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Review on the Origin, Transmission and Clinical Therapies of Covid-19

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ABSTRACT

In December 2019, Wuhan, Hubei Province, China, reported an outbreak of pneumonia of unknown cause. The Huanan Seafood Wholesale Market was found to be associated with instances of pneumonia. Inoculation of respiratory materials into human airway epithelial cells, Vero E6 and Huh7 cell lines, resulted in the isolation of a novel respiratory virus, which was later identified as a novel coronavirus linked to SARS-CoV after genome analysis (SARS-CoV-2). The beta coronavirus SARS-CoV-2 belongs to the Sarbecovirus subgenus.[1] Corona virus causes pneumonia, colds, sneezing, and coughing in humans, while it causes diarrhoea and upper respiratory infections in animals. Corona virus spread from person to person or animal to animal through airborne droplets. Corona virus enters human cells via the ACE-2 exopeptidase receptor on the cell membrane. WHO and ECDC recommended avoiding public places and close contact with infected people and pets.

Keywords: SARS-CoV-2, Immunoglobulin G, RT-PCR, Pharmaceuticals, Nutraceuticals

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INTRODUCTION

Thousands to millions of people have died as a result of several diseases and pandemics around the world. Despite advancements in medicine and research, emerging infections continue to pose a threat to human lives, global economic security, and the healthcare system. Acute respiratory syndrome with severe symptoms. The 2019-20 pandemic will be caused by coronavirus-2 (SARS-CoV-2). It is a novel coronavirus that was first discovered.[3] WHO abbreviates the virus as 2019-nCoV. It was discovered in a patient's throat swab. The Coronavirus Study Group called this pathogen severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease coronavirus disease 2019 (COVID-19) by the WHO. As of January 30, China had reported 7736 confirmed and 12,167 suspected cases, with 82 confirmed cases discovered in 18 other countries. The SARS-CoV-2 outbreak was declared a Public Health Emergency of International Concern by WHO on the same day (PHEIC). As of February 4, the fatality rate among confirmed cases in China was 2.1 percent, while the mortality rate among cases outside China was 0.2 percent, according to the National Health Commission of China. The death rate for patients admitted to hospitals ranged from 11% to 15%. COVID-19 is a moderately contagious virus with a high fatality rate, yet public reports and published research are fast expanding. The goal of this study is to describe current knowledge about COVID-19, including the causative agent, illness pathophysiology, diagnosis and therapy with nutraceuticals, and case management and preventative efforts.[4]

Origin of SARS

Adults in Wuhan, Hubei Province's capital and a key Chinese transportation hub, began presenting to local hospitals in December 2019 with severe pneumonia of unknown origin. Many of the early cases shared a connection to the Huanan wholesale seafood market, which also dealt in live animals. The SARS surveillance system was activated, and patients' respiratory samples were forwarded to reference labs for etiological research. China notified the World Health Organization about the outbreak on December 31st, and the Huanan sea food market was shut down on January 1st. The virus was identified as a coronavirus on January 7th, with >95% homology to the bat coronavirus and >70% similarity to SARSCoV. The virus was found in environmental samples from the Huanan sea food market, indicating that it originated there. The number of cases began to rise exponentially, with some of them not having had any contact with the live animal market, indicating that human-to-human transmission was taking place. On January 11th, 2020, the first death was reported. The outbreak was fuelled by the enormous Chinese influx over the Chinese New Year.[5] People returning from Wuhan reported cases in other Chinese provinces and other

countries (in rapid succession, Thailand, Japan, and South Korea). On the 20th of January, 2020, the transmission to patient care staff was described. Wuhan's 11 million residents were placed under lockdown on January 23rd, with entry and departure restrictions in force. The curfew was quickly extended to other Hubei cities. COVID-19 cases have been documented in countries outside of China in people who have never visited China, implying that local human-to-human transmission is taking place. Symptomatic persons returning from China are being isolated and tested for COVID-19 at airports across the world, including India. It was quickly discovered that the illness may be spread from asymptomatic people and even before symptoms appeared. As a result, nations such as India, which evacuated their residents from Wuhan through special aircraft or had travellers returning from China, isolated anyone who was symptomatic or otherwise for 14 days and tested them for the virus. CoV-2- Scientists have questioned the origin of the new coronavirus SARS-CoV2 since its discovery.[6-9] SARS-CoV-2 is thought to be the result of laboratory experiments. However, genomic evidence contradicts this theory, indicating that SARS-CoV-2 did not originate from a previously identified virus backbone. SARS-CoV-2 has unique features that distinguish it from other coronaviruses, according to genome analysis and comparisons with previously known coronavirus genomes: optimal affinity for the angiotensin converting enzyme 2 (ACE2) receptor and a polybasic cleavage site at the S1/S2 spike junction that determines infectivity and host range. SARS-CoV-2 looks a lot like bat SARS-like coronaviruses; hence bats could be the reservoir host. RaGT13 is almost identical to SARS-CoV-2, with the exception of certain variations in the spike receptor binding domain (RBD), which could explain the discrepancies in ACE2 affinity between SARSCoV-2 and SARS-like coronaviruses. SARS-polybasic CoV-2's cleavage site is absent in pangolin beta-coronavirus, which shares many similarities with SARS-CoV-2. Furthermore, the RBD sequence of the spike protein (S) implies that it evolved naturally. The most recent common ancestor of SARS-CoV-2 dates the epidemic to late November or early December 2019, which is consistent with the initial cases recorded. Thus, human transmission occurred after the zoonotic event but before the polybasic furin cleavage site was acquired.[11-15]

Epidemiology reservoirs and transmission

Since December 12, 2019, an epidemic of an unknown acute respiratory tract illness has been spreading through Wuhan, China, perhaps linked to a seafood market. Several studies have shown that the bat could be a possible SARS-CoV-2 reservoir. However, there is no indication that SARS-CoV-2 originated in the seafood market. Bats, on the other hand, are a natural reservoir for a wide range of CoVs, including SARS-CoV and MERS-CoV-like viruses. Although bats are not

available for sale in this seafood market, COVID-19 was examined throughout the genome to Bat CoV RaTG13 and found 96.2 percent overall genome sequence identity, suggesting that bat CoV and human SARS-CoV-2 may have an ancestor. Furthermore, protein sequence alignment and phylogenetic research revealed that comparable receptor residues were found in many taxa, implying that alternate intermediate hosts, such as turtles, pangolins, and snacks, exist. SARS-CoV-2 is transmitted mostly amongst family members, including relatives and friends who have had close contact with patients or incubation carriers. According to reports, 31.3 percent of patients who have recently travelled to Wuhan and 72.3 percent of patients who have had contact with Wuhan locals. COVID-19 patients were infected by healthcare personnel in 3.8 percent of cases, according to the National Health Commission of China's report released on February 14, 2020. SARS-CoV and MERS-CoV, on the other hand, are thought to spread mostly through nosocomial transmission. Infections of healthcare workers were found in 33–42 percent of SARS cases, while transmission between patients was found in 62–79 percent of MERS-CoV cases. The major route of SARS-CoV-2 transmission was thought to be direct interaction with intermediate host animals or ingestion of wild animals. SARS-source(s) CoV-2's and transmission routine(s) are yet unknown. [15-20]

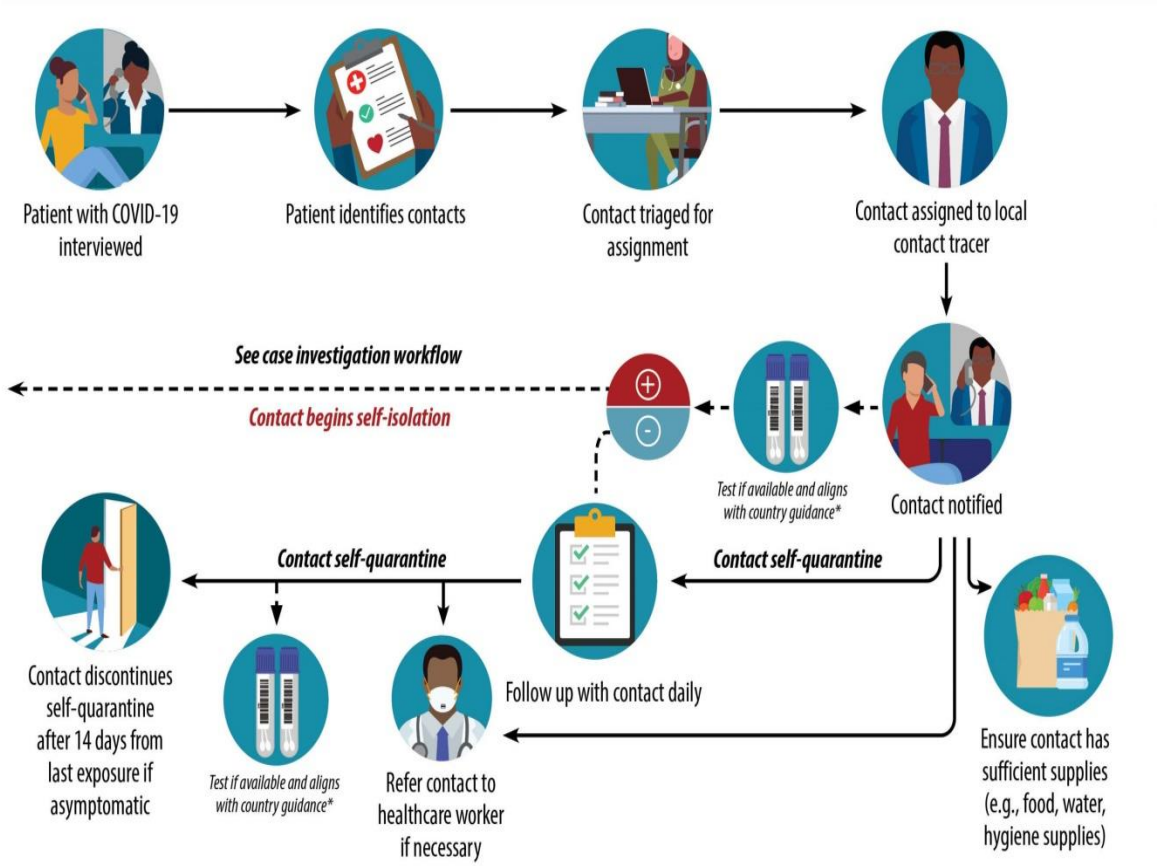

Figure 1: Steps from transmission to cure Covid-19

Diagnosis

Reverse transcription polymerase chain reaction (RT-PCR) is used to identify SARS-CoV-2 RNA, which is most typically collected from nasopharyngeal (NP) swabs. The CDC recommends collecting NP swabs from asymptomatic people in the United States. Instead, symptomatic patients should have their bilateral anterior nares and mid turbinates sampled. If an NP swab is not possible, an oropharyngeal (OP) swab could be used. Sputum collection is also advised by the CDC in individuals who have a productive cough, although sputum inducement is not. A lower respiratory tract sample should also be taken through bronchioalveolar lavage (BAL) when clinically indicated (i.e., patients who are mechanically intubatedSARS-CoV-2 testing accuracy is yet unknown. It has been highlighted that RT-PCR testing for SARS-CoV-2 may be mistakenly negative due to insufficient viral load if the specimen is collected too early or too late in the disease course, or due to technical problems such as incorrect handling or shipping. Patients with characteristic computed tomography (CT) chest abnormalities (bilateral peripheral distribution with multifocal lower lung involvement) who tested negative on RT-PCR have been documented. When compared to upper respiratory tract samples, lower respiratory tract samples (i.e., BAL) are more likely to provide a positive result. In a study of 205 individuals, 93 percent of BAL specimens were positive (14 out of 15), compared to 72 percent of NP swab specimens (72 out of 104). As a result, if initial testing is negative but clinical suspicion is high, the WHO advises repeating the test, ideally from a lower respiratory tract specimen if available. The antibody response in COVID-19 patients is unknown because SARS-CoV-2 is a newly found virus. Currently, RT-PCR-based viral RNA is the gold standard diagnostic method for COVID-19 infections, although various research suggest that serologic antibody testing could be used to help diagnose COVID-19 infections. These are especially effective in individuals with asymptomatic infections and suspected patients with negative RT-PCR-based viral RNA. Furthermore, when used in conjunction with RT–PCR-based viral RNA testing, these assays may increase the sensitivity of COVID-19 pathogenic diagnosis. The median seroconversion time for total antibodies, immunoglobulin-M (IgM), and immunoglobulin G (IgG) against SARS-CoV-2 was day-11, day-12, and day14, respectively, in research conducted by Zhao et al. among 173 patients with SARS-CoV-2 infection.[20-25]

Investigational approaches and adjunctive therapies

Unfortunately, no vaccine or proven effective therapy against SARS-CoV-2 infection has been developed too yet. While many experiments are presently underway, including much-needed randomized controlled trials (RCTs), supportive care remains the mainstay of therapy. Depending

on the severity of the sickness, this can range from symptomatic treatment to ventilator support for individuals with ARDS. This includes early detection and treatment of superimposed bacterial infections and/or sepsis. Many of the current clinical trials are looking into pharmaceuticals that have previously been used to treat SARS and MERS. These will be covered in greater detail further down. Chloroquine/Hydroxychloroquine Antimalarial medications chloroquine and hydroxychloroquine are commonly used. Hydroxychloroquine is a chloroquine derivative with fewer drug-drug interactions and a higher safety profile than chloroquine. In vitro, both chloroquine and hydroxychloroquine limit SARS-CoV-2 growth and reduce viral replication in a concentration-dependent manner. The more powerful hydroxychloroquine was discovered. Both chloroquine and hydroxychloroquine have been suggested as potential inhibitors of SARS-CoV-2 replication. They could achieve this by altering the pH at the cell membrane's surface, preventing fusion as well as nucleic acid replication, glycosylation, and viral assembly and release. Chloroquine was found to be efficacious and safe in patients with SARS-CoV-2 pneumonia in multi centre clinical studies conducted in China. Hydroxychloroquine is now being studied in the United States in multiple RCTs for treatment of SARS-CoV-2 infection, as well as pre- and post-exposure prophylaxis. Treatment with hydroxychloroquine, azithromycin, or both was not related with significantly lower in-hospital mortality in a retrospective cohort analysis involving 1,438 patients hospitalized in metropolitan New York. The observational approach, however, may limit the interpretation of these findings. 821 asymptomatic people were randomly assigned to receive either placebo or hydroxychloroquine 4 days following exposure to someone with verified COVID-19 in another randomized, double-blind, placebo-controlled experiment in the United States. When used as post exposure prophylaxis within this interval, hydroxychloroquine did not prevent sickness or confirmed infection due to COVID-19. The US Food and Drug Administration (FDA) cancelled the emergency use permission for chloroquine phosphate and hydroxychloroquine sulphate in select hospitalized COVID19 patients granted on March 28, 2020 on June 15, 2020. They claim that the risks of major cardiac events and other serious side effects exceed the potential benefits of using them.[25-27]

Azithromycin

Because of its anti-inflammatory properties, azithromycin is commonly utilized in individuals with chronic pulmonary inflammatory diseases and/or community-acquired pneumonia. There is, however, limited evidence that azithromycin in conjunction with chloroquine/hydroxychloroquine is effective in the treatment of ARDS in individuals infected with SARS-CoV-2. In a 36-patient open-label non-randomized clinical trial in China, combining hydroxychloroquine and

azithromycin reduced the detection of SARS-CoV-2 RNA in upper respiratory tract specimens, indicating a synergistic impact in the treatment of SARS-CoV-2 infection. However, the clinical benefit of this combination was not addressed in this investigation. Another small observational trial in China found that treating SARS-CoV-2 in hospitalized patients with hydroxychloroquine and azithromycin had no clinical benefit and no evidence of fast viral RNA clearance. Both hydroxychloroquine and azithromycin can cause QTc prolongation, which can result in deadly arrhythmias. As a result, they should be taken with caution in those who have a long QTc or who have certain medical problems like hepatic or renal impairment. Remdesivir is a new nucleotide analogue that binds to nascent viral RNA chains and inhibits viral replication by causing premature termination. Remdesivir has been demonstrated to be an effective antiviral agent against beta-coronaviruses like SARS-CoV and SARS-MERS in mice, non-human primates, and in vitro, and it is now being tested in clinical studies for the treatment of Ebola virus. Remdesivir is particularly successful in reducing SARS-CoV-2 infection in vitro, according to a study conducted in China. Another study released recently found that 68 percent of patients with severe SARS-CoV-2 infection (36 out of 53) improved clinically, with 57 percent being extubated and 47 percent being discharged. Despite promising results in vitro, in vivo in animal models, and in compassionate-use studies in humans, the FDA has yet to approve remdesivir for use as a standard-of-care medication due to a lack of solid data on safety and efficacy in humans. Giliad, a biopharmaceutical start-up, has begun two phase 3 clinical trials in COVID-19 patients to assess the drug's safety and efficacy.[27-30]

Lopinavir-Ritonavir

Lopinavir-ritonavir is a protease inhibitor combination used to treat HIV infection. Although this medicine has been shown to have in vitro efficacy against SARS-CoV, it does not appear to be of any assistance during the current outbreak. A 199-patient randomized, controlled, open-label trial compared the use of lopinavir–ritonavir treatment to standard care alone, which included antibiotics, vasopressors, renal replacement therapy, extracorporeal membrane oxygenation (ECMO), and/or supplemental oxygen/invasive ventilation if needed. When compared to those getting standard-care alone, gastrointestinal adverse events were more common in the lopinavir–ritonavir group; nevertheless, total adverse events were more common in the standard-care group.

Favipiravir

In China, favipiravir is an RNA polymerase inhibitor that is used to treat influenza. By inhibiting the RNA-dependent RNA polymerase (RdRp) enzyme, favipiravir can prevent RNA viruses from

replicating. As a result, favipiravir may exhibit antiviral action against the RNA virus SARS-CoV-2. Clinical trials using this medication to treat SARS-CoV-2 infection are presently underway.[30-32]

Importance of Nutraceuticals

Due to their supposed "immune-boosting" properties, sales of dietary supplements and nutraceuticals have soared during the epidemic. However, nothing is known regarding the effectiveness of these dietary supplements and nutraceuticals in the fight against the new coronavirus (SARS-CoV-2) and the disease it produces, COVID-19. Based on the evidence available to date, this review presents a critical overview of the potential preventive and therapeutic usefulness of numerous dietary supplements and nutraceuticals. Vitamin C, vitamin D, and zinc, for example, are commonly thought to help with respiratory infections and immunological function. Some supplements may be subject to limited government oversight, so consumers should be careful of misinformation and deceptive promises. However, additional research is needed to see if dietary supplements and nutraceuticals can help prevent and treat SARS-CoV-2 and COVID-19 infections. This review sheds light on which nutraceuticals and supplements are involved in COVID-19 recovery and preventive biological processes.[33]

Zinc

Zinc is a nutritional supplement with antiviral properties. Zinc is a trace metal that is necessary for the maintenance of immune cells involved in adaptive and innate immunity. It can be gained from dietary sources or supplementation. Zinc picolinate, zinc acetate, and zinc citrate are examples of supplements that can be taken orally as a tablet or a lozenge. Meat, seafood, nuts, seeds, legumes, and dairy products are all good sources of zinc. Zinc's role in immunological function has been well investigated. Zinc is a key signalling chemical, and its levels can affect the host's defence mechanisms. Zinc can control leukocyte immunological responses and activate the nuclear factor kappa-light-chain-enhancer of activated B cells in inflammatory circumstances like infections, affecting cytokine output. Zinc supplementation, in particular, can boost natural killer cell counts, which are crucial for the host's fight against viral infections. Zinc is being studied for its potential anti-COVID-19 effects as a result of these immune-related actions. Zinc supplementation has been linked to lower infection rates and antiviral immunity. Zinc deficiency was linked to greater susceptibility to infection in a randomized, double-blind, placebo-controlled trial that lasted a year and concluded that zinc deficit may be averted with supplementation. When zinc is given within 24 hours after the onset of symptoms, clinical trials show that it can reduce the duration and intensity of symptoms associated with common colds. COVID-19 patients had significantly lower zinc levels than healthy controls, according to an observational study, and zinc-deficient COVID-

19 patients (those with levels less than 80 g/dl) had more complications (70.4 percent vs 30.0 percent, p = 0.009) and potentially longer hospital stays (7.9 vs 5.7 days, p = 0.048) than patients who were not zinc deficient. In vitro research has shown that combining zinc (Zn2+) and zinc ionophores (pyrithione) can disrupt the replication mechanisms of SARS-CoV-GFP (a fluorescently tagged SARSCoV-1) and a number of other RNA viruses in coronaviruses. There are now over twenty clinical trials registered with the goal of using zinc as a COVID-19 preventive or treatment measure. However, many of these studies suggested using zinc in combination with hydroxychloroquine and azithromycin, and it's unclear how the lack of evidence for hydroxychloroquine will affect zinc research. In one retrospective observational trial, hospitalized COVID-19 patients were given hydroxychloroquine and azithromycin with zinc sulphate (n = 411) against hydroxychloroquine and azithromycin alone (n = 521) in New York University Langone hospitals. Because of the lack of efficacy and probable adverse effects associated with hydroxychloroquine and azithromycin against COVID-19, zinc is the only medication employed in this trial that is still being considered as a therapeutic agent. While the addition of zinc sulphate had no effect on hospitalization time, ICU stay time, or patient ventilation time, univariate analysis showed that zinc increased the frequency of patients released and decreased the need for ventilation, ICU referrals, and mortality. A smaller retrospective study at Hoboken University Medical Center in New Jersey, however, found no link between zinc supplementation and hospitalized patient survival. As a result, it's uncertain whether zinc plays a role in COVID-19 healing. Additional studies are now looking into combining zinc with other supplements like vitamin C or n-3 PUFA. Though there is now limited evidence to suggest zinc supplementation has any beneficial effects against the current novel COVID-19, the clinical trials that are currently underway will provide vital information on the efficacy of zinc in COVID-19 prevention and/or treatment. Given the low risk of infection and the possible link between zinc shortage and sickness, keeping a balanced diet to guarantee adequate zinc status may be desirable for those looking to lower their risk of infection

Vitamin C

Vitamins B, C, D, and E have also been mentioned as possible COVID-19 nutrient supplement therapies. Due to its long history of use against the common cold and other respiratory infections, vitamin C has been postulated as a potential treatment agent against COVID-19. Vitamin C can be gained from foods like fruits and vegetables or from supplements. Because of its actions on diverse immune cells, vitamin C plays an important role in enhancing immunological function. It impacts inflammation by modifying cytokine production, lowering histamine levels, promoting T- and B-

lymphocyte differentiation and proliferation, increasing antibody levels, and guarding against the deleterious effects of reactive oxygen species, among other COVID-19 pathology-related actions. Vitamin C is used by the body during viral infections, as seen by reduced levels of vitamin C in leukocytes and urine vitamin C. These levels revert to normal after infection. Vitamin C doses as low as 0.1 g/d have been found to maintain normal vitamin C plasma levels in healthy people, but greater doses of at least 1-3 g/d are required for critically ill patients in ICUs. Vitamin C insufficiency does appear to be prevalent among COVID-19 patientsCOVID-19 is also linked to the formation of microthrombi and coagulopathy, both of which contribute to the disease's typical lung pathology. However, these symptoms can be alleviated by early vitamin C infusions, which inhibit endothelial surface P-selectin expression and platelet-endothelial adhesion. In a case study of 17 COVID-19 patients, intravenous vitamin C lowered D-dimer levels, which are substantially increased in COVID-19 patients. As a result, preliminary evidence suggests that vitamin C level and supplementation may be related to COVID-19 results. However, larger-scale vitamin C research has shown mixed findings. According to a new meta-analysis, regular vitamin C supplementation reduces the duration of the common cold, however supplementation with vitamin C (> 200 mg) does not reduce the incidence of colds. Vitamin C has been shown in trials to reduce patients' susceptibility to lower respiratory tract infections including pneumonia. Vitamin C supplementation reduced the length of stay of patients in intensive care units (ICUs) by 7.8% (95 percent CI: 4.2 percent to 11.2 percent; $p = 0.00003$) in twelve trials, according to another meta-analysis. Furthermore, in six trials ($p = 0.003$), high doses (1-3 g/day) significantly shortened the length of an ICU stay by 8.6%. In three trials in which patients required mechanical breathing for more than 24 hours, vitamin C reduced the length of the intervention by 18.2 percent (95 percent CI 7.7% to 27 percent; $p = 0.001$). Despite these findings, the CITRUS ALI RCT of 167 patients found no benefit from a 96-hour vitamin C infusion to treat ARDS. According to Carr et al. [99], clinical trials studying vitamin C in the context of COVID-19 have now commenced. These studies will look into the use of intravenous vitamin C in COVID-19 patients who are hospitalized. In Wuhan, China, the first study with preliminary results was conducted. In univariate survival analysis, the administration of 12 g/12 hrs of intravenous vitamin C for 7 days in 56 critically sick COVID-19 patients resulted in a promising reduction in 28-day death ($p = 0.06$). Indeed, on day 7 of vitamin C infusion, IL-6 levels had dropped significantly ($p = 0.04$), according to the same study. Additional research in Canada, China, Iran, and the United States will help to determine whether vitamin C supplementation influences COVID-19 outcomes on a larger scale. Even though evidence for the use of vitamin C is beginning to surface, it will be some time before we

know how successful it is as a therapy. Clinicaltrials.gov presently has around fifteen trials that are either recruiting, active, or in the planning stages (as of January 2021). These trials, once completed, will give critical evidence on the efficacy of vitamin C as a COVID-19 infection treatment. However, the majority of supplemental research focus on intravenous vitamin C infusion in severely ill individuals. As a result, there are few research looking into the potential prophylactic delivery of vitamin C by oral supplementation for healthy people or SARSCoV-2 positive patients who are asymptomatic. Once again, vitamin C is an important part of a healthy diet and poses little danger, but its potential preventative or therapeutic effects against COVID19 remain unknown. Individuals should ensure that they obtain the appropriate dietary requirement of vitamin C to maintain a healthy immune system. The FDA recommends 75-90 mg/d, but the European Food Safety Authority recommends 110 mg/d.

Vitamin D

Vitamin D has emerged as the most promising preventive and therapeutic candidate against SARS-CoV-2 among all the supplements currently being studied. Vitamin D is linked to several elements of immunological health and antiviral defence and can influence both the adaptive and innate immune systems. Vitamin D can be obtained by diet or supplements, although it is mostly biosynthesized by the body in response to UVB solar exposure. Vitamin D insufficiency has been linked to an increased risk of infection. Vitamin D deficiency increases the incidence of acute respiratory infections and ARDS in individuals. Vitamin D levels are normally evaluated by the longer lasting and more abundant precursor 25-hydroxyvitamin D, which is implicated in adaptive and innate responses due to its low concentration and short half-life of a few hours. Vitamin D is an immunomodulator of antigen presentation cells, dendritic cells, macrophages, monocytes, and T- and B-lymphocytes, and its receptor is found in a variety of immune cells. Vitamin D administration may be beneficial for maintaining a healthy immune system due to its putative immunomodulating characteristics. Early in the pandemic, it was thought that a person's vitamin D status could influence their risk of contracting COVID-19. The current pandemic began in Wuhan, China, during the winter, when 25-hydroxyvitamin D concentrations are at their lowest due to a lack of sunlight, whereas the number of cases was low in the Southern Hemisphere, where it was nearing the end of summer and higher 25-hydroxyvitamin D concentrations would be higher. This caused researchers to wonder if the SARS-CoV-2 pandemic had a seasonal component, and if vitamin D levels might have played a role. Though COVID-19 is thought to be seasonal, there are a number of other factors that can influence vitamin D levels. These determinants include, among others, an individual's nutritional state, age, occupation, skin colour, potential comorbidities, and

variations in sunshine exposure due to latitude. Indeed, each degree of latitude north of 28 degrees was linked to a 4.4 percent increase in COVID-19 mortality, implying that vitamin D levels are linked to COVID-19 mortality through UVB light exposure. Additional studies of various quality have studied some of the potential relationships between vitamin D and COVID-19 observed early in the pandemic as the pandemic progressed. Indeed, research are beginning to look into whether vitamin D and COVID-19 have a preventive and/or therapeutic link. In a study conducted in Switzerland, 27 SARS-CoV-2 positive patients had 25-hydroxyvitamin D plasma concentrations that were significantly lower (11.1 ng/ml; p = 0.004) than those of SARS-CoV-2 negative patients (24.6 ng/ml; p = 0.004), an association that held when patients over 70 years old were stratified. A Belgian observational study of 186 SARS-CoV-2 positive patients with pneumonia symptoms, where 25-hydroxyvitamin D plasma concentrations were monitored and CT images of the lungs were obtained upon admission, appears to validate these findings. Between the SARS-CoV-2 patients and 2,717 season-matched sick controls, there was a substantial variation in 25-hydroxyvitamin D levels. Both female and male patients had lower median 25-hydroxyvitamin D concentrations and a greater rate of vitamin D insufficiency than the control group (18.6 ng/ml versus 21.5 ng/ml; p = 0.0016). (58.6 percent versus 42.5 percent). When the comparisons were stratified by sex, evidence of sexual dimorphism emerged, with female patients having equal levels of 25-hydroxyvitamin D to female controls, but male patients were deficient in 25-hydroxyvitamin D compared to male controls (67 percent versus 49 percent; p = 0.0006). Vitamin D deficiency was shown to be lower in males as radiological illness stages progressed (p = 0.001). Several more studies back up these findings, indicating that vitamin D level may be an independent risk factor for COVID-19 severity in COVID-19 patients compared to population-based controls. Indeed, serum 25-hydroxyvitamin D concentrations above 30 ng/ml, indicating vitamin D sufficiency, appear to be associated with a decrease in serum C-reactive protein, an inflammatory marker, as well as increased lymphocyte levels, suggesting that vitamin D levels may modulate the immune response by reducing the risk of cytokine storm in response to SARS-CoV-2 infection. COVID-19 fatality was found to be higher in patients with severe COVID-19 and low serum 25-hydroxyvitamin D levels (mean level 6.2 ng/ml; 97 percent vitamin D deficient) compared to asymptomatic non-severe patients with higher vitamin D levels (mean level 27.9 ng/ml; 33 percent vitamin D deficient) in an Indian study. Vitamin D deficiency was linked to greater levels of inflammatory markers such IL-6, ferritin, and tumour necrosis factor in the same study. These findings contribute to a growing body of evidence suggesting a link between low 25-hydroxyvitamin D levels and COVID-19 occurrence and severity.[34]

Vaccination strategies

To prevent a pandemic, many efforts have been made to develop COVID-19 vaccines, with the S-protein of SARSCoV-2 being used in the majority of developing vaccine candidates. As of July 2, 2020, there are 158 vaccine candidates in research for SARS-CoV-2, with 135 of them in preclinical or exploratory stages. Currently in phase I/II clinical studies are mRNA-1273 (Moderna), Ad5-nCoV (CanSino Biologicals), INO-4800 (Inovio, Inc.), LV-SMENP-DC, Pathogen-specific aAPC (ShinzenGeno-Immune Medical Institute), and ChAdOx1 (University of Oxford) (WHO, 2020Inactivated or live attenuated viruses, protein subunits, virus-like particles (VLP), viral vector (replicating and non-replicating), DNA, RNA, nanoparticles, and other vaccines are used in the conduit. Various adjuvant technologies, such as AS03 (GSK), MF-59 (Novartis), CpG 1018 (Dynavax), and others, are now available to researchers for vaccine development to improve immunogenicity. Epitope discovery for SARS-CoV-2 vaccine candidates is also done using an immuno-informatics approach. It can be utilized to find important cytotoxic T-cell and B-cell epitopes in viral proteins.[35]

CONCLUSION

The current COVID-19 outbreak is unmistakably a global public health issue. There has been rapid progress in our understanding of the pathogen, how it infects cells and causes disease, and disease clinical features. Because of the rapid spread of disease, countries around the world should pay more attention to disease surveillance systems and scale up country readiness and response activities, such as forming quick response teams and increasing the national laboratory system's capabilities. It is recommended that combination of nutraceuticals and pharmaceuticals be used to better prevent and control the risk of COVID-19 disease. We have also started using the vaccines that are currently available on the market, but we need to raise public awareness about the need of immunization.

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