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Importance of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Virus Viral Components: A Comprehensive Review

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Abstract In recent times, a new viral origin, known as SARS COV-2, has been identified as responsible for the pandemic. SARS COV-2 is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) associated mainly with breathing or respiratory problems. This review shows details about the virus and its components and transmission. The world is fighting and trying to develop a cure or vaccine against the virus. SARS-CoV-2 commonly presents itself with fever and pneumonia resulting in dyspnea, respiratory insufficiency and damage to the lung, resulting in morbidities and mortality. Besides the breathing system that is attacked by the virus, other organs and organic systems can suffer the inconvenience of the infection, such as, for example, the brain, gastrointestinal tract, renal system, hepatic system, hematological, cardiovascular and immune system. Coronaviruses (CoV) are enveloped positive-strand RNA viruses found in a host of animals and humans, which belong to the family Coronaviridae and subfamily Coronavirinae, the order of the nucleoside sequences. Though rare, CoVs can mutate and cross animal-wildlife barriers, returning to perpetuate the public health crisis. It is a large virus with a genome size of about 30 kb. The genome has 14 open reading frames, with the four major structural proteins: the spike (S), envelope (E), membrane (M) and nucleocapsid (N) proteins at the 3 end of the genome. It is the S protein, through the receptor binding domain, that is essential for binding to the ACE2 receptor and its priming by transmembrane serine protease 2 allows the virus to enter the host cell through membrane fusion with the host cell membrane.

Key Words Pandemic, Public Health, Respiratory Infections, SARS-CoV-2, Viral Transmission

INTRODUCTION

In December 2019, an outbreak emerged in Wuhan, a city in China. The illness resembled infections of unknown viral origin, such as the previous severe acute respiratory syndrome associated with the coronavirus 2 (SARS-CoV-2) in 2002-2003 and Middle Eastern respiratory distress syndrome (MERS-CoV) 2012-2013 in Saudi Arabia. Coronaviruses (CoV) are enveloped positive-strand RNA viruses found in a host of animals and humans, which belong to the family Coronaviridae and subfamily Coronavirinae, the order of the nucleoside sequences [1-7]. Though rare, CoVs can mutate and cross animal-wildlife barriers, returning to perpetuate the public health crisis. Not much is recognized or clearly defined about their evolution yet. CoVs can cause a range of diseases, including minor upper respiratory infections in humans to severe lower respiratory infections and are often clinically identified. The treatment indicated for CoVs is unfortunately and only, based on symptomatic and supportive therapy, in addition to the use of traceable isolates with modest success [8-13].

The objectives of the review were to show details about the virus and its components and transmission. The selection of articles and journals was based on high ranked ones.

Epidemiology of SARS COV-2

The pandemic of novel coronavirus is a matter of international concern and in such situations, it is ultimately important to provide timely information regarding the virus and its spread. The epidemiology, source and genome of the SARS COV-2 virus are firstly elucidated. Then, the subsequent virus spread is linked to population movement [14-18].

The basic reproductive number is estimated to be around 3 and its confidence interval marks an overall risk assessment relative to the secondary attack rate. There is evidence that the population fatality rate may vary by admissible risk factors. Datasets of estimates are based on the exportation of cases outside Wuhan. During the second and third weeks of January 2020, the virus spread led to deaths and a vital increase in the number of confirmed cases detected and worldwide exportation. Efforts to cut off the spread of the disease led to a partially reduced growth rate. To date, the confirmed cases of SARS COV-2 have been escalating day by day in Hubei. The data show that self-sustained human-to-human transmission has not yet been established among regions outside the Wuhan area. But with increasing invasion, the proportion of human-to-human cases with good exposure history will continue to multiply [19-23]

Global Spread of the Virus

As of 22nd November 2020, SARS COV-2 was still spreading globally with a cumulative figure of 57,785,259 persons affected and 1,373,448 deaths reported. The spread of this virus is making it difficult for people to know who may be infectious, leading to questions about how transmission occurs. Studies have reported that patients infected with the SARS COV-2 virus can transfer the virus to people through respiratory droplets, close contact and air. The air transmission route has been highlighted as the major path leading to the SARS COV-2 virus spreading worldwide due to similarities in virus signatures detected in sewage and the virus identified in symptomatic SARS COV-2 patients, while the importance of fecal-oral transmission potential due to the exact fecal/anal existence of the asymptomatic viral shedding employed by SARS COV-2 remains largely unknown. Controversial studies have shown waterborne transmission to be possible [24-27]. There is limited body of studies on the transmission of the virus, which needs more future studies.

Key Statistics and Trends

The proportion of confirmed cases per 100,000 population in the Americas, i.e., the incidence of cases, exceeds the proportion in every other region or country. The number of known cases of SARS COV-2 has increased substantially over time from almost zero in the very beginning of March to over 1.3 million by the end of the month, with the number of new cases growing at an exponential rate. Around 32,411 persons have died because of infection by the pandemic virus. The number of new deaths increased by 53% over the same time. Although the number of deaths increased rapidly, the rate of increase was slower than the rate of increase in the number of new cases. Consequently, the proportion of deaths decreased from 3.67% at the beginning of the month to 2.46% by the end of the month [28-31].

The disease has spread from eight countries, with new deaths confirmed in 42 of 50 countries, or 84% of all countries within the region. Over 99% of all deaths have been reported by two countries. Although the number of new deaths increased substantially, the rate of increase in the number of new deaths slowed down during much of the month. Even so, a sustained, exponential increase in the number of cases globally resulted in the deaths increasing enough to keep fatalities on an upward exponential trajectory for the next week. There was a two-day window that could have been used to slow the exponential increase in deaths and cases, only to be allowed to close. At this rate, Earth begins to run out of time to control the spread. Up to 80% and 90% of the global and United States populations, respectively, might have to be quarantined to control the spread and flatten the curve [32,33]

Virology and Pathogenesis of SARS-COV-2

SARS-CoV-2 belongs to a family of viruses known as coronaviruses. It is an enveloped virus with a single-stranded RNA genome. It is a large virus with a genome size of about 30 kb. The genome has 14 open reading frames, with the four major structural proteins: the spike (S), envelope (E), membrane (M) and nucleocapsid (N) proteins at the 3 end of the genome. The positive-sense single-stranded viral genome is effectively translated into a long polypeptide, which is cleaved by viral proteases and host proteases into smaller proteins. It is the S protein, through the receptor binding domain, that is essential for binding to the ACE2 receptor and its priming by transmembrane serine protease 2 allows the virus to enter the host cell through membrane fusion with the host cell membrane. SARS-CoV-2 replicates mainly in the upper respiratory tract and spreads into the lower respiratory tract to infect type I and II pneumocytes and alveolar representative cells. The damage to the lungs appears to be the main cause of mortality from the virus, although there is now a recognized range of clinical phenomena that can occur over the course of infection. In addition to these effects, damage to other organs has been reported, including the kidney, liver and heart. The interplay between the SARS-CoV-2 virus and the host immune system is significant. The cytokine release syndrome has been shown to be one of the key factors in disease progression. Additionally, strong antibody responses and the presence of high neutralization activity could contribute to disease recovery [34-38].

Structure and Genome of the Virus

SARS COV-2 is an acute respiratory infectious disease. It is caused by the type of coronavirus SARS-CoV-2 that was first detected in the city of Wuhan, Hubei province, China and has spread rapidly across the world. The number of confirmed cases of SARS COV-2 has now reached almost 1,700,000. The virus is a cause of great concern because it has high morbidity and infectivity. In some cases, it can even be lethal. The structure and genome of the virus will be the starting point in finding the most effective measures to control and destroy the disease. For instance, the virus is composed of a spike-like glycoprotein corona, which is a unique morphological characteristic of the virus, but also the most important structure for its infectivity, providing multiple targets of antibodies for research. Genomes encode 6-11 structural proteins related to virus infection, assembly and release [39-42].

The origin and evolution of the SARS COV-2 virus have received a great deal of concern and attention. The virus is closely related to the genome sequence of six strains of highly homologous bat-derived coronavirus. In addition, the tract in the SARS COV-2 virus that is highly homologous to the pangolin coronavirus indicates the close species relation. Whereas the receptor-binding domain in the SARS COV-2 virus does not seem to be derived from the pangolin coronavirus. The virus invades the host primarily through a specific interaction between the corona spike glycoprotein and receptor protein and its high sequence homology is related to homology models, suggesting a high-risk mismatch in the receptor [43-45]. Only by clarifying the infection characteristics and pathogenic mechanisms of the SARS COV-2 virus and related proteins, to provide new targets for structure-based design or virtual screening of small molecular inhibitors, could the contagion be controlled and its harmfulness effectively minimized. Therefore, this paper provides the most recent state of structures and genomes of the current understanding of various research accomplishments and provides detailed information for the subsequent structural-functional research [46, 47] (Figure 1).

Mechanism of Infection

Coronaviruses contain the S (Spike) protein on the surface. The S-protein is a large type I spike glycoprotein that mediates the host cell receptor binding and membrane fusion processes. Both the S1 and S2 subunits are critical for viral infection, with the S1 subunit containing a receptor binding domain and the functional ganglioside binding sites. The S-protein is the most important determinant of host cell specificity, the site of host receptor binding and the distal position of glycosylation in many coronaviruses and other animal coronaviruses. Coronaviruses use glycosylated S-proteins to bind sialic acid receptors during the first steps of infection and internalization. The L protein is the largest subunit packed with RNA to synthesize new viral genomes and the second copies of viral proteins. Particles appeared as small, rounded S-protein-covered portions at the extracellular level. It has been reported that the nucleocapsid protein of some other coronaviruses is in the endoplasmic reticulum-Golgi intermediate compartment. Thus, the subcellular location of SARS COV-2 and other coronaviruses remains to be further studied [48,49].

In general, coronaviruses use endocytic pathways to enter the host cell after binding the receptors on the cellular surface. For instance, one coronavirus enters the host cell by clathrin-mediated endocytosis. The subgroups have not been widely studied, but a coronavirus belonging to a specific group has been found to use the clathrin-mediated endocytosis pathway. It is known that the early and late endosomes are involved in the entry of the virus into the host cell, after which the pH of the late endosome decreases. The fusion of the virus S-protein with the endosome membrane begins, which can be triggered by the reduced pH, mediating the release of viral RNA from the nucleocapsid protein into the cytosol. Conclusively, the virus hijacks the host to generate synthesized viral proteins and then replicate the complete virion forms. Subsequently, those virions release from host cells and become the transmission medium between hosts. The release mechanism of all coronaviruses depends on the complex interaction with host cell organelles and the virions' envelope, which is the above-mentioned endocytosis [50,51].

Clinical Manifestations and Complications

Over one year and a half after the emergence of severe acute respiratory syndrome coronavirus-2, well known as the SARS COV-2 virus, the world is still unable to answer many questions about this virus. It is reported that the clinical presentation of SARS COV-2 varies from no symptoms to severe complications and multiorgan failure. Therefore, knowing the various ranges of clinical symptoms and complications in patients with SARS COV-2 is essential for helping each patient as soon as possible and also for obtaining the appropriate measures to control and prevent the further disease [52-54].

The virus was initially discovered to cause severe pneumonia and subsequent case reports or series of patients have described atypical clinical phenotypes, other than respiratory system invasion. Multiple system organ failure and sepsis-like presentations have been reported. Patients with SARS COV-2 may present with extrapulmonary symptoms, including cutaneous findings, headache or dizziness, neurologic deficits, musculoskeletal symptoms, gastrointestinal complaints, loss of smell or taste and cardiovascular complications. In laboratory findings of SARS COV-2, it is reported that changes occur in various magnitudes such as leukopenia, leukocytosis, neutropenia, neutrophilia, hypocalcemia, hypokalemia, lymphopenia, lymphocytosis, thrombocytopenia, thrombocytosis, etc., besides increased indexes of infection [55-57].

Symptoms of SARS COV-2

SARS COV-2 has been causing a lot of casualties and economic loss globally. Knowing the comprehensive

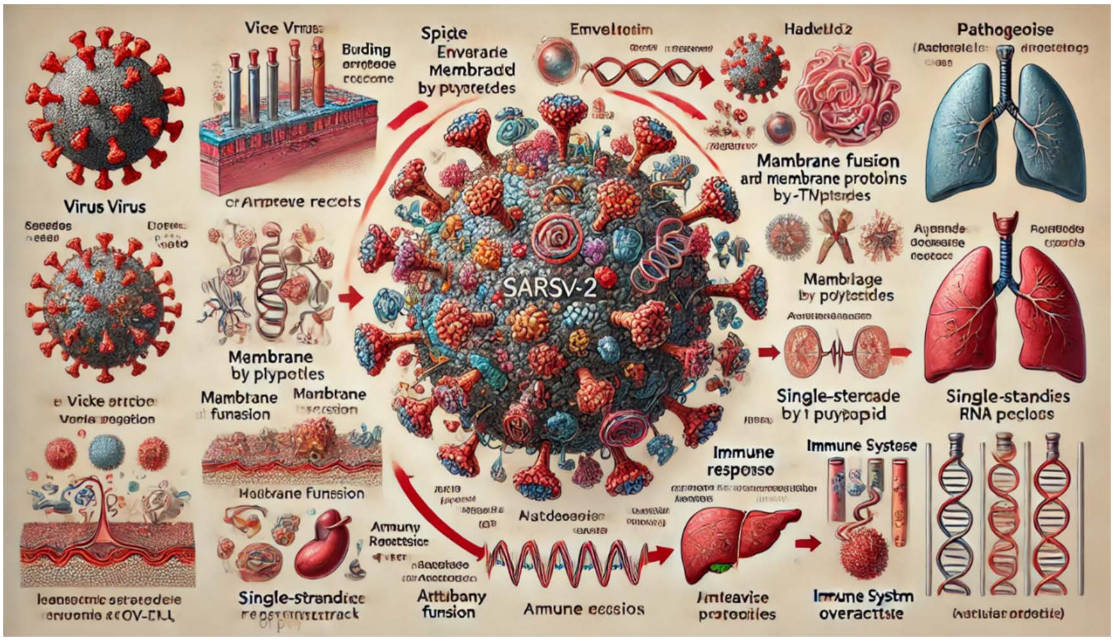

Figure 1: SARS COV-2 Virus pathogenesis

symptoms of SARS COV-2 can help detect the disease timely and protect individuals around the patients. There are many suspected individuals, but not all of them can timely receive medical examination. At some points, the medical examination resources are very limited, which makes it even harder for people who are not feeling so bad to receive medical examination. At those times, it is very important to know the most typical SARS COV-2 symptoms and distinguish them from other common flu symptoms. Some of the common flu symptoms are sore throat, cough, runny nose, congestion, fever, fatigue, headache, muscle soreness and watery eyes [58, 59].

The symptoms of SARS COV-2 include fever, cough, chills, repeated shaking accompanied by chills, difficulty in breathing, muscle pain, headache, sore throat, new loss of taste or smell, nausea or vomiting, diarrhea and many other less common symptoms. Fever, dry cough and tiredness are commonly discovered and less likely common symptoms are aches and pains, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell, a rash on the skin, or discoloration of fingers or toes. Some cases can also be asymptomatic, which means infected people do not have symptoms. People of all ages who come into close contact with SARS COV-2 patients or people who have been to high-risk areas should be vigilant. Although any of the above symptoms may be mistaken for symptoms of common flu, SARS COV-2 symptoms usually start slowly and are often mild at the beginning. It is therefore very important to take everyday preventive actions to stay healthy and timely receive medical examination when patients don't feel well [60,61].

Severe Cases and Risk Factors

Most of the clinical cases suffered only mild respiratory symptoms and recovered, while those with severe and critical cases mainly presented as pulmonary toxicity with dyspnea and hypoxemia, especially via acute respiratory distress syndrome. Patients with severe cases were often elderly males with comorbidities, such as chronic obstructive pulmonary disease, diabetes, hypertension and malignancy. At the time of admission, severe cases were usually presented with respiratory failure and hypoxemia, while others were accompanied by elevated serum levels of D-dimer and decreased lymphocyte counts. It is worth mentioning that for elderly patients, especially men, smoking cessation and alcohol restriction should be suggested to protect themselves in advance. The severity of the disease in males was suggested to be related to the alcohol impact on ACE2, as alcohol could promote the activity of ACE2 [62, 63].

The statistically significant risk factors for patients with severe SARS COV-2 were analyzed, including age ($\geq$70 years or the cut-off value from the receiver operating characteristic curve), blood type A and coexisting chronic diseases or dysfunctions, including hypertension, diabetes, heart diseases and chronic renal impairment. Additionally, the ratio of hepatic enzymes, albumin and blood components in severe cases, such as an increase in D-dimer, especially meeting the criteria for disseminated intravascular coagulation, an increased number of neutrophils and a decrease in lymphocytes, would represent the prognosis of the patients. Therefore, it is recommended to adopt a combination of risk factor screening for the assessment of patients, especially those with severe and critical cases that require intensive interventions [64,65].

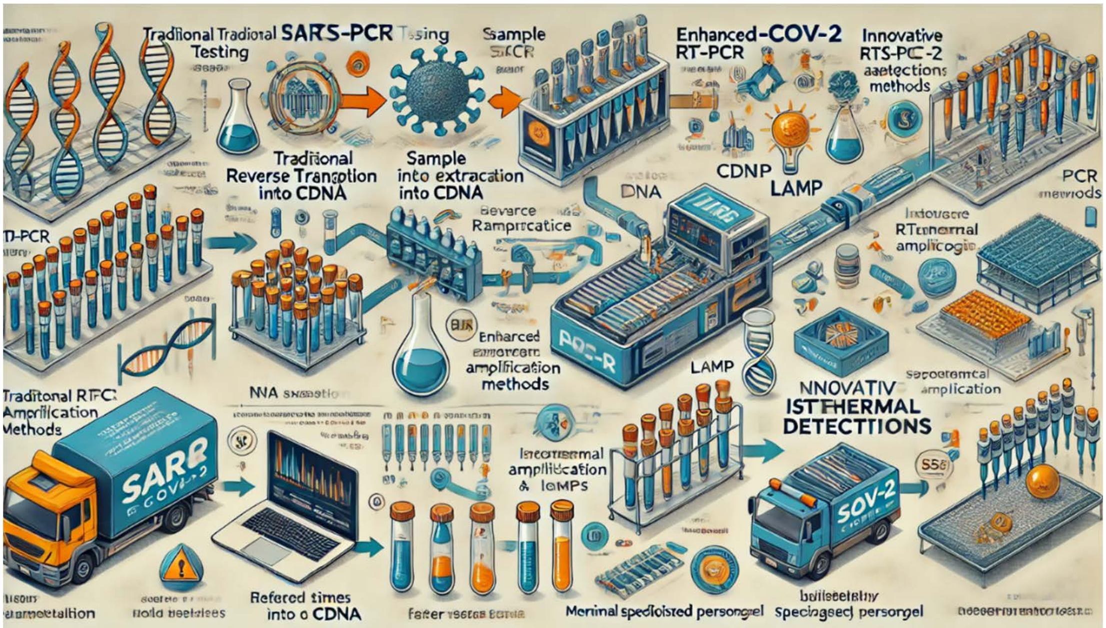

Figure 2: RT-PCR process for the detection of SARS COV-2 virus

Diagnostic Methods

As an RNA virus, SARS-CoV-2 can be readily detected with standard reverse transcription polymerase chain reaction. Traditional rRT-PCR testing has shown its accuracy and reproducibility in detecting minority populations, which greatly reduces the risk of false-negative results. The method is very appropriate for centrally located, highly organized laboratories, though results can take up to 5-6 hours to become available. Recently developed techniques can be paired with RT-PCR detection to improve sensitivity, thereby allowing for faster and more accurate SARS COV-2 detection. In addition to certain technology, a series of innovative technologies for the rapid detection of SARS-CoV-2 has been developed [66]. Some experts have developed a series of isothermal approaches for SARS-CoV-2 detection, some of which show promise for scaling up to high levels of throughput. This method offers several advantages in terms of its ability to minimize the need for specialized personnel, reduce the time required for diagnostic testing and result in lower costs. While containment in certain locations is particularly difficult due to a lack of resources or suitable laboratory facilities, isothermal technology is ideally suited to field diagnostics, which can often expedite results and improve overall accuracy related to specific medical or public emergencies [67] (Figure 2). False positive results could be an issue here. Primers and techniques should be applied correctly to minimize errors.

PCR Testing

Polymerase Chain Reaction (PCR) testing. This test is used to diagnose SARS COV-2. Molecular diagnostic tests commonly called PCR tests detect genetic material from the SARS COV-2 virus and can help diagnose active SARS COV-2 infection. Potential patients can either collect respiratory samples themselves and send them to a testing provider or visit a healthcare provider to have the sample collected and sent. Laboratorians use a process called reverse transcriptase polymerase chain reaction (RT-PCR) to diagnose SARS COV-2. For this method, healthcare providers collect samples from patients and ship them to the laboratory. There, an RNA extraction step is used to isolate the SARS-CoV-2 RNA that is present in-patient samples. Then, the PCR technique is used to make millions to billions of copies of a specific area of the SARS-CoV-2 genome. This is done using the SARS-CoV-2 genetic material and specially designed chemicals called reagents [68-70].

The PCR testing is more accurate than rapid testing methods for detecting the presence of an active SARS COV-2 infection. PCR tests are not perfect, however and there is some risk that people with SARS COV-2 will receive false-negative results. A false-negative result could occur if the sample collected does not have enough viral material in it or if the sample is not collected and processed correctly. Any molecular test may be associated with a false-negative result depending on a variety of factors, including the time from sample collection to the time of testing. To increase the accuracy of molecular tests, healthcare providers may collect samples from multiple areas of the respiratory system at the same time or at different times. It is very important for patients to discuss with their healthcare provider which type of test they may have had done and what the results may mean. Consulting the healthcare provider is more important than relying on what is said online [69-71]. The CRISPR offers advancements in the diagnosis of the virus in high accuracy.

Antigen Testing

Rapid antigen tests can be used in generalist or specialized clinics by healthcare professionals after a brief training course. Compared with other molecular tests, the advantages of using these devices include shorter analysis times, reduced costs, simpler logistics and no requirement to send the sample to the laboratory [72]. However, the false negative rate is high, especially when there is a low viral load and these tests should be performed at the earliest possible time and under conditions (presence of symptoms or contact with infected people). Their use is not recommended in people with no symptoms and at low risk. Their specificity is high, so a positive test result is reliable. These tests play a fundamental role in controlling and preventing the spread of the infection. However, since a negative test result cannot rule out infection, rigorous complementarity of physical distancing measures, barrier measures and self-isolation after contact or post-travel with infected persons is essential [73,74].

Indeed, precautions are to be exercised with these tests. Capacity is therefore to be increased and more individuals are to be tested. These tests are to be performed in clusters requiring quick decisions to detect cases in areas with known active transmission or at the start of local or national outbreaks. They are also to be used in agglomerations of cases. With rapid antigen testing, the spread of the virus can be significantly limited in situations where the timing of the test is pivotal. Repeated testing is particularly useful for screening people in care facilities. Antigen testing also makes it possible to better stratify contacts in areas where there has been known active transmission and, thus, to optimize the use of PCR tests according to the risk of infection [75,76].

Serological Testing

Antibodies, as well as virus antigen detection tests, are currently under research to detect acute infection. The detection of both IgM and IgG antibodies is recommended simultaneously within 7 days after illness onset. However, in the early stage (0-7 days after the onset of clinical symptoms) of SARS COV-2, the sensitivity of the IgM test is only 14.4%. After receiving nucleic acid detection, it is more important to make a serological diagnosis of suspected or positive individuals. Serology results can be reported immediately after detection and can complement the perceived SARS COV-2 infection [77-79].

After SARS-CoV-2 antigen enters the human body, an immunological reaction occurs. Then, the immune system will produce the corresponding IgM and IgG antibodies to resist and dispose of the antigen. After the SARS-CoV-2 antigen enters the body, the corresponding antibodies (IgM and IgG) will multiply in the human body. After the virus nucleic acid is negative, the antibodies increase and an effective immune response occurs at the acute stage. Serum can be collected to detect IgM and IgG for diagnosis. When there is an IgM and IgG antibody test result that is positive, the diagnosis and differentiation should be considered. At the maximum concentration of antibodies, both IgM and IgG antibodies are positive. When the IgM is positive, the infected person has the active SARS-CoV-2 virus and vice versa. The serological test kit includes the double antigen sandwich method and the indirect method. The double antigen sandwich method with colloidal gold nanoparticles and fluorescent microspheres has ultrahigh sensitivity [80]. It can recognize the corresponding antigen with high affinity. The approximate test results can be observed within 3-7 minutes. These methods have a wide range of applications in clinical and epidemiological research because of their thorough capacity, simplicity and short detection time. For negative results, the throat swab nucleic acid real-time test needs to be reviewed. The repeat throat swab nucleic acid real-time test should be reviewed after 24 hours and the serology rapid test should be reviewed after one week. The detection threshold is for IgM; the detection rate is for IgG. These results can provide the basis for rapid screening and diagnosis of acute infection. The results also have certain epidemiological significance. Only after the throat swab nucleic acid real-time test is negative and repeated at four consecutive points 24 hours apart, is it possible to begin scientific and safe treatment, immune isolation, or discharge of the patient [81,82].

Preventive Measures

In the scenario of high contagiousness and fatal consequences, both public and individual awareness strategies should be recognized as effective viral prevention plans. The following section highlights the different measures that can be pursued at individual and societal levels, focusing on human behavior as the major challenge in defeating any type of emergency or disaster. Preparing and training society regarding a future pandemic emergency is becoming a main objective. In fact, a robust population always has significant knowledge regarding rules and behaviors to be adopted to reach goals for successfully managing such dramatic events [83,84].

At an individual level, while the world is waiting for effective vaccines, only preventive strategies based on awareness may help in reducing the risk of infection by interrupting the chain of transmission. A non-exhaustive list of recommended preventive equipment includes respirators and/or masks, gloves, eye protection or face shields, gowns, hand hygiene products, waste disposal supplies and surface cleaning supplies. In addition to a series of concrete indications, the necessity to implement individual training to reach good personal prevention behavior is stressed. Furthermore, a range of measures can be advised at community levels; such measures differ from those for individual prevention action due to other objectives and can be distinguished as non-pharmaceutical interventions. Some of these should be urgently initiated today. The importance of implementing measures focused on vulnerable communities is confirmed following other case studies or health reports related not just to this pandemic, but also to other health emergencies [85, 86].

Social Distancing

Social distancing is a tool used to physically separate people from one another to stop or slow down the transmission of SARS COV-2. Social distancing is an important way to decrease the risk of SARS COV-2, especially for those who are at higher risk. There are several ways in which social distancing can be implemented. The first one is enforcing schools and universities to be closed. The second one is to postpone or possibly cancel public events, especially those that generate mass gatherings such as churches, religious activities, sporting events, weddings and others [87]. The third is to avoid crowding by controlling and regulating the number of people. Next is to have a very limited number of guests during mourning occasions. In addition, social distancing can also be enforced through telecommuting, a concept in which people work and perform their jobs from home. This can be carried out on several different levels when it comes to the requirement of having no office gatherings. In some companies, the essential employees need to be identified and assigned to be physically present in the office during an outbreak to assist with the telecommuting employees. With the current improvement and advancement of communication technology, this concept of telecommuting can easily be carried out [88].

There are also ways to break the chain of transmission during an outbreak by changing cultural mindset behaviors. This involves going against traditional customs and religious beliefs of crowded mass gatherings at religious activities, weddings and other events during the outbreak. Efforts must be made to change these practices by encouraging people to use technology to avoid crowded gatherings. These changes may result in a friction of cultural barriers and norms among communities, but it is crucial as this may cause people to distance themselves physically further apart from each other. Social distancing can also be implemented on a national or regional scope by a partial or complete transportation-free zone [89]. The area can be divided to have resources such as shops and markets. When there is an outbreak within a community, measures such as identifying and isolating the propagators can be implemented since those who show symptoms of being contagious may end up asymptomatic during the early stage of the incubation period. Infected carriers of SARS COV-2 often do not know that they are infected as they do not display any symptoms. This demands the practice of wearing a mask in all social interactions for at least two weeks from the point of potential exposure or from the time there was identification of being in the presence of a contagious individual until the person is completely free from the virus. Since there is currently no approved vaccine available for SARS COV-2, this practice is crucial especially if the carrier is in close contact with others and during the point of contact from the asymptomatic propagators [90].

Mask-Wearing Guidelines

The use of masks in the community is recommended to help slow the spread of SARS COV-2. The masks should have more layers of fabric, cover the nose and mouth completely and fit without gapping when speaking or breathing. It is recommended that in addition to wearing masks, attention should also be paid to hand hygiene, avoiding crowds and poorly ventilated spaces and complying with quarantine, isolation and other public health recommendations. It is also recommended that transportation safety measures be followed and preventive health behaviors be adopted, including practicing physical distancing, using facial masks and maintaining good hand hygiene. Since masks can be contaminated by virus-containing respiratory secretions present on the inner or outer surfaces of the mask, such physical contact can lead to self-contamination and infection. Proper hand hygiene is required before wearing and after removing masks [91]. Touching one's face, mask, or other objects, such as mobile phones and personal belongings, is associated with limitations in infection prevention measures because the mask touched by a contaminated hand may be contaminated and contribute to the subsequent spread of SARS COV-2. Furthermore, it is essential to avoid accidental self-contamination when using a mask by washing or sanitizing hands before touching the mask [92].

Treatment and Therapeutics

The sudden appearance and rapid spread of the SARS COV-2 virus raised immediate concerns about the lack of adequate treatments. Several types of vaccines were developed during the pandemic and satisfactory but not uniform results were obtained. There are recommendations for the administration of other types of vaccines if they do not conflict with SARS COV-2 vaccines. For example, the vaccine for influenza is recommended before or at the same time as that for SARS COV-2. Vaccines should be administered hand in hand when the start of the problem is not clear. It should be stressed that the vaccine for a particular person should be based on their situation, including age, previous diseases, other treatments and so on. Obviously, vaccination is the preferable approach based on the disease's propensity to spread easily, making prophylaxis highly recommended. However, treatments must also consider existing widespread infection and the continuously evolving nature of the virus [93].

Hence, a great window of opportunity with significant challenges opened up. During the first phase, which is now past, attention was primarily focused on finding healing solutions to minimize the probability of poisoning those still healthy. Optimizing general prophylaxis also occurs when the beginning of a disease is not identifiable with certainty, with the risk that contagion is already occurring. During this phase, the first vaccines were developed and used, with good but not perfect results. Other precautions, especially the use of face masks and distancing, were used in this phase but were not available in the earliest phase [94]. Monoclonal antibodies come with high therapeutic effects; however, new monoclonal antibodies according to newly mutated strain should followed.

Approved Drugs and Vaccines

Currently, there is no vaccine developed against SARS-CoV-2. RNA-based vaccination is a novel approach that might be very powerful. Antigens generated by mRNA have no critical immune response against potential antibody formation, so they might generate effective immune responses. An RNA vaccine directed towards the SARS-CoV spike protein was used in Balb/c mice, which induced the cells to produce neutralizing antibodies to the virus and conferred protective long-term immunity. Specific antiviral antibodies in the serum were detected within 5 days of the initial immunization, fitting with a quick immune response. This vaccination appeared to be effective and offered partial protection against SARS-CoV in a brief timeframe. SARS-CoV and MERS-CoV studies suggest that memory T cells and neutralizing antibodies in survivors during infections are important in overcoming CoV infection. Whether the immune response is adequately protecting and whether any antigen compatibility occurs in relation to new SARS-CoV-2 vaccines are questions that should be considered [95]. As it is well known, research on novel CoV vaccine development is still in its early stages and more animal model studies and clinical studies should be developed. Furthermore, important issues such as related prions and vaccine development, including the development of the affected CoV attack motif or the ability to block viral entry by antibodies, are among the topics awaiting detailed investigation. It will be a significant improvement, especially for the current SARS-CoV-2 epidemic, when the anticipated vaccines and therapeutic approaches are shared and made public throughout scientific communities without delay [96].

Experimental Treatments

Vaccination procedure is the most effective in viral illnesses. Vaccination studies against the new type of SARS COV-2 pandemic virus have been urged due to the short natural history of the virus. The first mention of vaccination against SARS COV-2 was during the offshore departure in March 2020. As a matter of fact, to say "the first" is not so correct, to tell the truth, as studies continue to be a priority. Each new vaccine candidate is announced in a very short time of each other, but the first mention is accepted to be in that way, some sense in which it was announced before starting the phase-I studies of the vaccine. Vaccine studies have a natural essential stepwise progression; some modern vaccine development approaches can even further reduce the number of steps. Various vaccine studies in various stages of the ongoing clinical trials are in progress for SARS COV-2 [97].

As has been seen, the fact that the structure of the vaccine antigen is deoxyribonucleic acid is the only common characteristic in vaccine studies whose current statuses are different. Vaccines using different technologies are also included in these ongoing studies. While mRNA vaccine candidates are not in preclinical research processes and are in phase-I studies, recombinant viral vector and inactivated virus platform-based vaccine candidates at phase-I/II are at different levels. It is also observed that a similar level has been reached in the development stages of the subunit, synthetic peptide, mRNA and inactivated virus vaccine platforms [98].

Public Health Responses

In response to the emergence and rapid spread of SARS COV-2, many governmental and non-governmental organizations have implemented several public health measures. Such measures include efforts to detect new cases and provide care to the sick, efforts to increase public knowledge, changes to societal behaviors to control and stop the spread of the condition and informational guidance for making decisions. Given the increasing numbers of people affected by this pandemic, attaining the best outcomes depends on maximizing public health support that is evidence-based and constantly updated. Public health measures considered for community-wide use should include case identification, isolation of ill individuals, tracing contacts, quarantine of contacts of the cases, social distancing approaches, personal protective measures, hand hygiene, cough etiquette, use of therapeutics, public health learning and maintenance of essential community services [99]. To stem the spread of SARS COV-2, given that affected populations are geographically dispersed, is an enormous challenge. This requires global public health support and the implementation of community-focused interventions that are effective in reducing the spread of infectious diseases. Public health response strategies have been focused on reducing the speed of transmission and on increasing support for communities that are considered to be at highest risk for complications due to SARS COV-2. Personal efforts to intersect diseases are also critical. Collaboration across all areas of government, such as education, transportation, labor and others, is important. Both governmental and non-governmental organizations, multilateral organizations and the business sectors need to engage in efforts to minimize community harms caused by SARS COV-2. Different countries are at different stages in their SARS COV-2 outbreak; therefore, it is essential that public health measures for SARS COV-2 be regularly updated [100].

Governmental Policies and Interventions

Governments have been leading an integrated response to fight the SARS COV-2 virus through a set of drastic interventions. Monitoring compliance in such situations has been more direct with few sanctions and actions are predominantly coercive. The feasibility of traditional policy instruments is limited where information and time are of high value. Carrying out aggressive decentralization of data, control and response capacities has been a more effective approach than spatially agnostic policies [101]. Differences in location-based demographic and economic structures, local formal and informal institutions and existing SARS COV-2 problems and responses justify different local strategies to dampen the disease's trajectory. SARS COV-2 lockdowns are essential weapons to tackle the outbreak and have made dramatic contributions to disease control. Such a decision has crucial behavioral, time-sensitive, as well as political economy policy dimensions, sparking a wave of discussions about the effectiveness, consequences and timing of such policy measures [102].

All efforts focused on stopping the movement of people, goods and international flows of vital equipment and medical supplies, while also ensuring the continuity of economic activities. There has been a dilemma due to the costs and trade-offs associated with such negative externalities - those with negative consequences arising from the market decisions made by others and those involved in the oversupply of politics - about the ethical legitimacy of economic shutdowns, which may bring short-run rescue but much bigger long-term costs. Substantial resources have been committed to helping companies preserve jobs and maintain the structure of economies, providing safe and easy access to liquidity for economic players in liquidity difficulties and providing capital through real economy financing in case of solvency difficulties [103,104].

Economic Impact of the Pandemic

The SARS COV-2 pandemic has not only been a challenge to the health sector of countries around the world but has also had a significant and adverse impact on the economy. Measures implemented by countries to mitigate the spread of the virus include frequent hand hygiene, disinfection, the use of masks, social distancing and partial or complete confinement of the population, taken with the goal of reducing the number of contacts with others, which could effectively contain the spread of the virus. However, it has temporarily or permanently paralyzed several sectors of the economy, causing job and income losses for millions of people and they have had to face diverse hardships such as maintaining companies that had to cease their activities, schools and the payment of rent, water, electricity, among other expenses. The economic ramifications of such measures to control the outbreak of SARS COV-2 are a critical cause of great concern in all countries of the world [105].

Last year and early this year brought severe economic hardship and a loss in value in many countries around the world. The impact has sent the world into a state of profound uncertainty and, in turn, has motivated states and other grantees to set new forms of governance, regulations and laws in motion, some of which intend to limit and regulate economic transactions, production, trade and property [106]. The damage has been done. Similar large crises have continued to cause destruction and painful hardship for many over the past century and the causes of those crises are broadly understood. A similar pattern of excessive risk-taking has been observed this time, leading to disturbing new financial patterns and relationships: too much borrowing, risk-taking, insufficient savings, or the repayment of debt. The great international recession occurred; rock bottom was reached and economic growth, prompt regulation and customer warranty were evidenced by the discourse values to influence and reprogram investors and their intentions. The best predictors of profitability were a timely restart of stimulus and consumer-oriented aid packages. The main objects of matter were not only financial aid to the public or work [107].

Global Financial Consequences

Financial markets have been hit in several ways during the SARS COV-2 crisis. The pandemic has had strong effects on real economic sectors, disrupting supply chains and reducing the demand for travel. More importantly, it has caused many businesses to sustain heavy losses, particularly in those sectors that have been most affected, such as tourism, hospitality and oil and gas industries. Analysts have often focused on the equity markets, but much of the action has taken place in the corporate credit markets. Primary and secondary markets in corporate bonds witnessed a sell-off, with prices falling at rates comparable to those of falling equity prices and with liquidity drying up for the hardest-hit corporate borrowers. Investors also liquidated their holdings and shifted into safer assets, causing a spike in demand for safe and liquid assets, best represented by U.S. Treasury bonds and the U.S. dollar [108,109].

Opinions have been formed on the impact of the COVID crisis on financial markets. Most studies provide an events study on the impact of the pandemic on equity markets. They highlight the fact that there is no room for any other factor driving stocks down during those critical weeks other than the COVID pandemic and its direct and indirect influence. The studies focus on stock markets and credit markets. It is mandatory that the macroeconomic consequences of SARS COV-2 will be brief and that next year's financial recovery will erase this decline. Results support the assumption that the general economic sentiment and the stock market demonstrate an unintentional tendency to recover on the way down [110].

Psychological and Social Impact

The SARS COV-2 outbreak is the first global event in the age of interconnected information, creating the so-called infodemic. This has generated myths and misconceptions that contribute to social disharmony and anxiety. To adequately address the psychological and social consequences of the pandemic, it is important to inform the population about its main characteristics, mode of transmission and available therapies. Efficient strategies are also urgently needed to tackle false information, to avoid responses to the crisis that are poorly adjusted to the reality of the outbreak and responses that worsen psychological consequences. While responding to the pandemic, it is important to simultaneously promote mental health. SARS COV-2 was first detected in Wuhan, Hubei Province, in December 2019 and quickly spread to other cities and countries [111]. In February 2020, the pandemic was declared when several countries in different continents had confirmed cases. The lack of pharmaceutical measures and information on SARS COV-2 has led to the implementation of public health measures. SARS COV-2 has imposed an immense economic, social and health impact globally, leading to severe consequences, such as mass unemployment and stress on economic health systems, all while requiring the implementation of measures to contain the pandemic. The SARS COV-2 pandemic significantly impacts all dimensions of society, including both economic and psychosocial aspects. The pandemic is first and foremost a health crisis, but it has also caused a social one, with psychological problems manifesting in many individuals.

Mental Health Challenges

The outbreak of deadly SARS COV-2 has not only affected physical health but also mental health. One of the major mental health challenges is the issue of stigmatization against SARS COV-2 patients and frontline workers, which causes stress among those infected. Long-term home quarantine also leads to mental health problems. For many people, during the time of SARS COV-2 infection, the focus is on diagnosing the infection based on how the person got infected. The main stigma and discrimination arise among health care workers while treating infected individuals [112,113].

People think that SARS COV-2 infected patients are worse than those with other infectious diseases, specifically Ebola and Acquired Immune Deficiency Syndrome. In Africa, it is observed that stigma manifests in different forms, such as social isolation, community ostracism and sabotage of health care. It is also noted that family members and health care workers are stigmatized, driving them out of their homes and communities. All these factors contribute to worries, discomfort and the need for care, as well as stress among SARS COV-2 infected individuals. During home quarantine, day-to-day life is disturbed, making quarantine very challenging for those diagnosed and infected with SARS COV-2 and therefore cortisol levels increase [114].

All people who are not infected with SARS COV-2 need to follow preventive measures such as quarantine and social isolation. Many pieces of evidence suggest that quarantine leads to various health problems, including sleep disturbances, low mood, stress, decreased security and health status. SARS COV-2 infected individuals experience emotional problems and everyone is aware of their diagnosis. Stigmatization can cause social, emotional and personal difficulties. During home quarantine, individuals become stressed because they feel more isolated, uncomfortable and worried. They also feel that they have ruined their lives and become less social and approachable. There is a frequent need for care and help in everyday activities. On this basis, stress plays an important role in enhancing an individual's vulnerability to the development of various health conditions, including mental disorders. Sometimes, home quarantine leads to post-traumatic stress disorder, such as financial loss and job insecurities [115,116].

CONCLUSION

The SARS-CoV-2 pandemic and its spread have had a deep and wide impact not only on human society but also on how we view viral spread and healthcare responses. To appropriately fight a virus, one must understand its spread. SARS COV-2 has demonstrated not only how fast a virus can spread through modern travel but also how fear and misinformation can play such a major role in public policy. Understanding the similarities and differences between "viruses" of information and knowledge and viral agents may provide clues to how such "viruses" may be combatted. The genome has 14 open reading frames, with the four major structural proteins: the spike (S), envelope (E), membrane (M) and nucleocapsid (N) proteins at the 3 end of the genome. It is the S protein, through the receptor binding domain, that is essential for binding to the ACE2 receptor and its priming by transmembrane serine protease 2 allows the virus to enter the host cell through membrane fusion with the host cell membrane. Future studies should be done on variant evolution, long COVID studies and vaccine improvements.

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