settings. Adequate funding and policy support are essential to strengthen mental health systems and address the increased needs arising from the pandemic. The pandemic has resulted in significant social and economic disruptions, including job losses, financial strain, and social isolation. Future directions will focus on implementing strategies to mitigate these impacts. This includes providing financial support, unemployment assistance, and targeted interventions to vulnerable populations [184]. Promoting job creation, supporting small businesses, and strengthening social safety nets are important for restoring stability and well-being in communities. Building resilience and promoting effective coping strategies will be essential in the aftermath of the pandemic. Future efforts will involve implementing mental health promotion programs that equip individuals with skills to manage stress, anxiety, and emotional well-being [185]. This includes providing education on self-care, stress reduction techniques, and fostering social support networks. By empowering individuals with the tools to navigate challenges, it is possible to enhance their overall resilience and well-being. The pandemic has highlighted the importance of community support and social cohesion in times of crisis. Future directions will involve strengthening community networks and fostering a sense of belonging and solidarity [185]. This includes encouraging community engagement, supporting grassroots organizations, and promoting initiatives that bring people together. By strengthening social connections and fostering a sense of collective responsibility, communities can support each other during times of recovery and rebuilding. The pandemic has also brought to the forefront issues of stigma and discrimination related to COVID-19 and mental health. Future efforts will involve combating stigma and promoting a culture of inclusivity and acceptance. This includes raising awareness, providing education, and challenging negative stereotypes surrounding mental health and COVID-19. By addressing stigma, individuals are more likely to seek help, and communities can foster an environment of understanding and support [186]. The COVID-

19 pandemic has highlighted the significant health inequities that exist globally and has further exacerbated these disparities. As we move forward, it is imperative to address these inequities, promote equitable access to healthcare, and improve health outcomes for vulnerable populations. Future efforts should focus on addressing the social determinants of health that contribute to health inequities. This includes tackling poverty, improving access to education, addressing housing insecurity, and addressing systemic racism and discrimination [187]. By addressing the root causes of health disparities, we can create a more equitable foundation for health. Ensuring equitable access to healthcare services is crucial for achieving health equity. Future directions should involve reducing barriers to healthcare, including financial barriers, geographic barriers, and cultural and linguistic barriers. This includes expanding healthcare coverage, strengthening primary care systems, and implementing strategies to reach underserved populations. Tailored interventions should be developed to meet the specific needs of vulnerable populations. Improving health education and literacy is essential for empowering individuals and communities to make informed decisions about their health. Future efforts should focus on promoting health literacy, providing accurate and accessible health information, and addressing health disparities in health education curricula. This will enable individuals to navigate healthcare systems, make informed choices, and take proactive steps towards better health outcomes. Robust data collection and analysis are essential to identify and monitor health inequities [187]. Future directions should prioritize collecting disaggregated data on health outcomes, healthcare utilization, and social determinants of health across diverse populations. This data can inform evidence-based policies, interventions, and resource allocation to address health disparities effectively. Strengthening health systems, particularly in low-income and marginalized communities, is crucial for achieving health equity. Future efforts should involve investing in healthcare infrastructure, training healthcare professionals, and ensuring the availability of essential medical resources in underserved areas [188]. This includes strengthening primary healthcare, improving the quality of care, and promoting culturally responsive and patient-centered approaches. Addressing health inequities requires international collaboration and resource sharing. Future directions should involve global partnerships to promote knowledge exchange, capacity building, and resource sharing. This includes sharing best practices, lessons learned, and innovative approaches to address health disparities. By working together, countries can leverage collective expertise and resources to combat future pandemics and promote health equity on a global scale.

Conclusion

The COVID-19 pandemic has profoundly impacted global health, economies, and societies, presenting numerous challenges that demand innovative solutions and collaborative efforts. It has presented numerous challenges that require innovative solutions and collaborative efforts. This review has examined various aspects of COVID-19, including its transmission mechanisms, vaccine development hurdles, treatment strategies, supportive care approaches, natural remedies, and future implications. One of the most significant achievements in combating COVID-19 has been the rapid development and deployment of effective vaccines. These vaccines have played a pivotal role in reducing disease transmission and severity, offering hope for a gradual return to normalcy. However, there are still challenges to overcome, such as ensuring equitable access to vaccines for all populations worldwide. The pandemic has underscored the importance of preparedness and the need for resilient healthcare systems. Moving forward, efforts should prioritize strengthening disease surveillance, improving diagnostic capabilities, and enhancing healthcare infrastructure to effectively respond to future outbreaks and protect vulnerable populations. Addressing the long-term health effects of COVID-19, including both physical and mental consequences, is equally vital. The recognition and understanding of "long COVID" or post-acute sequelae of SARS-CoV-2 infection (PASC) will guide future research and interventions to support the well-being of individuals who have recovered from the disease. Moreover, the pandemic has revealed existing health inequities, emphasizing the need to address disparities and ensure equitable access to healthcare for all populations. International collaboration and resource-sharing will be crucial in combating future pandemics and promoting health equity on a global scale.

Abbreviation

ACE2: Angiotensin-converting enzyme2; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BNEF: Bloomberg New Energy Finance; COVID-19: Coronavirus Disease; Ca2+: Calcium ion; CCL3: Macrophage Inflammatory Protein-1 Alpha (Human Recombinant); CD4: Cluster of Differentiation 4; CO_2: Carbon Dioxide; COVAX: COVID-19 Vaccines Global Access; CPK: Creatine Phosphokinase; CRP: C-Reactive Protein; CT: Computed Tomography; D-Dimer: A protein fragment present in the blood after a blood clot breaks up; DNA: Deoxyribonucleic Acid; DOACs: Direct Oral Anticoagulants; ECMO: Extracorporeal Membrane Oxygenation; ESR: Erythrocyte Sedimentation Rate; FDA: Food and Drug Administration; FP: Fusion Peptide; G-CSF: Granulocyte Colony-Stimulating Factor; GDP: Gross Domestic Product; GHG: Greenhouse Gas; H1N1: Influenza A Virus; HIV: Human Immunodeficiency Virus; HR: Human Resources; ICU: Intensive Care Unit; IEA: International Energy Agency; IFN-γ: Interferon-gamma; IL-10: Interleukin-10; IL-2: Interleukin-2; IP-10: Interferon-Gamma-Inducible Protein 10; ITC: Isothermal titration calorimetry; IV: Intravenous; JAK: Janus Kinase; LDH: Lactate Dehydrogenase; LLF motif: Hydrophobic motif; LMWH: Low Molecular Weight Heparin; MERS-CoV: Middle East Respiratory Syndrome coronavirus; mRNA: Messenger RNA; NA: Neuraminidase; NASA: National Aeronautics and Space Administration; NO_2: Nitrogen Dioxide; ORFs: Open reading frames; PCR: Polymerase Chain Reaction; PPE: Personal Protective Equipment; PT: Prothrombin Time; R&D: Research and Development; RNA: Ribonucleic Acid; RT-PCR: Reverse Transcription Polymerase Chain Reaction; S2: A portion of the spike protein; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; TNF-α: Tumor Necrosis Factor Alpha; UN: United Nations; WHO: World Health Organization; X-ray: X-ray

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Availability of data and materials

Data will be available by emailing dramalibrahim29@gmail.com

Authors' contributions

The conceptualization and design of the study were primarily carried out by Amal Ibrahim Hassan. Both authors, Amal Ibrahim Hassan (AIH) and Eithar Kareem Al Adham (EKAA) were involved in the analysis and interpretation of the data. Furthermore, both authors contributed equally to the review, editing, and writing of the manuscript. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

We conducted the research following the declaration of Helsinki. The "Review Articles" need no ethic committee approval.

Consent for publication

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Competing interest

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