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ANGUISH OWED BY COVID-19 PANDEMIC: NEED OF CONSIDERATION TO BOOST IMMUNITY THROUGH FOOD HABITS AND AYUSH RECOMMENDATIONS

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ABSTRACT: World Health Organization (WHO) designated the COVID-19 or more commonly called Coronavirus disease, a "public health emergency of international concern" on January 30, 2020, and declared it a pandemic on March 11, 2020, which threatens human wellbeing around the world. With no proven pharmacological treatment, therapy (such as plasma, bacteriophage, virophage) drug approved by Food and Drug Administration (FDA) against COVID-19 and the frequent transmission of infection resulting in progression of infected person; made the situation more critical. The critical pandemic situation created by COVID-19 realized that nutrition becomes a priority to boost immune function as what we eat can have severe health impacts and medical consequences. The present assessment focused on enhancing awareness among people to maintain a healthy lifestyle through balanced food, nutrition, and eating habits, and AYUSH recommendations to overcome inevitably caused distress due to pandemic situation.

INTRODUCTION: The whole world faces a very critical situation created by a small tiny entity with single-stranded RNA as genetic material, which contains 29891 nucleotides, encoding for 9860 amino acids; prevalently called Corona Virus Disease (COVID-19) ¹. The single-stranded RNA viruses of COVID-19 encode for four enzymes which is essential for the viral life cycle. This novel strain of the corona family has shown its severity as it enters inside mammalian cells through a collaboration interaction of viral spike glycoprotein and a receptor-Angiotensin-converting enzyme (ACE2) for Severe acute respiratory syndrome coronavirus (SARS-CoV-1) and SARS-CoV-2 and dipeptidyl peptidase 4 for Middle East respiratory syndrome coronavirus (MERS) ².

They are due to the worldwide rapid and exponential spreading of disease caused by COVID-19 and its lethal impacts; World Health Organization (WHO) labelled it as pandemic due to a raised threat to human life. The severity of this zoonotic disease upshot to the pandemic situation, which has long-term impacts on the emotional, behavioural, social, economic and political state of affairs. Variations in COVID-19 severity made the situation more critical to elucidate genomics and genetic pathways linked to susceptibility and transmission of SARS-Cov-2 infection.

The symptoms of COVID-19 identified have resemblance with flu or common cold symptoms, including nasal congestion, shortness of breath, runny nose, sputum production, sore throat, fever, fatigue, body aches, diarrhoea, and also loss of taste, the smell in some cases. Distinct phases of its clinical symptoms include three phases: Phase 1 (Asymptomatic with no chest imaging findings and clinical signs); Phase 2 (Pulmonary with decreased oxygen levels, persistent cough and shortness of breath, blood clotting and Phase 3 (Hyper

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inflammatory with the hyperactivated immune system, Acute respiratory distress syndrom, hypoxia, bronchitis, pneumonia, respiratory failure, shock and other organ failures). According to WHO reports, approximately 80% of individual have been recovered without taking special treatment. However, immune-compromised, older and patients with upper respiratory tract infection are at “high risk” becomes critically ill with more severe symptoms, such as acute respiratory distress syndrome, septic shock, difficulty breathing,

metabolic acidosis, requires special medical treatment. But the rate of such cases is one out of every six people who get infected by COVID-19. According to world meters COVID-19 data updated on May 12, 2021; there were 1,60,340,059 Coronavirus cases with 3,331,779 deaths and 138,118,893 recovered cases reported³. Up until 210 countries and territories worldwide and two international conveyances (based on the United Nations Geoscheme classification) are affected by Coronavirus COVID-19 **Fig. 1**.

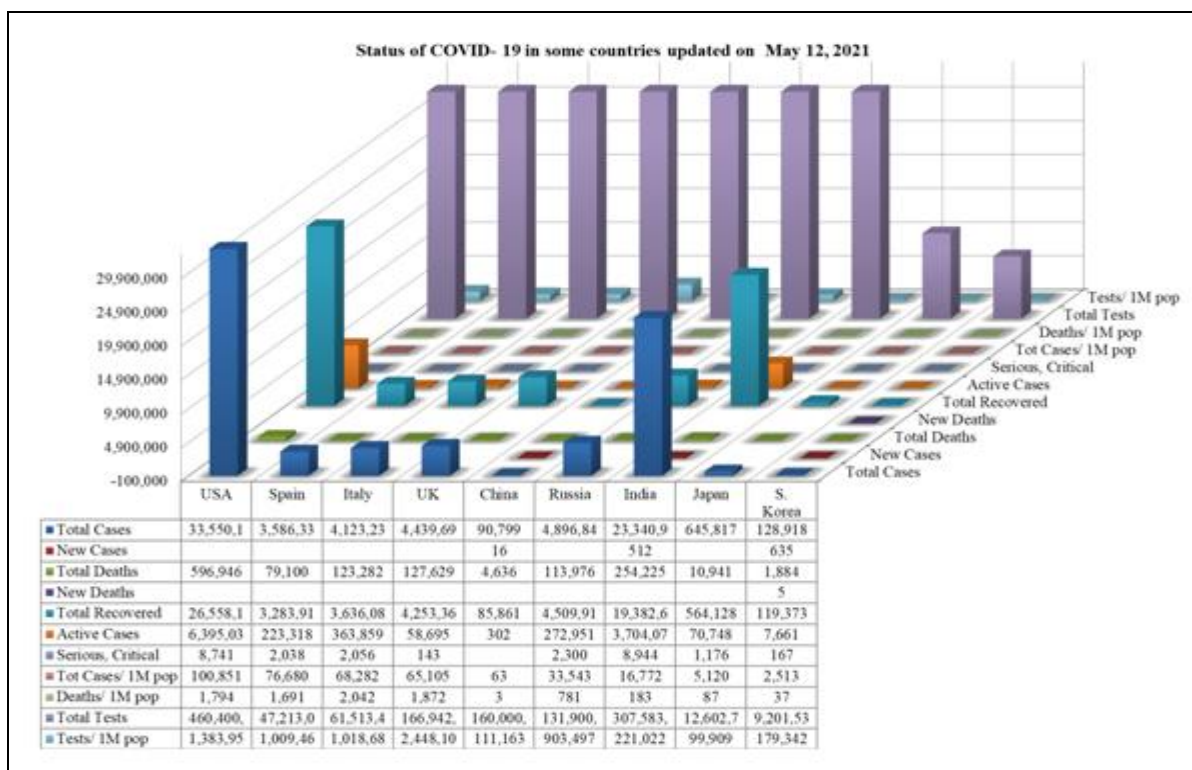


FIG. 1: GRAPH SHOWING CURRENT STATUS OF COVID-19 IN SOME COUNTRIES. (Source-<https://www.worldometers.info/coronavirus/#countries>)

Various agencies like the Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), and the WHO are continuously working on animal/human trials in search of the antiviral activity of several drugs. They regularly post updates regarding the spread of the disease with infected cured and death cases throughout the world and provide suggestions and possible remedies to handle potential infection caused by COVID-19. The Food and Agriculture Organization has suggested in this pandemic situation to follow the regulations of physical distancing along with acceptable hygiene practices as the best protection option for self and adjoining population against COVID-19⁴. The transmission of COVID-19 infection is widespread and mainly

through person-to-person contact. Therefore, the first line of defense to prevent virus transmission is to avoid gathering in groups or crowds of all sizes. Keen-sighting the severity of such a critical situation, most countries have employed a nationwide lockdown and physical distancing regulations to avoid gathering and mass. These regulations have promoted the three most dominating ways to escape from COVID-19 infection, *i.e.* quarantine (for infected person), self-isolation and social distancing. The situation resulting from the conditions mentioned earlier indirectly has a significant impact on people's lifestyle, leading to the shift in physical, social and psychological behaviour and the change in food and eating behaviour. The condition of quarantine

and self-isolation executed shifting consumer preference to local, homegrown ingredients and home-cooked recipes/food items to avoid eating out, which consequently minimizes the risk of having frontage on COVID-19 infections through food. The trend of cooking at home and eating home-cooked food has reduced the transmission vector for coronavirus, for example, food handlers at restaurants and grocery stores. The current pandemic situation has realized that the immune response is vital for the control and resolution of COVID-19. Keeping the above facts in mind, it was planned to carry out a study with a collection of existing data and generation of information to support and boost the immune system via balanced food, nutrition and eating habits, which may further help as a small effort in our campaign against COVID-19. The foundation of good health may always be coupled with the proper functioning of the immune system⁵. We focus on highlighting the

current status of COVID-19 worldwide and shed systematic light on the role of food, nutrition, and eating behaviour and Ayurvedic, Yoga and Naturopathy, Unani, Sidha, and Homeopathy (AYUSH) recommendation on humans' health and wellbeing to fight against COVID-19.

Covid-19 Outbreak and Progression as Pandemic: The outbreak of coronavirus disease by the newly identified β -coronavirus was first reported in Wuhan, China, in December 2019¹. WHO Country Office in China did the first reporting on December 31, 2019; however, there was some previously published literature that has reported the emergence of such symptomatic individuals with an unidentifiable causative agent; before December 2019 and classified as "pneumonia of unknown etiology". The progression of this virus from an outbreak to a pandemic situation **Table 1** is persistent.

TABLE 1: HIGHLIGHT ON PROGRESSION OF COVID-19 OUTBREAK AS PANDEMIC

Date	Place	Causative agent	Progression as	Announced by	Evolution
December 31, 2019	Wuhan, Hubei province, China	Unknown	unexplained low respiratory infections, pneumonia of unknown etiology	WHO Country Office in China	Emergence
February 11, 2020	-	CoV was a "COVID-19," an acronym of "coronavirus disease 2019"	-	WHO Director-General, Dr. TedrosAdhanomGhebreyesus	Outbreaks
January 30, 2020	spread to 18 countries	Covid 19 outbreak	four countries reporting human-to-human transmission	International Health Regulations (IHR, 2005), was declared by the WHO a Public Health Emergency of International Concern (PHEIC)	Epidemic
February 26, 2020,	United States.	Initially, 2019-nCoV and termed as SARS-CoV-2 virus	Because it has shown similarity to the one that caused the SARS outbreak (SARS-CoVs). Major pathogens of emerging respiratory disease outbreaks	experts of the International Committee on Taxonomy of Viruses (ICTV)	
February 28, 2020	-	CoV-created situation is quickly evolving.	COVID-19, the epidemic to the "very high" level	WHO raised the threat to the CoV	
March 11, 2020	outside China	COVID-19	COVID-19 cases have increased 13 times, and the number of countries involved has tripled, with more than 118,000 cases in 114 countries and over (4,000 deaths)	WHO	Pandemic

Etiological Factors of Covid-19 Infection: COVID-19, an enveloped circular virus-containing single-stranded RNA as genetic material belonging to the family Coronaviridae. The subfamily

Orthocoronavirinae includes four genera alpha, beta, delta, and gamma coronavirus. The human coronavirus (HCoV) is associated with alpha and beta CoV **Fig. 2**.

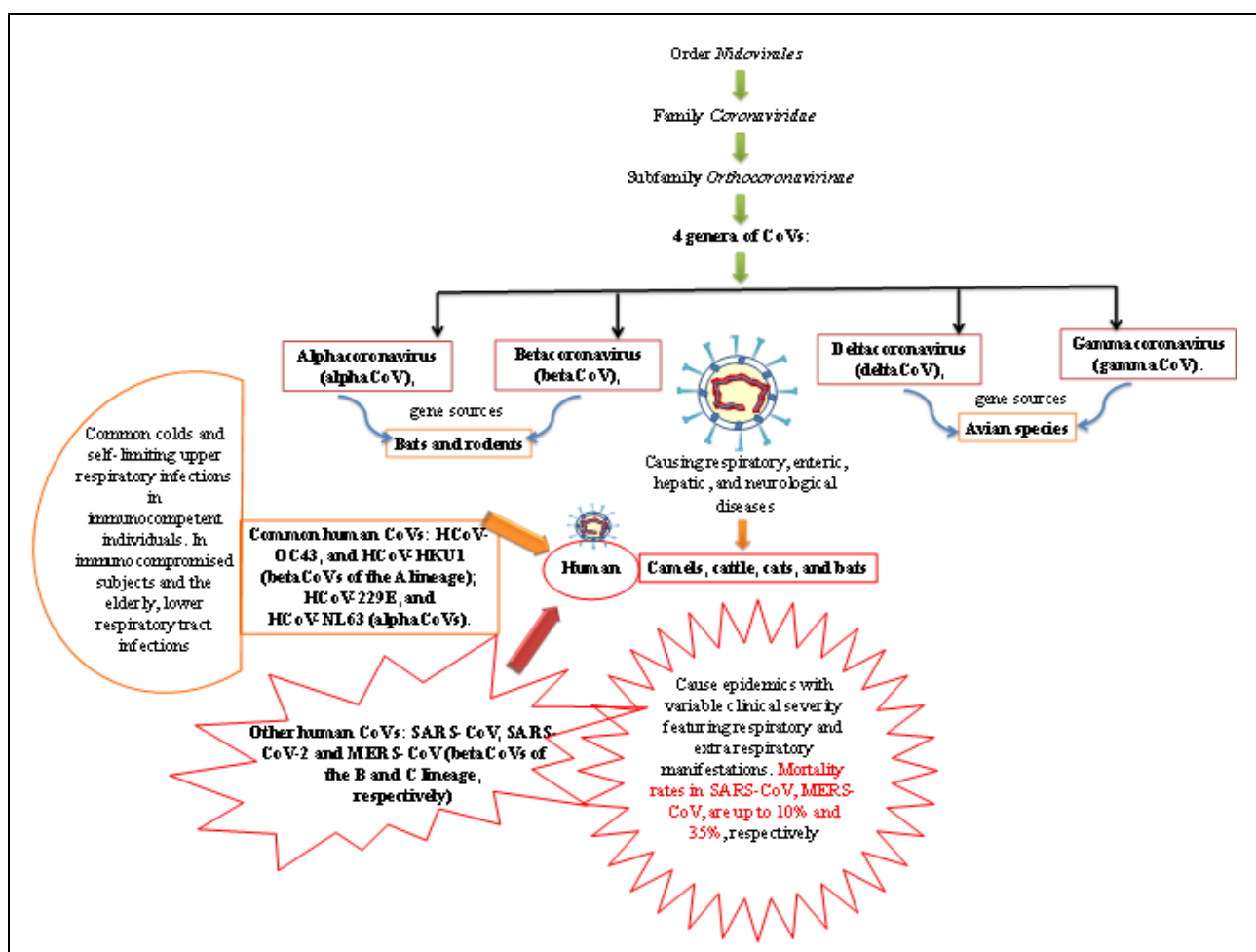


FIG. 2: PHYLOGENETIC DISTRIBUTION OF CORONAVIRIDAE FAMILY MEMBERS WITH ITS ETIOLOGICAL FACTORS ASSOCIATED WITH HUMAN INFECTION

So for a reason, the International Committee on Taxonomy of Viruses (ICTV) has been named the virus SARS-CoV-2. COVID-19 causes infection, including acute respiratory disease similar to the SARS-CoV, using the same receptor site, angiotensin-converting enzyme 2 (ACE2). Clinically COVID-19 transmission is very much rapid from human-to-human utilizing respiratory tract infection resulting in flu-like symptoms having high fever, cough, and fatigue in infected patients and more complicated in some immune-compromised diseased person, aged, pregnant woman and also children.

Treatment Strategy and Preventive Measures Follow-up:

Diagnostic Methods: The clinical diagnosis of COVID-19 is based on nucleic acid detection in the nasal and throat swab sampling or other respiratory tract samplings by real-time PCR and further confirmed by next-generation sequencing. So far, in China, the initial identification of the SARS-

CoV-2 by a viral research institute has already been made, which was based on the morphological observation through classical Koch's postulates by using electron microscopy⁶. Based on the prior experience of SARS-CoV and MERS-CoV generated epidemic, there are some treatment strategies against coronavirus⁷. Most research agencies and laboratories are continuously working on the patent analysis of Coronavirus related biologics and therapies such as therapeutic antibodies, cytokines, and nucleic acid-based medicines targeting virus gene expression and different vaccines type⁸. A diagnostics one-step test, *i.e.* TruenatTM beta CoV test, is also performed to detect the virus at an early age validated by the TruelabTM workstation of the Indian Council of Medical Research (ICMR) as a screening test⁹. According to ICMR, the confirmatory test followed by the RT - PCR test of the throat and nasal swab confirms the diagnosis of COVID-19 infection. Raybiotech also develops another qualitative detection of Coronavirus (COVID-19) IgM/IgG

Rapid Test Kit kit to diagnose novel coronavirus (SARS-CoV-2) by identifying SARS-CoV-2 IgM antibodies in whole human blood from a finger prick. The Government of India has, with the help of the ministry of electronics. IT has launched a Digital Assessment Tools called "AarogyaSetu app", which will help ascertain the people for the risk of infection by the Coronavirus. This app is based on the calculation of interaction with others, using cutting-edge Bluetooth technology, algorithms and artificial intelligence in a smartphone. Once the app is installed, it detects other nearby devices with AarogyaSetu installed. Then, it started calculating the risk of infection based on sophisticated parameters if one or a few of these contacts were tested positive. Some studies also suggested Bacteriophage therapy as an alternative treatment for human disorders¹⁰. Some specific researches are also going on to find out the possibility of bacteriophages or more precisely called virophages (bacteriophages with new capsids) for their antiviral activity against COVID-19.

Probable Therapeutic Options: WHO recommended oxygen therapy, broad-spectrum antibiotics and extracorporeal membrane oxygenation (ECMO) to almost all patients as the first line of treatment¹¹. In more severe and critical cases, the rescue treatment involved convalescent plasma and immunoglobulin G delivery according to the patient requirement and condition¹². Lopinavir/Ritonavir (Protease inhibitors), Chloroquine (9-aminoquinolin), Ribavirin (protease inhibitor), Oseltamivir (neuraminidase inhibitor), Penciclovir/Acyclovir (Nucleoside analogue) are some of the potent antiviral drugs approved for trials against COVID-19 infection¹. Recently, WHO also has taken the initiative and coordinated for repurposing drugs against COVID-19, referred to as 'Solidarity'.

A trial consists of the four most promising therapies in which 90 countries confirmed their participation. Furthermost suitable treatments in this solidarity trial include the clinical trial on the following drug as given below:

1. Remdesivir
2. Lopinavir/Ritonavir
3. Lopinavir/Ritonavir with interferon beta and
4. Chloroquine

The trial will compare four treatment options against the standard of care to assess their relative effectiveness against COVID-19. By enrolling patients in multiple countries, the Solidarity trial aims to rapidly discover whether any drugs slow disease progression or improve survival. Along with who solitary trial INSERM Discovery trials were also in advance with planning randomized, open-label interventions to be conducted very recently. Besides this development of Antiviral vaccines are the priority, and a lineup of studies by different researchers are going on. These antiviral vaccines may fall into one of the following categories: inactive or live-attenuated viruses, virus-like particle (VLP), viral vectors, protein-based, DNA based, and mRNA-based vaccines. Like other CoVs, the virus causing COVID-19 is also sensitive to ultraviolet rays and heat. It can be inactivated by using lipid solvents sc as ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform. COVID 19 vaccination program had been started across the world. Vaccination of COVID 19 was created on January 16 2021, concerning the letter DO No. T22020/14/2020-Imm dated January 14 2021, Government of India, Ministry of health and family welfare, Nirman Bhavan New Delhi, Government of India, was circulated in all states and union territories (UT). In India, two vaccines with their trade name COVAXIN, and COVISHIELD, are approved for emergency uses^{13,14}.

Earlier, the Plant materials such as lectins, tannins, and shikimic acid had shown antiviral activity against the influenza virus. Galactose, glucose, and N-acetylgalactosamine, containing other categories of plant materials, have also been reported for their antiviral action against severe acute respiratory syndrome coronavirus (SARS-CoV) and the feline infectious peritonitis virus¹⁵. One of the studies revealed the possibility of convalescent plasma (CP) transfusion to save severe patients and reported that one dose (200 mL) of CP was abided by ten severe cases of adult followed by maintenance of neutralizing antibodies prominently resulted in vanished viremia in 7 days¹⁶. Apart from this, the main recommendation given by WHO for the prevention of COVID-19 are as follows:

- Avoid nearby contact with infected people (acute respiratory infections)
- Frequent hand-washing (minimum 20sec for soap), especially after direct contact with infected or ill people and their environment.
- Avoid insecure interaction/contact with farm or wild animals.
- Maintain distance with infected people while coughing and sneezing, covering your face with disposable tissues or clothing while coughing and sneezing, and washing hands.
- It was advised to health care facilities that they should enhance standard infection prevention and control practices in hospitals, specifically in emergency wards and departments.

Mitigation Tactics: Balanced Food Nutrition and Eating Habits Against Covid-19:

According to WHO recommendation, the most vital tactics for robust health is proper nutrition and hydration. Balanced diets lean towards healthier and stronger immune systems with reduced risk of chronic illnesses and infectious diseases. As per current ongoing research, COVID-19 has declared a respiratory virus and is not a foodborne disease. No single study has concluded with evidence that this disease may spread through contact with food or food packaging from touching an infected person. However, the virus COVID-19 may survive on surfaces for a certain period. So far, it is strongly recommended and encouraged to wash hands regularly after random intervals, especially after touching frequently handled objects like doorknobs or handles. Researchers suggested one of the reasons for COVID-19 pandemic emergence may be due to the preference and appetite for particular food like pangolin meat, exotic meats *etc.*, in China and Vietnam.

Initially, the COVID-19 epidemic began as rapid animal-to-human infection representing death due to severe atypical pneumonia cases, after wide spreading of COVID-19 in a brief period around 210 countries all over the world; WHO declared it as pandemic and advised to strictly followed the social distancing, Quarantine, self-isolation along with acceptable hygienic practices to reduce the

spread of the virus. As the COVID-19 infection is spread mainly through person-to-person contact at a fast rate, it poses an extra burden on medical resources in developed and developing countries.

Most of the states declared lockdown and quarantined, which is associated with an interruption from work routine and promoting work from home¹⁷. Such situations have created stress due to unbreakable news of COVID-19 infections and death cases results in sleep disturbances; panic food security. Along with this boredom due to paused working, staying at home for an extended period of lockdown and increased monotony most often related to overeating as a consequence of overriding signals of hunger and satiety^{18,19}. These psychological conditions are not suitable for health as they may push overeating, food craving, increased salivation, and continuous seeking /thinking about food, resulting in a higher intake of comfort food²⁰ that are rich in sugar, energy, fats, and carbohydrates. WHO also recommended counselling and psychosocial support to people because proper nutrition and hydration may improve health and immunity, but they are not magic bullets. It is also essential to mention that people suffering from chronic illnesses (suspected or confirmed COVID-19) may require mental support and diet to ensure their good health. It is evident from the literature that no food items, dietary supplements and nutraceuticals can prevent the infection caused by COVID-19. However, maintaining a healthy lifestyle, including a balanced diet with good eating habits, may significantly support and boost a healthy immune system²¹. WHO suggested that adequate and balanced nutrition is vital before, during and after COVID-19 infection²². Therefore, change in eating habits with a healthy eating plan through smart food choice (includes vegetables, fruits, whole grains, and fat-free or low-fat dairy products, lean meats, poultry, fish, beans, eggs, and nuts) help to protect from these health problems.

As depicted in **Fig. 3**, the diet must include all type of food from all five food groups with plenty of fruits and vegetable as a source of antioxidants and fibres, an essential fatty acid source, with limited intake of salt, sugar, and fat, along with plenty of water for hydration.

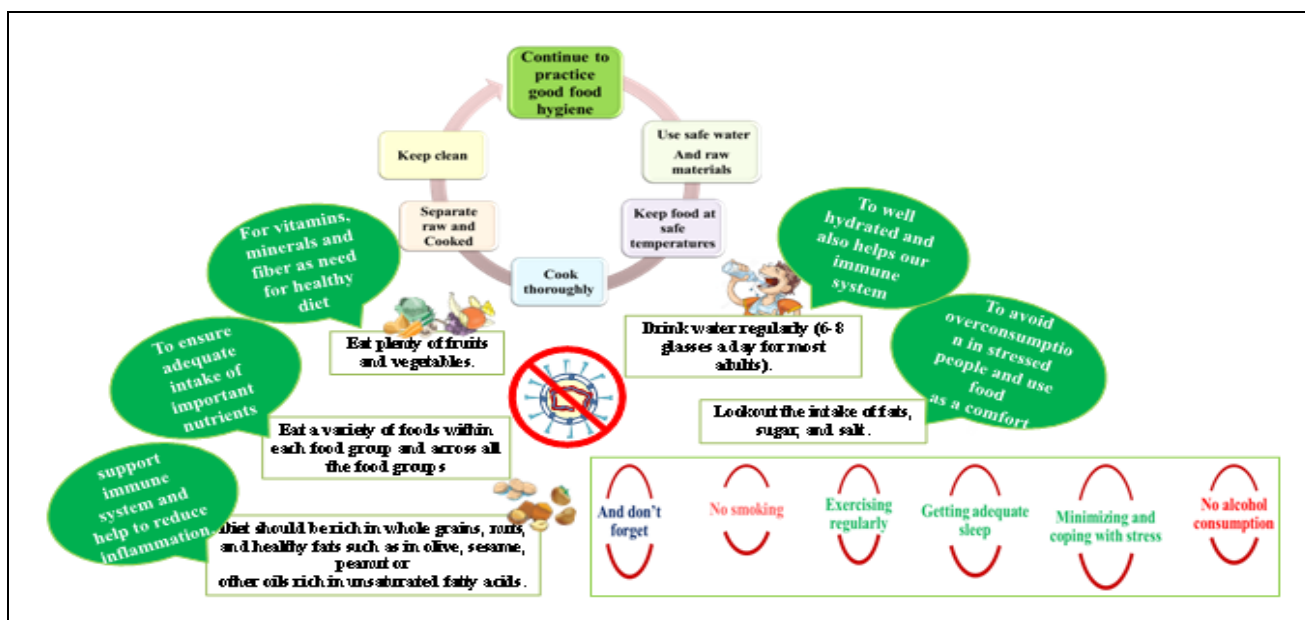


FIG. 3: ROLE OF BALANCED FOOD, NUTRITION AND EATING HABITS BEFORE, DURING AND AFTER COVID-19 INFECTION. (Source- www.emro.who.int/nutrition/nutrition-infocus/nutrition-dvice-for-adults-during-the-covid-19-outbreak.html 3/7)

More consumption of eating sugar, fatty foods, and fried foods will kill the gut bacteria, thereby decreasing serotonin and immunity. As a consequence of reduced satiety and calorie intake regulated by tryptophan, serotonin helps in lowering carbohydrate and fat intake and inhibits neuropeptide Y (the most potent hypothalamic orexigenic peptides)²³. A healthy weight following a low diet may also be vulnerable to significant health risks associated with the emergence of such COVID-19 illness and even death. A balanced diet and good eating habits such as no consumption of alcohol, no smoking, avoidance of stress, adequate sleep, and regular exercise help improve immunity as 80% of immunity cells are present in the digestive tract²¹. By following some small healthy changes in eating habits may result in better health. Some of the required changes in eating routine and their consequences are listed below.

- Don't skip breakfast and have a healthy breakfast-reflecting on meals enhances the feeling of hunger, which will lead to more eating than average at the next meal.
- Diet should be rich in fruits, vegetables-antioxidants help to reduce free radicals.
- Increase preference for Low-fat dairy products (low-fat milk and yoghurt) and steamed or baked food items instead of fried ones- lowers cholesterol level.
- Intake of whole-grain foods- increased Dietary fibre, which helps in improved digestion and bowel motion.
- Intake of milk and milk product before sleeping milk and milk product protein contains the sleep-inducing amino acid tryptophan.
- Eat snacks on a plate instead of the package- control over food intake.
- Chew gum when you cook or free- a reduced temptation to snack.
- Avoid meals high in calorie more than required and enjoy healthy eating as pleasure, avoid eating too fast- for better digestion and absorption of nutrients in the bloodstream.
- Rinse and wash canned fruits and vegetables to remove excess salt or sugar- helps in reducing stressed conditions as it leads to overeating.
- Avoid intake of Comfort foods (sugary foods) - to avoid food craving in boredom generated by Quarantine and self-isolation in lockdown.
- Increased physical activity- energies the body by burning the extra calories.

CoV-2 includes mainly two key host factors, *i.e.* ACE2 and TMPRSS2, which were investigated to determine its unique genetic susceptibility from ~ 81,000 human genomes across different populations. The functional polymorphisms in ACE2 and TMPRSS2 may influence the significantly different incidence and mortality rates among COVID-19 patients from other people ²⁶. Recently a study suggests that TMPRSS2 variants and their resulting expression may have more influence on COVID-19 severity ²⁷.

Along with this, susceptibility to SARS-CoV2 and severity of COVID-19 is also found to be in the association between the genetic variability in Major Histocompatibility Complex (MHC) class I

genes (human leukocyte antigen [HLA] A, B, and C). It was also reported that Specific HLA-B*46:01 gene product exhibits the lowest binding capacity to SARS CoV-2 virulent peptides and represented more severity as individuals with this allele may be more susceptible to COVID-19 disease owing to reduced capacity for the presence of viral antigen to immune cells. In contrast to this, the HLA-B*15:03 encoded protein has the most remarkable ability to present highly conserved SARS-CoV-2 peptides that are probably present among all commonly known human coronaviruses ²⁸ suggested that patients with this HLA genotype probably be more likely to develop immunity. *AyushKwath* herbal constituent found to have some role in increasing the immune response **Table 2**.

TABLE 2: IMMUNE-MODULATORY EFFECTS OF SOME MAIN CONSTITUENT OF AYUSHKWATH

Herbal constituent of <i>AyushKwath</i>	Chemical compound	Immune-modulatory effects	Reference
Sunthi (ginger)	nevirapine, β -sitosterol, 6-gingerdiol, germacrene, methyl-6-shogaol, 6-gingerol, α -linalool, 6-shogaol, gingerdion, zingiberene,	inhibit viral replication; among these the most potent inhibitors of reverse transcriptase (RT) enzyme is β -sitosterol, which is predicted to be used as non-nucleoside reverse transcriptase (NNRTIs) HIV-1 inhibitors	29, 30
Marich(<i>Piper nigrum</i>)	piperine	regulate the balance of the cytokines production of Th1, Th2, Th17, and Treg cells, reduce the accumulation of inflammatory cells, inhibit the expressions of GATA3, IL-4, IL-6, IL-1 β , ROR γ t, IL-17A and TNF- α , increase INF- γ and IL-10 secretions in BALF (Broncho-alveolar lavage fluid) and increase macrophage activation and T and B cell proliferation	31, 32
Dalchini (Cinnamon bark)	cinnamaldehyde, benzaldehyde, cuminaldehyde and terpenes	regulator of monocyte/macrophage-mediated immune responses by inhibition of PI3K, PDK1 and NF- κ B activation of signaling components. Activation of CD29 and CD43 suppress both the production of nitric oxide (NO) and up-regulation of surface levels of co-stimulatory molecules (CD69 and CD80) and pattern recognition receptors (TLR2 and CR3)	33
Tulsi (<i>Ocimum sanctum</i>)	ursolic acid, carnosol, rosmarinic acid, cirsilineol, apigenin, eugenol, and cirsimaritin present in	Increased haemoglobin concentration, enhanced SRBC agglutinin titers, decreased cyclo-oxygenase (CoX)-2 and lipoxygenase (LOX)-5 enzymes activity, suppression of NF- κ B classical pathway, up regulation of IL-2, IFN- γ and TNF- α and down regulation of IL-1 β ; production of SRBC antigen-specific antibodies, representing as major defense mechanism for assessment of T-cell-dependent antibody responses	34, 35

The associating immune-pathogenesis of COVID-19 with immune-modulatory effects of herbs utilized in the preparation of *AyushKwath* may be an alternative; before infection and during the non-severe stage to enhance immune response, safeguarding public health in early recovery with mild symptoms³⁶. Although the dose of each herb is mentioned in API (The Ayurvedic Pharmacopoeia of India), more intensive research, including pre-clinical and clinical trials, needs to be done for the valuation of the safety and effectiveness of such polyherbal formulation.

CONCLUSION: It's today's urge of the pandemic situation to keep our immune system boosted up through balanced nutrition and maintaining a healthy diet along with following regulations of social distancing and acceptable hygienic practices for prevention against COVID-19 infection and its ill consequences. It is urgently necessary to implement more emphasis on intake of healthy food containing immuno-supportive nutrients, balanced diet, diet plan, eating habits, and a positive mindset as the best way to mitigate such negative situations posing towards ill-health impacts. We can only hope if we stay safe and healthy, there will be a lesser chance of getting to the risk of severe medical complications of unintended COVID-19 infection. The Ayurvedic formulations recommended by AYUSH are the reservoir of mostly new structural and chemical diverse compounds and also have high immune-modulatory and protective activities. These have chemical diversity, which might motivate the researchers to develop unique formulation/decoction with scientific validation to identify specific bioactive compounds responsible, their mechanism of action, and ways to regulate the activity of these compounds on COVID-19 related immunological factors. Keen insights over unexplored *in-vitro*, *in-vivo* and clinical studies are needed to explore in search of its potential targeted activities in immunity enhancement against SARS-CoV-2. This can be concluded that if more strong the immunity, there will be less susceptibility to viral infections. According to a famous medical phrase, 'prevention is better than cure.

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written – original draft; reviewed, and edited. Dr. Raghvendra Raman Mishra has to Supervise and corrected. Both authors have read and approved the final version.

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