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Learning from COVID-19 for Mitigating the Next Possible Pandemic: Nutrition, Lifestyle, Risk Factors and Non-Pharmaceutical Interventions

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Abstract

The COVID-19 pandemic has sparked a paradigm change in pandemic preparedness measures, motivating an investigation of non-pharmaceutical therapies. This research dives into the lessons learned from COVID-19 to strengthen our strategy to prevent future pandemics. The study aimed to extract valuable insights from the COVID-19 experience, extrapolating lessons learned to develop strong strategies that include diet, lifestyle, risk factors and non-pharmaceutical treatments. Nutrition and lifestyle influences on illness susceptibility were studied using a comprehensive examination of scholarly literature, reports and epidemiological studies. Role of essential risk variables was investigated in magnifying pandemic outcomes and the efficiency of non-pharmaceutical treatments in reducing infectious agent transmission. The analysis demonstrates the long-term utility of COVID-19 findings. This review emphasizes the importance of nutrition and lifestyle variables in determining susceptibility to infectious illnesses. Furthermore, a detailed examination of risk variables shows critical predictors of pandemic severity. Most significantly, the findings highlight the effectiveness of non-pharmaceutical measures, emphasizing their vital role in pandemic containment. This study has far-reaching ramifications that advocate for a paradigm change towards comprehensive pandemic preparation using the lessons learned during COVID-19. Research findings highlight the need for a multifaceted strategy, including diet, lifestyle changes, targeted risk reduction and non-pharmaceutical therapies. This study provides a road map for improving global resilience to potential future pandemics, calling for preventative strategies beyond pharmacological remedies.

Keywords: antioxidant; epidemiology; immunity; nutritional supplements; quarantine

INTRODUCTION

COVID-19's introduction, fueled by the new Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has sparked worldwide turmoil. SARS-CoV-2, discovered in a Wuhan wet market in December 2019, joins the ranks of seven previously detected coronaviruses, including SARS-CoV-1 (2002) and Middle East Respiratory Syndrome Corona Virus/MERS-CoV (2012), which caused severe respiratory illness. These coronaviruses traced back to bat reservoirs highlight the complicated zoonotic interaction. COVID-19's global toll encompasses over 150 million infections and 3.15 million deaths (April 2021), extending beyond physical afflictions to deeply unsettling mental health repercussions. Quarantine-related psychological stresses have

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been evident, including emotional fatigue, sleep disturbances and mood alterations (Brooks et al., 2020).

A genetic analysis reveals a plausible bat origin for SARS-CoV-2, with significant genomic similarities. As demonstrated in prior coronavirus instances, intermediate hosts play an important role in transmission dynamics. A SARS-like CoV found in deceased Malayan pangolins implies that they might serve as intermediate hosts (Liu et al., 2019). According to comparative genomic research, a genome connection of 88% exists between COVID-19 and bat-derived SARS (Wan et al., 2020). SARS-CoV-2 spreads to people via various mechanisms, including direct contact and droplet transmission (Wu et al., 2020). The search for intermediate carriers saw initial conjecture focus on snakes, which was later revised to emphasize mammalian and avian species (Basseti et al., 2020). This complex network of virus transmission, origin hypothesis and public health implications sheds light on the complicated nature of the COVID-19 epidemic.

W. Zhang et al. (2020) during their studies related to the comparison of the bat, pangolin and human coronavirus have suggested that the bat is the probable species of origin for the 2019 novel coronavirus (SARS-CoV-2) because both share 96% whole-genome identity, i.e., bat species *Rhinolophus affinis* from Yunnan Province. However, SARS-CoV and MERS-CoV usually pass into intermediate hosts, such as civets or camels, before moving to humans. This fact shows that SARS-CoV-2 was possibly transmitted to the human body by other animals. As the earliest COVID-19 patient reported having no contact with the seafood market, finding the intermediate SARS-CoV-2 host is vital to hinder interspecies spread. The research by Liu et al. (2019) from the Guangdong Wildlife Rescue Center of China identified the existence of a SARS-like CoV from lung samples of two dead Malayan pangolins with a frothy liquid in their lungs and pulmonary fibrosis. Their results showed that all virus coatings assembled from two lung samples (lung07 and lung08) exhibited low identities, ranging from 80.24 to 88.93%, with known SARS-CoVs.

Similarly, in other efforts to search intermediate carriers or reservoir hosts, different results have been found (Figure 1). At the start, two snakes were identified as a possible reservoir, but further studies showed that mammals and birds could be the only carriers for spreading COVID-19 among human beings (Basseti et al., 2020). Further genomic sequence analysis showed that COVID-19 is 88% identical with two bat-derived SARS (Wan et al., 2020). Further transmission occurs from person-to-person contact, either direct contact or by droplets through coughing/sneezing from infected persons (Wu et al., 2020).

COVID-19 infection symptoms appear after an incubation period of almost 5.2 days. The period from the onset of COVID-19 symptoms to death ranges from 6 to 41 days, with a median

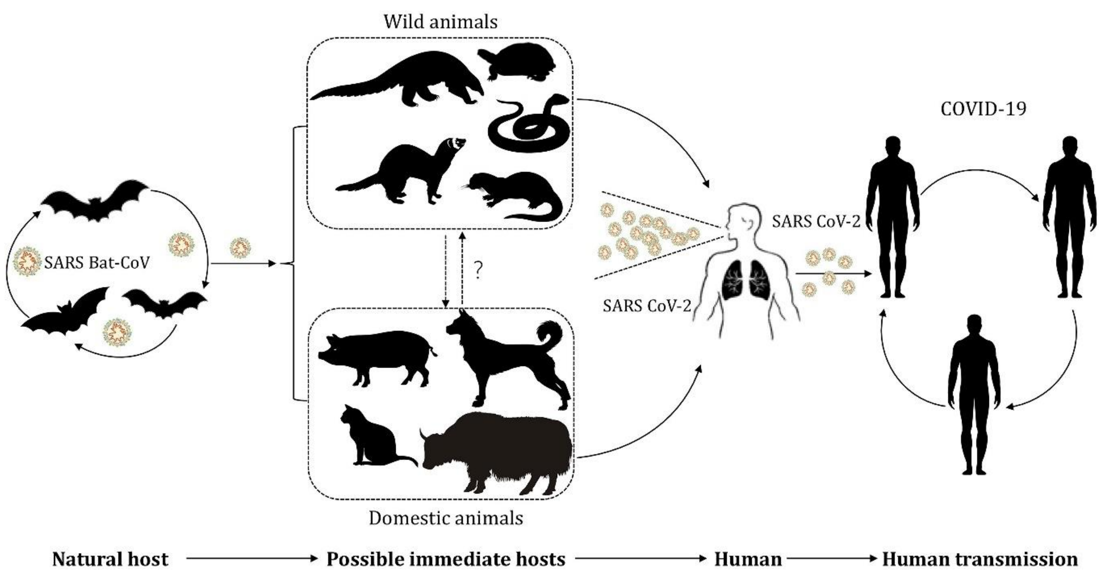

Figure 1. Potential transmission cycle for COVID-19 (Zhao et al., 2020)

of 14 days. This period is affected by the age and status of the person's immune system (Wang et al., 2020). The most common symptoms at the beginning of COVID-19 illness include systematic disorders such as fever, cough, fatigue, sputum production, headache, hemoptysis, acute cardiac injury, hypoxemia, dyspnoea, lymphopenia and diarrhea. Chest CT scan showed its symptoms as pneumonia. However, some unusual features such as RNAaemia, acute respiratory distress syndrome, acute cardiac injury, and incidence of grand-glass opacities can cause death (Huang et al., 2020). Unfortunately, interferon treatment for some cases showed no clinical effect and instead appeared to worsen the condition by progressing pulmonary opacities (Zhang and Liu, 2020). There are some similarities in the symptoms between COVID-19 and earlier beta-coronavirus, such as fever, dry cough, dyspnea and bilateral ground-glass opacities on chest CT scans; however, COVID-19 exhibited some distinctive clinical features that include the targeting of the lower airway as evident by upper respiratory tract symptoms like rhinorrhoea, sneezing and sore throat (Rothana and Byrareddy, 2020).

Since the coronavirus disease was declared as public emergency on January 30, 2019, World Health Organization (WHO), health institutions, the scientific community and pharmaceutical companies have joined hands in a continuous attempt to speed up the vaccine development process (WHO, 2020c). The response has been very positive since different vaccines were developed quickly by teams of scientists worldwide. Many countries have approved the COVID vaccination as well. Governments still ban social gatherings, making people follow standard operating procedures (SOPs) strictly regarding COVID-19 even though they have entered the vaccination phase. Due to the new strain's development of coronavirus, by time and area, it is still spreading.

In contrast to prior reviews on pandemic preparedness, this study takes a comprehensive approach by investigating the intricate interplay between nutrition, lifestyle, risk factors and non-pharmaceutical interventions. This research sheds light on the mental health components of pandemics by meticulously analyzing the development of SARS-CoV-2 and its worldwide ramifications. The findings highlight the critical role of intermediary species in zoonotic transmission by delving into the origins, transmission dynamics and intermediate hosts of COVID-19. Considering the importance of food and agriculture, researchers provide a comprehensive strategy for pandemic resistance by expanding the discussion to include immunity-boosting foods and lifestyle changes. This paper summarises the enormous implications of the research and emphasizes the importance of proactive global collaboration in the face of impending health crises (Ali, 2023).

MATERIALS AND METHOD

This study aimed to derive insights from the COVID-19 pandemic to develop strategies for mitigating potential future pandemics. To do this, a thorough examination of relevant literature was undertaken, which included scholarly papers, reports from health organizations, governmental recommendations and epidemiological studies. The review aimed to better understand the role of nutrition and lifestyle factors in infectious disease susceptibility, identify key risk factors that exacerbate pandemic outcomes and assess the effectiveness of non-pharmaceutical interventions in preventing the spread of infectious agents. Researchers hoped to distill practical recommendations for improving global pandemic preparation by synthesizing and analyzing the obtained data. This condition entailed critically evaluating existing material, identifying knowledge gaps and extrapolating lessons learned from the COVID-19 experience to propose measures encompassing dietary considerations, lifestyle modifications, risk factor mitigation and non-pharmaceutical interventions. The findings add to a comprehensive framework for proactive pandemic management, building on lessons learned from the continuing COVID-19 crisis to provide methods for effectively mitigating the effects of any future pandemics. This study emphasizes the significance of multidisciplinary collaboration and is a valuable resource for policymakers, healthcare practitioners and academics working to strengthen our worldwide defenses against infectious disease epidemics.

RESULTS AND DISCUSSION

Non-pharmacological treatment

To avoid the coronavirus severity, the only approach to manage the disease symptoms and prohibit mortality is non-pharmacological interventions (NPI) (Figure 2). People's activities are restricted/being separated in a non-healthcare facility with the aim of surveillance of symptoms or early detection of such persons who might be exposed to the COVID-19 virus. The global data showed that since November 7, 2020, the number of confirmed coronavirus cases has reached 56,716,141 and total deaths were 1,357,714. Globally, governments are enforcing quarantine to control the further spread of disease (Waris et al., 2020).

COVID-19 is a respiratory disease transmitted to others by close contact and fluid droplets. For this reason, WHO has recommended certain effective personal protective equipment (PPEs), including gloves, masks, safety goggles, disposable aprons and respirators, i.e., KN95 and FFP2, to prevent the viral disease. The efficacy of PPEs against the SARS-CoV-2 disease was depicted by Liu et al. (2020) through a cross-sectional study on the healthcare workers of Wuhan, China, which suggested these PPEs can help them not only protect from disease but also develop the protective immunity against disease (WHO, 2020b).

As 78% of the cases of COVID-19 arise due to close contact, many countries, including China, Iran, Malawi and Pakistan, governments had a partial lockdown of the whole country or ordered a smart lockdown (Nafees and Khan, 2020). However, this can affect the country's economy but can protect it from such contagious diseases. In the case of an intelligent lockdown, the hot spots (1.5 cases per 1000) are identified by restricting IPs to break the disease transmission cycle. This smart lockdown also leads to numerous testing, isolation and quarantine situations. Observation was carried out on behavior (epidemiology, quarantine effectiveness and outbreak trends) over different days of lockdown. Results revealed that extended lockdown, gradual social contact and return to activities with minimum reference are adequate for the pandemic (Vega, 2020).

Damour et al. (2020) observed the positive role of social media on the behavior of the public, influencing health protection from COVID-19. People can take preventive measures against contagious diseases by getting awareness by broadcasting brief messages to the concerned

Figure 2. Non-pharmacological interventions as preventive measures for COVID-19

population. Malecki et al. (2020) have estimated that if health workers and doctors can get ahead in shaping such awareness-based messages, the misinformation can be replaced with accurate information.

Different NPIs interact and work synergistically to combat COVID-19 (Regmi and Lwin, 2020). In India, the effect of NPIs on COVID was observed from minimum to herd immunity level. The average growth rate declined from 21 to 6% after the lockdown. So, this early stringent response by the Indian Government has slowed the COVID-19 epidemic (Patel et al., 2020). During the COVID-19 pandemic, most of the population is affected by mental health issues such as anxiety and depression. In a study in the Norwegian region, the risk factors and protective factors were recognized, and proper solutions were proposed to reduce such risks. The health policymaker must provide vivid and accurate knowledge about the duration of NPIs that would reduce the mental stress about the lengthy lockdown duration and increase the devotion to follow the NPIs (Ebrahimi et al., 2020).

The mortality rates per million in the United States and Peru were 0.061 and 0.069, respectively due to coronavirus SARS-CoV-2 (Rojas et al., 2020). Implementing strict NPIs in Peru showed a lower mortality rate than in the United States. The COVID-19 pandemic put socio-economic pressure on low and middle-income countries. The study has conducted an epidemiological-based option appraisal of many NPIs that can be done to lift the lockdown. For the low-income and middle-income countries, the rolling lockdown suggested by WHO was adopted and proved to be the best solution against COVID-19. Following is the consideration for epidemiological status, socio-economic cost, existing healthcare system and plans to sustain strategy (Chowdhury et al., 2020).

Need for nutritional supplements and healthy lifestyle interventions

Although the vaccination process has been started in many countries, we cannot neglect the preventive measures against the pandemic. Getting vaccinated does not mean we can ignore the SOPs and put ourselves and others at risk because the degree of effectiveness of those vaccines is still unknown. So, immunity booster foods/nutritional supplements, along with healthy lifestyle interventions, are a ray of hope for humans to fight against such calamity by strengthening immunity (Arshad et al., 2020).

A healthy lifestyle is directly linked with a stronger immune system. The human body's immune system and other vital functions work more effectively with synchronization and balance. There are some scientifically proven lifestyle behaviors and measures that strengthen immunity and ensure the general wellbeing to combat COVID-19 effectively. These are presented in Table 1.

Nutritional factors: Supplements management

The immune system plays a pivotal role in maintaining the integrity of human body functions, built on gut microbes protecting the human body from numerous diseases and harmful foreign bodies, including bacteria, viruses and parasites (Sajid et al., 2020). The immune system consists of two kinds of cells, T-cells and B-cells, which fight against the invading species directly, produce antibodies and fight the foreign molecules. Other than that, phagocytic cells including macrophages and neutrophils, can perform a specific function at the site of infection and eradicate the debris created from destroying cells (Reddy et al., 2018). This system remains active always and performs surveillance, but it becomes more active during the attack of any foreign body. The high activity will give rise to an increased metabolism, needing energy sources for biosynthesis and molecules and these molecules can get from diet. The immune system performs four different functions: forming the barrier against pathogens from entering the body, identifying the pathogens that already get entered into the host system, eliminating those pathogens and giving rise to immunological memory cells (antibodies produced in response to antiviral infection will circulate in the body after combating the infection and become active upon again attack) (Yang et al., 2020).

Immuno-enhancers

Vitamin A

Vitamin A either extracted from animal or plant sources, reduces mortality and morbidity and regulates the immune response element and its responses, particularly during different types of infection, including measles, diarrhea, respiratory diseases, malaria, human immunodeficiency virus (HIV) and tuberculosis, by increasing IgG, IgA, lymphocyte count, T-cell response

Table 1. Lifestyle interventions

Lifestyle category	Suggestions
Nutrition	➢ Maintain hydration 2 to 3 l day^{-1} (Monye and Adelowo, 2020) ➢ Adequate and unsaturated food intake includes fish (Omega 6 and Omega 3), avocado, nuts, olive oil, soybeans, canola oil, sunflower ➢ Maintain a healthy body mass index ➢ Limit junk food (Sodas, soft drinks, burgers, salt), saturated fat (cheese, ghee, and lard) and trans-fat consumption ➢ Consume more nutritious food (high in antioxidants and fiber, i.e., whole grains, fruits, legumes) ➢ Nutrient-dense and superfood consumption having nutraceutical properties (*Moringa oleifera*, *Psidium guajava*, *Allium cepa*, *Eucalyptus*, *Curcuma longa*, *Trigonella foenum-graecum*, *Piper nigrum*, *Zingiber officinale*, *Cuminum cyminum*)
Physical activity	➢ Aerobic exercise should be done 200 to 400 minutes weekly for 5 to 7 days with 65 to 75% maximal heart rate intensity. Plus, resistance exercises, including sit-ups and weights for one hour 2 to 3 times a week (Pavon et al., 2020)
Nap and night routine	➢ 7 to 8 hours of restorative sleep should be taken ➢ Reduction in sleep is associated with depressive symptoms (Gupta et al., 2020)
Anxiety management	➢ Limit anxiety by watching the news, stressful drama and current affairs; instead, use a reliable source, the WHO ➢ Consider using stress management techniques, i.e., Yoga (Sajid et al., 2006)

activation, natural killer cell and $CD4^+$ (Semba, 1998). *In vitro* and *in vivo* studies performed on murine RAW 264.7 cells showed that retinoic acid can cope with the disease norovirus by modulating gut microbiota, particularly lactic acid bacteria (LAB). The mechanism involved showed that on interferon (IFN-ß) up-regulation by oral administration of retinoic acid to produce antiviral properties against Nora virus (Lee et al., 2016), vitamin A can shorten the duration of pyrexia, cough and chest infection. WHO technical staff found out that children with vitamin A deficiency are more prone to respiratory illness and vitamin A overdose can cause vomiting, nausea and headache. Moreover, microbiota and vitamin A-rich food, i.e., fruits (mangos and papayas) and animal origin (liver, milk, cheese and eggs), are recommended to support and regulate the immune system and resist infectious diseases.

Vitamin B

Vitamin B complex (B1, B2, B3, B5, B6, B9 and B12) from plants, yeast and bacteria are directly involved in immunological regulations. B1 acts as a cofactor and regulates the trichloroacetic acid (TCA) cycle, responsible for energy generation and pro-inflammation activation of T-cells. B2 will activate and differentiate the immune cells by regulating fatty acid oxidation. B3 will suppress the production of pro-inflammatory cytokines. B5 acts as a cofactor for the CoA cycle and fatty acid oxidation that regulates host immunity. B6 contributes to intestinal immune regulation. B7 is involved in fatty acid metabolism. B9 inhibits the $CD8^+$ T-cell from entering the cell cycle's S phase. B12 contributes to immunity by regulating the natural killer cells and T-cells. B9 (folic acid) can inhibit the enzyme furin associated with viral and bacterial infection and prevent viral entry and activation in the body (Shakoor et al., 2021).

Hernandez et al. (2020) classified vitamin C as an antioxidant that can protect the lungs from respiratory inflammation when infused intravenously to protect from pneumonia caused by a coronavirus. It is a cofactor for many enzymes that regulate important biological functions, immune-stimulatory effect, antioxidant, vasopressin synthesis regulation and antiviral. It boosts the immune system, acts as an anti-inflammatory and removes the alveolar fluid that accumulates. Similarly, H. Chen et al. (2020) observed that combining vitamin C, curcumin and glycyrrhizic acid (VCG) was developed to cope with COVID-19 infection due to the immune and inflammatory response. VCG can potentially regulate innate immune response by acting on toll-like signaling pathways to promote the production of interferons and regulate the inflammatory response. The Go analysis suggested that vitamin C is involved in T-cell activation, platelet activation, homeostasis and blood coagulation. The bioinformatics analysis on the combination of vitamin C and glycyrrhizic acid depicts cell-to-cell adhesion, T-cell activation and response to bacterial invasion and proves that it has a pharmacological mechanism against COVID-19. The results of a study show that all the nutritional interventions of vitamin C should be taken before administration to the hospital as this can support the immune system strongly. It empowers the immune system, directly kills the viruses and decreases the death rate (Saul, 2020). Wibudi (2020) proved by randomized controlled trials that it can reduce the mortality in patients combating coronavirus. Also, the same was tested in Wuhan, China, and worked effectively. It concluded mitigation of symptoms arising from outbreaks by COVID-19 or any other viral infection by vitamin C is possible. Biancatelli et al. (2020) checked the collective effect of vitamin C and quercetin proved effective against COVID-19. It promoted the concept of multi-drug usage to be more effective. Quercetin has a broad range of antiviral properties with benefits that are cost-effective and lack severe side effects. Vitamin C can disrupt the virus entry enzyme replication and support the immune system by regulating IFN, T-cell, phagocytic activity and interleukins.

Arboleda and Urcuqui-Ichima (2020) observed that SARS-CoV-2 can lead to mild to high respiratory syndrome and vitamin D is a natural immune regulator, acts as an antimicrobial against respiratory viruses by up-regulating the antimicrobial peptide. Vitamin D can down-regulate the angiotensin converting enzyme 2 (ACE2) receptor and prevent the SARS-CoV-2 propagation, thus controlling cytokine storm’s pro-inflammatory response. Zhang and Liu (2020) suggested that vitamin D can protect from diseases relevant to immune deficiency and is also involved in regulating immune cells. Likewise, Grant and Baggerly (2020) proposed that higher doses of vitamin D help treat viral diseases. Ilie et al. (2020) observed a negative correlation between levels of mean vitamin D and the number of cases of COVID-19-related mortality. Spain and Italy show a high rate of vitamin D deficiency, being among the lower altitude countries, thus indicating high rates of mortality due to COVID-19 compared to higher altitude countries such as Norway, Finland and Sweden, which show less mortality rate and high immune-regulatory responses to combat COVID-19 (Laird et al., 2014). In a study, Meltzer et al. (2020) showed that the relative risk of COVID-19 positive was 1.77 times higher in patients deficient in vitamin D than in normal. Vitamin D is a secosteroid that acts as an immunomodulatory, antifibrotic, anti-inflammatory and antioxidant action (Ebadi and Montano-Loza, 2020).

Vitamin E

Vitamin E acts as a strong antioxidant, protects T-cells membrane, helps in immune synapsis formation and reduces the duration of viral infection (BourBour et al., 2020).

Selenium

Selenium deficiency can cause oxidative stress to the host and make the body more susceptible to virulent viral diseases. So, in combination with ginseng, it could enhance immunity and prevent free radical production. It shows redox activity against the SARS-CoV-2 virus (S. Zhang et al., 2020; Zhang and Liu, 2020).

Zinc

Kumar et al. (2020) observed that zinc is used as a prophylactic treatment to cure corona disease and play an essential role in the development and maintenance of immune cell. Pyrithione (zinc-ionophores) can inhibit the replication of the SARS-CoV-2 virus.

Iron

Iron plays an essential role in the development and maintenance of immune cells. Iron chelates, ferroptosis inhibitors and hepcidin modulators are recommended for such severe conditions of COVID-19 patients, as mentioned in Table 2 (Edeas et al., 2020).

Risk factors

No one in this pandemic is safe from the COVID-19 virus as it infects everyone. Nonetheless, there are specific groups of people who are more likely to get infected and have severe symptoms due to the disease than others. The reason is that those people have some medical conditions or attributes that make them susceptible to the disease.

Table 2. Immuno enhancers and their antiviral mechanism of action

Immuno enhancer	Mode of action
Vitamin A	Functions to increase IgG, IgA, lymphocyte count, activation of T-cell response, natural killer cells and $CD4^+$ (Semba, 1998)
Vitamin B complex	Regulate pathways of the body, i.e., TCA cycle, CoA cycle, fatty acid metabolism and production of natural killer T-cells (Shakoor et al., 2021)
Vitamin C	Vitamin C can disrupt virus entry and enzyme replication and regulates IFN, T-cell, phagocytic activity and interleukins (Biancatelli et al., 2020; H. Chen et al., 2020; Hernandez et al., 2020)
Vitamin D	Vitamin D can down-regulate the ACE2 receptor and can prevent the SARS-CoV-2 propagation. Can control cytokine storm (Arboleda and Uruqui-Inchima, 2020)
Vitamin E	Vitamin E can enhance T-cell-mediated function and signal transduction in T-cells or indirectly by reducing the production of suppressive factors such as prostaglandin E (PGE2). Thus, it enhances immunity directly and indirectly (Meydani et al., 2004)
Selenium	Redox activity against the SARS-CoV-2 virus (S. Zhang et al., 2020; Zhang and Liu, 2020)
Zinc	Regulates IFNs, cytokine potency and receptor binding. Thus, controls the immune response mechanism (Read et al., 2019)
Iron	Fe^{2+} chelator inhibits DNA and RNA virus replication (Edeas et al., 2020)

Age

Age factor is linked with various diseases such as cardiovascular diseases, respiratory diseases and other conditions that result in weakened immunity. Increased age, along with such diseases or lower immunity, escalates the chances of getting COVID-19 ailment, which results in extreme outcomes such as critical health conditions and even death. Therefore, age becomes a significant risk factor for COVID-19, as several scientific reports have reported it.

D. Chen et al. (2020) studied the clinical characteristics and the outcomes of older patients diagnosed with COVID-19. This study showed the mortality rate was 34.5% in older patients compared to the younger patients, whose percentage was 4.7%. In another study by Sun et al. (2020), the results support that older age raises the chances of death. Older age is also associated with the development of critical illness in case of COVID-19 infection compared to the younger individuals, i.e., admission to intensive care unit (ICU), invasive ventilation, etc. (Liang et al., 2020). Study by Starke et al. (2020) stated the isolated effect of age using the meta-regression technique. Disease outcomes considered for the study included infection severity, such as the risk of hospitalization, admission to ICU, intubation, death and other markers of severe disease due to COVID-19. People with older age with other comorbidities were at 5.2% and 13.4 % more risk of disease severity and death, respectively. After adjusting for important comorbidities (diabetes, hypertension, coronary heart/cerebrovascular disease, compromised immunity, previous respiratory disease, renal disease), only a 2.7% risk increase for disease severity and none was indicated for death. So, ignoring the age-related risk factors, older age poses no danger to the patient in terms of disease severity.

Gender

Morbidity and mortality rate due to COVID-19 disease differs between sexes, as evidenced by several recent reports. Peckham et al. (2020) evaluated reported cases globally from 90 pieces including 46 different countries including United States, adding up to 3,111,714 infected cases using a meta-analysis technique to declare that sex is a risk factor for the SARS-CoV-2 infection and severe outcomes as a result of the infection. It was concluded that male patients had almost three times higher risk of ending up in an intensive treatment unit (ITU) and risk of death than female patients. Study by Jin et al. (2020) focused on gender differences in patients with COVID-19. They concluded that the number of male patients who could not survive COVID-19 was 2.4 times that of female patients. In a study in which one hundred confirmed cases of SARS-CoV-2 from the province of Punjab, Pakistan, were enrolled, it was seen that male patients were 76% more prone to COVID-19 and its severe outcomes than females which the percentage was 24% (Sharif et al., 2020).

Some basic variations in the immune system functioning between men and women appear to be the reason behind the sex bias as reported in the COVID-19 pandemic. Fundamental differences between the two sexes in terms of innate and adaptive immune systems proved beneficial for females in combating COVID-19. Due to females have elevated numbers of $CD4^+$ T-cells (Abdullah et al., 2012), more efficient $CD8^+$ T-cell cytotoxic activity, and increased B-cell production of immunoglobulin compared to males (Hewagama et al., 2009). Other than that, women's bodies make IFN type 1, a stronger antiviral cytokine than men (Webb et al., 2019). Additionally, the rising level of IFN production in females correlates with the concentration of sex hormones and the already present two X chromosomes rather than in males. Sex chromosome constitution is also crucial in disease outcome as it holds a high density of immune-related genes (Laffont et al., 2014).

Changes in the immune system with age also differ between sexes. Males show a decline in B-cells and hastened immune aging as they age (Marquez et al., 2020). This condition also plays a contributory role to the sex bias observed in COVID-19. Along with behavioral changes, socio-cultural differences exist between men and women. For example, the more significant percentage of smokers globally are men and according to new research, smoking is also a risk factor for COVID-19 progression (Patanavanich and Glantz, 2020). Health-seeking behaviors and access to care also may incline men toward access to hospital and ITU admission (Bischof et al., 2020). In a recent study by Silvero et al. (2021), through invariable meta-regression, a link between the male sex and in-hospital death was shown, and it was concluded that the male sex does have a significant effect on mortality in COVID-19.

Ethnicity

Ethnicity is a complex entity composed of genetic makeup, social constructs, cultural identity and behavioral patterns. Certain ethnic groups or people of a specific race within a community are more likely to get infected by COVID-19 and develop severe health conditions than the majority. Ethnicity could be associated with virus spread through cultural, behavioral and societal differences, including lower socio-economic status, health-seeking behavior and intergenerational cohabitation (Pareek et al., 2020). In a study conducted by Izurieta et al. (2020), it was found that in the United States, being the minority and belonging to the specific race puts COVID-19 patients at higher risk of hospitalization and death. Compared to Whites, Blacks, Hispanics, and North American Natives they had a higher probability of dying with a prior COVID-19 diagnosis. Laurencin and McClinton (2020), in their first-of-its-kind study addressing the racial and ethnic disparities, found that Black Americans face more extensive infection and fatality cases compared to their population percentage in connecticut. Raine et al. (2020) performed a comprehensive study to assess the racial and ethnic distribution of COVID-19 outcomes relative to representation in the United States. State-level data from the American Community Survey (ACS) was assessed as representation quotients (RQ) (RQ > 1 is indicative of over-representation of a subgroup, and RQ < 1 shows that the subset is under-represented). They found that in COVID-19 incidence, White people had the highest number of confirmed cases, but the RQ was only 0.484. In the case of Hispanic/Latinx, American Indian/Alaskan Native (AIAN), Native Hawaiian/Pacific Islanders (NHPI) and Black people, RQ was greater than 1, which describes their over-representation. Regarding the mortality rate of each race, the RQ for White people was only 0.808. While for minority races like African American, Asian, AIAN and NHPI, the RQ was 1.792, 0.742, 0.829 and 0.352, respectively. Therefore, it can be concluded that minority races in America had more cases of COVID-19 infections and deaths.

Reasons for minorities getting more prone to COVID-19 include: first, racial/ethnic minority populations have a disproportionate burden of preexisting health conditions such as cardiovascular disease, obesity, asthma, HIV, diabetes, liver disease and kidney disease (Hooper et al., 2020). Second, racial/ethnic minorities and poor people have a lower socio-economic status that is linked with more inferior cell-mediated immunity. Moreover, they have reduced access to medical care, comorbidities, poor diet and life stressors, resulting in their weakened immune system (Dowd and Aiello, 2009). They also live in denser and more crowded places and are commonly associated with public-facing occupations, i.e., services and transportation, which also compromise physical distancing. As Yancy (2020) described, "social distancing is a privilege," and being able to isolate and work in a safe home with complete digital access and not facing financial problems are the privileges not enjoyed by all.

Obesity

Obesity is another significant risk factor as it diminishes the host immunity by a great deal, so people who are obese are at greater risk of COVID-19 disease susceptibility and severity compared to non-obese people. It has been proven by the studies that obesity influences the mechanical and inflammatory aspects of lung functions in a bad way, making obese people an easy target to undergo severe respiratory symptoms and proceed towards respiratory failure (Dixon and Peters, 2018). Besides, it stimulates the chronic activation of the immune system with higher rates of infectious complications. Along with the manipulated immune system, increased receptors for virus invasion, altered pulmonary physiology and prolonged viral shed together make the SARS-CoV-2 infection in obesity complicated (Zhou et al., 2021). In obese hosts, T-cell and B-cell both show reduced effectiveness, escalating the infection vulnerability. More research confirms the abnormality of activation and functioning of $CD4^+$ and $CD8^+$ T-cells, increased IL-5 production, and lower IFN-γ production in people with body mass index (BMI) above 30 kg m^{-2} (Xia et al., 2017).

Research also shows that obese people, after getting an infection end up badly with higher rates of hospitalization, admission to ICU and deaths reported in them compared to non-obese people. Reports suggest that in the United Kingdom, 38% of the patients admitted to ICU were obese (ICNARC, 2020). Similarly, in the United States, among COVID-19 patients, people with BMI > 30 kg m^{-2} were 1.8 and 3.6 times more at risk of getting admitted to ICU than those with normal BMI (Lighter et al., 2020). Considering the facts provided by the scientific reports in France, 76% of COVID patients admitted to the ICU were overweight (Simonnet et al., 2020). In China, it was seen that obese people were at a three-fold more significant risk of severe COVID-19 with a consequent more extended stay in hospital (Gao et al., 2020).

Diabetes

Diabetes is a worldwide health concern, with around 422 million people globally suffering from the disease (WHO, 2020a). In research, diabetes was the second-highest comorbidity in the COVID-19 epidemic. Diabetes worsens the infectious condition, with the patients showing increased morbidity and mortality rate compared to the general population (Tiwari et al., 2011). During the SARS pandemic, among patients who have diabetes, the rate of admission to the ICU, need for mechanical ventilation, and mortality was 3.1-fold more significant than that of non-diabetic patients (Booth et al., 2003). Another study performed by Silverio et al. (2021) showed that diabetes is undoubtedly linked with a higher risk of in-hospital mortality in COVID-19 patients. Chronic inflammation in diabetic patients might facilitate the cytokine storm, which eventually contributes to severe results of COVID-19 disease, even death (Maddaloni and Buzzetti, 2020). Studies showing the biochemical features of the coronavirus patient with diabetes indicate a higher neutrophil-to-lymphocyte ratio (NLR), high-sensitivity C reaction protein, and procalcitonin (Yan et al., 2020). Besides the higher NLR, in recent scientific studies related to diabetic patients of COVID-19, especially among severe cases, a significant minimization in the number of total T-cells and $CD4^+$ and $CD8^+$ T-cell subsets were seen, and they were functionally exhausted, leading to poor immune responses in COVID-19 pathogenesis (Qin et al., 2020). Continuous hyperglycemia in diabetic patients also results in a series of unusual metabolic changes, which elevate the production of superoxide and activation of inflammatory pathways, promoting the dysfunction of the immune system (Tiwari et al., 2011; Hameed et al., 2015). COVID-19 is a respiratory disease that gets worse in diabetic patients because diabetes damages the lungs as it is linked with physiological and structural abnormalities in lung tissues and attenuation in lung function (Teeter and Riese, 2008).

Cardiovascular disease

In the SARS-CoV-2 pandemic, cardiovascular disease (CVD) has been reported as one of the highest comorbidity among coronavirus patients. It has been supported by several studies that preexisting CVD can result in increased vulnerability to COVID-19 attacks and can pose serious health threats with worse clinical outcomes (Li et al., 2020).

In China, in a study that included 191 patients, 30% (48% of non-survivors) of the patients were found to have already present hypertension disease. In contrast, 8% (13% of non-survivors) had cardiovascular disease comorbidity (Zhou et al., 2020). In another study, out of 138 patients, 46% patients had one or more preexisting medical complications. Hypertension 31.3%, cardiovascular disease (14.5%), diabetes (10.1%) and malignancy (7.2%) were reported as the most common coexisting conditions. Also compared with the patients who were not admitted to ICU, patients who needed ICU care had a percentage of cases with comorbidities, including hypertension 58.3% vs 21.6% of those who did not require ICU care, cardiovascular disease 25.0% vs 10.8%, diabetes 22.2% vs 5.9% and cerebrovascular disease 16.7% vs 1.0%. A mortality report published by the National Health Commission of China in March 2020 confirmed that 35% of patients infected with COVID-19 had a hypertension history and 17% had coronary heart disease (Clerkin et al., 2020). The leading mechanisms responsible for cardiovascular complications in COVID-19 include direct myocardial injury in case which the SARS-CoV-2 virus binds with ACE2, a membrane-bound aminopeptidase which is highly expressed in heart other than lungs. This binding can result in a variation of ACE2 signaling pathways, which eventually causes myocardial injury. Acute systematic inflammation, which leads to injury to multiple organs, also makes the COVID-19 condition critical in cardiovascular disease patients (Bansal, 2020). A recent study by Silverio et al. (2021) observed that hypertension was no longer found significant in its relation to mortality after adjustment for age. It does not result in a fatal outcome. Nonetheless, as the knowledge about the COVID-19 disease and its association with other preexisting medical conditions is evolving, there are chances that not all previous results present facts. More research is required in this field to understand COVID-19 fully.

The relevance of learning from COVID-19

Given the shifting nature of pandemics and their potential global effect, we must look beyond the immediate aftermath of COVID-19. Although the epidemic no longer dominates headlines, the lessons it has taught us are crucial in preparing for future outbreaks of equal proportions. This review aims to derive broad ideas that can be used to predict pandemics of a similar sort by looking into the processes and reactions that constituted the COVID-19 era. Recognizing that the essence of this study extends beyond COVID-19, researchers strive to develop transferable and adaptable conclusions to a variety of new infectious disease situations.

Critical assessment and discussion

A review article is more than just a collection of information; it serves as a spark for critical thinking and dialogue. This study goes beyond summarising previous findings. Researchers have threaded a critical appraisal of current knowledge throughout the study, addressing the empirical findings and the conceptual foundations of the themes presented. This study aims to inspire meaningful debate and reflection within the scientific community by challenging assumptions, finding gaps, and investigating the implications of given facts.

This paper highlights the COVID-19 pandemic's lasting importance as a crucible of discoveries, paving the way for more robust pandemic preparedness systems. Researchers transcend the limitations of urgent emergencies by painstakingly traversing the terrain of nutrition, lifestyle variables, risk drivers and non-pharmaceutical therapies, providing a radical path for the arena of pandemic mitigation. A key theme surpasses medicinal solutions' typical bounds: the critical need for overall readiness. Nutrition and lifestyle variables, sometimes neglected in conventional techniques, emerge as powerful moderators of illness susceptibility, highlighting the importance of overall wellbeing as a fundamental pillar of pandemic resistance. The sophisticated assessment of risk drivers yields actionable insights, directing efforts towards focused mitigation consistent with the particular characteristics of emerging infectious diseases. This study, moreover, advocates the critical role of non-pharmaceutical therapies, conclusively establishing their usefulness in pandemic containment. As the globe grapples with the repercussions of COVID-19, these initiatives stand as potent weapons of reaction, capable of containing infection and protecting communities. This appeal for all-hazards preparation is not a solo effort; it invites multidisciplinary collaboration and global solidarity.

The implications of this study ripple beyond academic discourse. They resonate in the corridors of policy formulation, healthcare delivery and societal resilience. As researchers transition into a post-pandemic landscape, this research assumes the mantle of a guiding beacon—a compendium of wisdom that informs collective action. It urges us to embrace the lessons inscribed in the annals of COVID-19, facilitating the emergence of a future where pandemics no longer catch us unawares. In essence, this study serves as a testament to the enduring value of understanding, adaptation and innovation in the face of unprecedented challenges. It crystallizes the knowledge from the pandemic and transforms it into a blueprint for holistic preparedness. As we chart a course through uncertain terrain, this research is a testament to our collective resilience—a commitment to learning from adversity and empowering future generations to stand firm in the face of the unforeseen.

CONCLUSIONS

The findings underscore the necessity of a comprehensive approach that integrates nutrition, lifestyle modifications, targeted risk reduction and non-pharmaceutical interventions. This study serves as a roadmap for enhancing global resilience against potential future pandemics, with a transformative framework that informs future strategies, emphasizing the power of holistic interventions. This study redefines our understanding of pandemic mitigation and paves the way for an era of comprehensive, adaptable and resilient preparedness. This thorough evaluation of the COVID-19 pandemic points to interesting future research and practical applications. Future research can contribute to a more robust and proactive global response to prospective pandemics by harnessing the lessons learned from COVID-19 and embracing a multidimensional strategy beyond pharmaceutical cures.

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