COVID-19 and its Long term Implications: A Literature Review

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Abstract

In the year 2019, early December, Hubei Province, Wuhan city of China was hit by a disease causing virus, later named as corona virus. The COVID-19 spread instantly causing a severe respiratory disease, which also proved to be fatal. The medical name of the virus was declared as SARS-CoV-2, which was later declared as a health emergency by the World Health Organization (WHO). The year 2020 was hit the hardest with the disease, where it was declared as a global pandemic by WHO. More than 40,000 laboratory cases were confirmed as on 14th February, 2020, with more than 1500 deaths confirmed at the global level. Various Governments were forced to close their borders and also to implement numerous measures of control like wearing masks at public places and work from home for offices. The endeavor of this article is to understand the spread of this disease in the year 2020 through publically available literature in order to understand the pandemic and assess its long term implications. This literature review examines the causal agent, pathogenesis and immunological responses, epidemiology, diagnosis, treatment, and management of the disease, as well as control and preventative efforts.

Keywords: Novel Corona Virus, Prevention, Detection

Introduction:

The Chinese Health Agency reported a number of cases of unknown pneumonia causing virus in Wuhan City, Hubei Province Central China at 31 December 2019 to the WHO. Cases have been reported from 8 December 2019, with many patients working or living near the local Huanan Seafood wholesale market, while numerous other cases did not have any link to the market. A new corona virus, previously abbreviated as 2019NCoV, was detected by WHO on January 7 in a patient's saliva sample. The study group in China later termed the Corona virus as SARS-CoV-2, which was a major respiratory disease. Generally, WHO termed it as COVID-19.

In China, 7736 confirmed cases and 12,167 suspected cases were registered as of January 30, while in 18 other countries the number of confirmed cases was 82. On the same day, WHO selected the SARS-CoV-2 epidemic as a Public Health Emergency of International Concern (PHEIC). The National Health Commission of China, declared 2.1 percent fatality rate on February 4th, on the other hand, fatality cases around the world was 0.2

percent. Admitted patients mortality rate was 11 percent to 25 percent. COVID19 is quite infectious, with a high mortality rate, but the knowledge available in public reports and published research is rapidly expanding. This literature review describes the knowledge on COVID-19 in the year 2020, from the perspective of its diagnosis and treatment, along with control and prevention efforts.

Origin of the Virus:

According to Tang (2020), SARS-CoV-2 is a member of the Nido virales order and family Corona viridae. The family is divided into two subfamilies, Coronavirinae and Torovirinae. The four genera that make up the subfamily Coronavirinae are as follows: Human coronaviruses (HCoV)-229E and HCoV-NL63 are classified as Alphacoronaviruses; HCoV-OC43, SARS-HCoV, HCoV-HKU1, and Middle Eastern respiratory syndrome coronavirus (MERS-CoV) as Betacoronaviruses; Viruses from whales and birds are classified as Gammacoronaviruses; and Viruses isolated from pigs and birds are classified as Deltacoronaviruses. Like SARS-CoV and MERS-CoV, which are also extremely dangerous viruses, SARS-CoV-2 is a betacoronavirus. Positive-sense single-stranded RNA virus (+ssRNA) in an envelope is called SARS-CoV-2.

SARS-CoV-2 is thought to be a new betacoronavirus that infects humans. Phylogenetic analysis of the SARS-CoV-2 genome reveals that the virus is genetically distinct from SARS-CoV (approximately 79% similarity) and MERS-CoV, but closely related (with 88% identity) to two bat-derived SARS-like coronaviruses collected in 2018 in eastern China (bat-SL-CoVZC45 and bat-SL-CoVZXC21). A closer examination revealed that the virus is more closely related to BatCoV RaTG13, a bat coronavirus previously reported in Rhinolophus affinis from Yunnan Province, with 96.2% total genome sequence identity. This was determined using the genome sequences of SARS-CoV-2, RaTG13, and SARS-CoV. Recombination events between SARS-CoV-2 and other bat-borne viruses, including BatCoV RaTG13, SARS-CoV, and SARSr-CoVs, were not detected in the study. All things considered, our research points to bats as the possible original host of this virus.

To ascertain whether any intermediate hosts aided in the virus's transmission to humans, more investigation is necessary. For a number of reasons, bats are unlikely to be the animal that is specifically to blame for the virus's spread to humans. Huanan Seafood Wholesale Market sold a variety of non-aquatic animals, including mammals, but no bats were sold or located; (2) SARS-CoV-2 and its close relatives, bat-SL-CoVZC45 and bat-SL-CoVZXC21, have a relatively long branch (sequence identity of less than 90%), indicating that those viruses are not direct ancestors of SARS-CoV-2; and (3) other animals have served as intermediate hosts (civets and likely camels) for other coronaviruses, like SARS-CoV and MERS-CoV, where bats are the natural reservoirs (Feng, 2020).

Corona virus: The Transmission

It's unclear how the Huanan Seafood Wholesale Market contributes to the spread of disease. This market was connected to a large number of early COVID-19 cases, suggesting that SARS-CoV-2 was transmitted from animals to people. On the other hand, genetic research revealed evidence that the virus entered the market from an unidentified region where it spread more quickly, possibly preceding human-to-human transmission. Groups of afflicted relatives and medical professionals have confirmed that person-to-person transmission occurs. Less than 10% of patients had market exposure after January 1, while more than 70% had none at all. It is believed that person-to-person transmission happens between intimate contacts, mostly through respiratory droplets released when an infected individual sneezes or coughs. Fomites have been shown to be a major source of SARS-CoV transmission.

There is disagreement over whether illness can spread asymptomatically. A study that was released on January 30, 2020, stated that the transmission of the disease was asymptomatic; however, it was subsequently found that the patient, who had symptoms prior to the transmission, was not contacted by the researchers directly. Similar claims of asymptomatic transmission were made in a more recent study that was published on February 21. However, the validity of such studies may be compromised by errors in self-reported symptoms or interactions with other cases and fomites. Research on the characteristics of illnesses is dynamic and subject to selection bias (Stratton, 2020). The average incubation period, according to a study, was 5.2 days (95% confidence interval [95%CI]: 4.1-7.0). It has been demonstrated that the incubation period can last up to 19 or 24 days, however case to case varies.

According to the researcher's analysis of 138 COVID-19 patients, 41% of them acquired SARS-CoV-2 while they were in the hospital. In addition, a different study involving 425 patients found that the frequency of cases among medical staff grew over time. Most likely, extended close contact with a high virus concentration is what caused these cases. As of February 12, 2020, 24 countries outside of China had 441 confirmed COVID-19 cases reported; on January 13, 2020, Thailand reported the first imported case. Of these nations, eleven have documented local transmission; Singapore has reported the highest number of cases (47 confirmed cases) (Burki, 2020).

Infection: The Risk Factors

Male adult patients between the ages of 34 and 59 have the highest prevalence of SARS-CoV-2 infection. Individuals with chronic comorbidities, such as diabetes and cardiovascular and cerebrovascular disease, are also at an increased risk of contracting SARS-CoV-2. Severe cases are more common in people 60 years of age and

older, as well as in people with underlying medical conditions like diabetes, cerebrovascular disease, and cardiovascular disease (20, 30). Coinfections with fungi and bacteria may also be linked to severe symptoms. Fewer cases of COVID-19 in children under the age of 15 have been reported. No cases of COVID-19 in children under the age of 15 were discovered in a Wuhan study involving 425 patients, which was published on January 29. However, as of January 2020, 28 pediatric patients had been registered. Although the majority of pediatric patients with the infection have mild symptoms without a fever or pneumonia and have a good prognosis, the clinical characteristics of these patients vary. Another study found that a child was asymptomatic despite having radiological ground-glass lung opacities. In conclusion, compared to adults, children may be less likely to be ill or, if they are, may show milder symptoms. Because of this, their parents might decide against going to therapy, which would understate the incidence of COVID-19 in this age group.

Response of Immune System:

Like the majority of other coronaviruses, betacoronavirus is highly species specific, but even slight genetic alterations can significantly change tissue tropism and host range. The emergence of SARS-CoV and MERS-CoV-caused deadly zoonotic diseases in human history is a prime example of the viruses' adaptability. Humans were the ultimate host for both viruses, with the palm civet and dromedary camel serving as intermediate hosts for MERS-CoV and SARS-CoV, respectively. Bats served as the natural reservoir for both viruses. Because they can facilitate greater contact between a virus and a new host, intermediate hosts undoubtedly play a significant role in cross-species transmission. This interaction allows the virus to undergo additional modification necessary for effective replication in the new host. Comprehensive surveillance is essential to track SARS-CoV-2'sfuturehost adaptability, viral evolution, infectivity, transmissibility, and pathogenicity due to its potential to cause a pandemic (Murphy, 2016).

Numerous molecular interactions, including receptor interaction, determine the virus host range. Despite differences in amino acids at some critical positions, the envelope spike (S) protein receptor binding domain of SARS-CoV-2 was found to be structurally similar to that of SARS-CoV. Additional structural analysis strongly implies that SARS-CoV-2 may enter cells through the host receptor angiotensin-converting enzyme 2 (ACE2), which is also the receptor through which SARS-CoV can infect alveolar type 2 (AT2) pneumocytes, which are responsible for the synthesis of pulmonary surfactant, and the epithelium of the airways. The coronavirus spike protein can be divided into two domains in general: S2 is crucial for the fusion of cell membranes, while S1 is in charge of receptor binding.SARS-CoV and SARS-CoV-2'sS1domains have about 50 conserved amino acids in common, while most viruses derived from bats have a higher degree of diversity. Further proof that SARS-CoV-2 has developed the capacity to spread from person to person comes from the identification of multiple essential residues (Asn501 and Gln493) that mediate the binding of the SARS-CoV-2 receptor binding domain to ACE2.

Even though SARS-CoV-2'sreceptorbinding spike protein sequence is more similar to SARS-CoV, SARS-CoV-2'swholegenome is more closely related to bat-SL-CoVZC45 and bat-SL-CoVZXC21. Species specificity is not solely determined by receptor recognition, though. As soon as SARS-CoV-2 binds to a host cell's receptive receptor, it enters the cell and starts the innate immune response. In order to effectively infiltrate the novel host, SARS-CoV-2 needs to be capable of inhibiting or evading the host's innate immune signals. The mechanism by which SARS-CoV-2 evades immune response and causes pathogenesis is, however, largely unknown. Given the clinical similarities between SARS and COVID-19, SARS-CoV-2 may share a pathogenic mechanism with SARS-CoV. The type I interferon (IFN) system produces more IFN-stimulated genes (ISGs) in response to SARS-CoV infections, which prevent the virus from replicating. SARS-CoV generates at least 8 viral antagonists to thwart this antiviral effect; these antagonists regulate the production of IFN and cytokines while avoiding ISG effector activity (Hossain, 2009).

Inhibiting viral replication and spread requires the host immune system's reaction to viral infection, which includes inflammation and cellular antiviral activity. Pathogenesis, however, will arise from a combination of the virus's lytic effects on host cells and strong immune responses. Studies show that fever and a dry cough are common symptoms in patients with severe pneumonia. 10% of patients died, and some patients progressed quickly with Acute Respiratory Stress Syndrome (ARDS) and septic shock, which was followed by multiple organ failure.

Inflammatory damage patterns are similar in patients with COVID-19 and SARS. Proinflammatory cytokines (e.g., IL-1, IL-6, IL12, IFNη, IP10, MIP1A, and MCP1), which are associated with severe lung inflammation, are found in higher concentrations in the serum of SARS patients. Compared to healthy individuals, SARS-CoV-2 infected patients have higher plasma levels of proinflammatory cytokines like IL1β, IL-2, IL7, TNF-α, GSCF, and MCP1.

Compared to non-ICU patients, patients in the intensive care unit (ICU) have significantly higher levels of GSCF, IP10, MCP1, and TNF-α, suggesting that a cytokine storm could be the fundamental cause of the severity of their illness. Unexpectedly high levels of anti-inflammatory cytokines, such as IL10 and IL4, were observed in those patients—an uncommon observation for an acute phase viral infection. As previously mentioned, an additional noteworthy finding is that SARS-CoV-2 primarily affects older adult males, with very few cases reported in children. Similar findings were observed in SARS-CoV-infected monkey models, which demonstrated that the virus more commonly infected elderly Cynomolgus macaques than young ones. The virulence mechanisms and host genes of SARS-CoV-2, which enable the virus to transcend species boundaries and cause fatal infections, require further investigation.

Clinical manifestations:

Clinical characteristics of the 2019-CoV infection are comparable to those of the SARS-CoV infection; fever, dry cough, dyspnea, chest pain, lethargy, and myalgia are the most common symptoms. Headache, lightheadedness, nausea, vomiting, diarrhea, and stomach pain are less frequent symptoms. The initial 425 confirmed cases in Wuhan report fever, dry cough, myalgia, and exhaustion as the most common symptoms; sputum production, headache, hemoptysis, abdominal pain, and diarrhea are less common. About 75% of the patients experienced bilateral pneumonia.

The fact that comparatively few COVID-19 patients exhibit obvious upper respiratory tract symptoms like rhinorrhea, sneezing, or sore throat suggests that the virus may prefer to infect the lower respiratory tract as opposed to SARS-CoV and MERS-CoV infections. There are similarities between non-pregnant and pregnant women. Severe outcomes including hypoxemia, acute ARDS, arrhythmia, shock, acute cardiac injury, and acute renal injury have been reported in COVID-19 carriers. About 17% of the 99 patients in the study had ARDS, and 11% of them passed away from multiple organ failure [8]. Eight days was the median time between the onset of symptoms and ARDS.

Diagnosis:

Useful screening and diagnostic technologies are necessary for the implementation of isolation and quarantine protocols, the control of patient care, and the prevention of the COVID-19 virus. While SARS-CoV-2 is spreading, a community may see an increase in the prevalence of other respiratory infections. The World Health Organization (WHO) released COVID-19 case surveillance guidelines on January 31, 2020. According to WHO guidelines, individuals who meet certain requirements should first be screened for respiratory diseases that are more common in that area and during that season. The sample should be sent to a referral laboratory for SARS-CoV-2 testing if a negative result is found.

Case definitions vary by nation and are subject to change as epidemiological conditions in a given area do. A confirmed case in China as of January 15, 2020, needs to show clinical symptoms like fever, pneumonia, and a low white blood cell count, in addition to an epidemiological link to Wuhan within two weeks. The epidemiological requirement was changed on January 18, 2020, to include communication with anyone who had visited Wuhan during the preceding two weeks. Eventually, the case definitions no longer included the epidemiological relationship.

Case definitions were proposed by the World Health Organization. A patient is considered suspected of having COVID-19 if they meet one of the following criteria: (a) they have a history of severe acute respiratory infections (fever and cough that require hospitalization), and no other cause fully explains the clinical presentation. (b) they have any acute respiratory illness and have traveled to or resided in China within the 14 days prior to the onset of symptoms. Those whose SARS-CoV-2 test results are unclear or who test positive for the pan-coronavirus assay but have no other respiratory pathogens found in the lab are considered probable cases. A verified case is one in which a laboratory has confirmed irrespective of the symptoms and clinical signs.

The CDC advises obtaining specimens from the upper respiratory tract (nasopharyngeal and oropharyngeal swabs) and, if at all feasible, the lower respiratory tract (sputum, tracheal aspirate, or bronchoalveolar lavage) for patients who meet the diagnostic requirements for SARS-CoV-2 testing. The tests are carried out in government-designated laboratories in each nation. Patients with COVID-19 frequently have elevated lactate dehydrogenase, prolonged prothrombin times, and lymphopenia in their lab tests. Compared to non-ICU patients, patients admitted to the ICU had more abnormalities in their lab work. Aspartate aminotransferase, creatine kinase, creatinine, and C-reactive protein levels were elevated in some people. The majority of patients' serum procalcitonin levels are normal (Burki, 2020). Patients with COVID-19 have higher than normal levels of MCP1, IP10, IFN-γ, and IL1β. Elevated levels of GCSF, IP10, MCP1A, MIP1A, and TNF-α are observed in ICU patients.

The Radiology Findings:

Depending on the patient's age, immunological status, comorbidities, disease progression, and early medical intervention, radiology findings may vary. Researchers studied 41 of the first cases of 2019 CoV infection, and all 41 patients had abnormal results on chest computed tomography (CT scan) and pneumonia. Another study involving six participants also found abnormalities on the chest CT scan; all of them had multifocal patchy ground-glass opacities, especially in the vicinity of the lungs' periphery. Research indicates that consolidative pulmonary opacities and bilateral pulmonary parenchymal ground-glass opacities are the most frequent findings on a chest CT scan.

In some cases, the extension and increased density of lung opacities showed that patients five days or more from the start of the disease and those 50 years of age or older had consolidated lung lesions, compared to patients four days or fewer and patients fifty years of age or younger who had mild to moderate disease development. On chest CT scans of ICU patients, bilateral multiple lobular and subsegmental regions of consolidation are frequently observed. One of the 99 patients in the study experienced a pneumothorax while having imaging work done.

Treatments:

Like MERS-CoV and SARS-CoV, COVID-19 does not yet have a specific antiviral treatment. Isolation and supportive care, which may include oxygen therapy, fluid management, and antibiotics, are the best treatments for secondary bacterial infections. A rapid progression to ARDS and septic shock, followed by multiple organ failure, was observed in certain COVID-19 patients. Because of this, the initial care for COVID-19 patients needs to be concentrated on early suspect identification and stopping the spread of the illness through immediate isolation and infection control measures. Though if a vaccine were available right now, its uptake might not be sufficient. According to a study, at the beginning of the H1N1 pandemic in the United States in May 2009, roughly 50% of people intended to get vaccinated; by January 2010, that number had dropped to 16% (Hossain, 2009).

The drugs were examined in compliance with earlier research on SARS and MERS therapeutic therapies. Overall, there isn't much proof to support the claim that these antivirals greatly enhance clinical results. A. COVID-19 patients have been treated with antiviral medications like oseltamivir in addition to empirical antibiotic therapy. Remdesivir, which was first created to treat the Ebola virus, is now being used in the US to treat COVID-19 infections that were brought in from abroad. Three out of four COVID-19 patients showed clinical benefit from a brief study combining Lopinavir/Ritonavir, Arbidol, and ShufengJiedu Capsule (SFJDC), a traditional Chinese medicine. A clinical trial is currently in progress to investigate the safety and effectiveness of interferon-α 2b and lopinavir-ritonavir in COVID-19 patients. Broad-spectrum antivirus Ramsedivir has demonstrated both in vitro andin vivo efficacy against SARS-CoV-2.

Control and prevention strategies:

Unquestionably, COVID-19 was a dangerous illness that drew attention from all across the world since it first appeared in 2020. According to some estimates, it has killed or infected more people than SARS and has a higher rate of reproduction. As with SARS-CoV and MERS-CoV, it is believed that severing the chain of transmission is essential to controlling the spread of the illness. In health care settings, different approaches should be applied on a local and global level. Regretfully, medical settings have the potential to be a significant hub for the spread of viruses. Triage, appropriate infection control procedures, case isolation, and contact tracing are essential to preventing the virus from spreading in clinics and hospitals, as the SARS model illustrates.

When suspected cases showed up at medical facilities exhibiting symptoms of respiratory disorders (such as runny nose, fever, cough), they were required to strictly follow the triage protocol and wear a face mask to contain the virus. They shouldn't have to wait in the facilities with other people who are seeking medical

attention. They should have easy access to respiratory hygiene supplies and be kept in a separate, well-ventilated room that is about two meters away from other patients. In addition, a confirmed COVID-19 case that needs to be hospitalized had to be placed in a single patient room with negative air pressure, meaning that there should be at least six air changes every hour. High efficiency particulate air (HEPA) filters were used to filter exhaust air, and medical personnel entering the room wore personal protective equipment (PPE) like gloves, gowns, facemasks, and eye protection (Tang, 2020).

Isolating afflicted individuals was the most effective way to stop the spread of disease in a communal setting. Chinese health officials, for instance, moved quickly to quarantine suspects and their close associates and isolate sick patients. Contact with animal fluids or tissues, as well as eating meat from wild animals, was to be avoided because there were still conflicting theories regarding the virus's animal origins (for instance, some studies link the virus to snakes, while others link it to bats). Additionally, it was crucial to teach the public how to identify unusual symptoms like persistent coughing or dyspnea so that people could seek medical care and the virus can be identified early.

Reducing social gatherings, closing schools temporarily, isolating homes, closely monitoring ill people, providing life support (such as an oxygen supply or mechanical ventilator), practicing good hand hygiene, and donning facemasks were all recommended actions in the event of a widespread community transmission. One of the first actions made by Chinese authorities to slow the global spread of COVID-19 was the closure of Wuhan. In these cases, air travel was also restricted unless there was an urgent need for medical attention. In order to detect possible cases, airports and borders set up temperature checks or scanning; to identify the outbreak's origin and provide information for the next pandemic , more research on the virus is essential.

Conclusions:

Without a doubt, the COVID-19 pandemic affected public health throughout the world. Our knowledge of the pathogen, how it infects cells and causes disease, and the clinical features of disease has advanced quickly. Governments everywhere should increase their attention to disease surveillance systems and step up country readiness and response activities, like forming rapid response teams and strengthening the capabilities of the national laboratory system, in light of the rapid spread of the disease.

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