Nutrition Odds to Even out Corona

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ABSTRACT

The pandemic of coronavirus disease-2019 (COVID-19) has taken the world unaware. Spread of the novel coronavirus, severe acute respiratory syndrome–coronavirus-2 (SARS–CoV-2), has reached a pandemic status. Elderly and people with comorbidities (obesity, type 2 diabetes) are hit the hardest with this respiratory disease. Optimum nutritional status is one of the important forms of defense against the process of existence of new viral pathogens. Nutritional malnutrition (imbalanced intake of macronutrients as well as micronutrients) is rampant, both in developing and the developed world; therefore, it is important to check the nutritional status of the patients for studying the cause of the viral disease. Overall immunity is suppressed in case of micronutrient deficiency since it affects cell-mediated and adaptive immune response leading to irregularity of immune response. Nutrition knowledge and research has widened the horizons of prevention and cure of dreaded virus threats, such as COVID-19. It identifies further progress in basic and clinical research for incorporating the type of foods which can make our immune system strong enough to resist the infections. Enhancement of public health is of utmost concern and this has to be from natural things rather than artificially incorporated.

Keywords: COVID-19, Immunity, Nutrition.

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INTRODUCTION

The pandemic of coronavirus disease-2019 (COVID-19) has taken the world unaware. Spread of the novel coronavirus, severe acute respiratory syndrome–coronavirus-2 (SARS–CoV-2), has reached a pandemic status. Elderly and people with comorbidities (obesity, type 2 diabetes) are hit the hardest with this respiratory disease. Data confirm that in areas where there is an increased consumption of typical western diets (WD) which contain high amounts of refined carbohydrates, simple sugars, and saturated fats and, on the contrary, devoid of fiber and essential micronutrients in the form of vitamins and minerals, these comorbidities are the highest. Innate immunity gets chronically activated by this type of dietary intake thus inhibiting the adaptive immune system which is an important in host defense against virus.¹ A huge network of molecules, cells, tissues, and organs work in a complex setup to form the body's immune system. Age old diseases emerging with new properties of pathogens as well as new diseases are rapidly increasing the world-wide mysterious disease load and coronavirus is one of them. Optimum nutritional status is one of the important forms of defense against the process of existence of new viral pathogens. Nutritional malnutrition (imbalanced intake of macronutrients as well as micronutrients) is rampant, both in developing and the developed world; therefore, it is important to check the nutritional status of the patients for studying the cause of the viral disease.

Some of the immune-supporting nutrients which may change the response of host to the pathogen are important micronutrients in the form of vitamins and minerals,² but these have to be backed by adequacy of all macronutrients in the diet. Three main barriers, i.e., skin, cellular response, and humoral immune response, provide protection to body. Qualitatively as well as quantitatively, various vitamins promote systematic immune processes by regulating T-lymphocytes, antibodies, and cytokines formation. Overall immunity is suppressed in case of micronutrient deficiency since it affects cell-mediated and adaptive immune response leading to irregularity of immune response.

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NUTRITION AND GENETIC MAKEUP IN RELATION TO VIRAL SEVERITY

Except for nutritional status of the host, all other proposed explanations (such as environmental changes, lifestyle changes) regarding cause of the pathogens have been studied. Recent reviews show that there may be a strong influence of host nutritional status not only on host response to the pathogen but also on the genetic makeup of the viral genome. These studies have reviewed that by simply withholding selenium or vitamin E, which are the critical and decisive cellular antioxidants, or by overfeeding prooxidant nutrient, such as iron, the oxidative stress of host animals was increased thus elevating the viral severity and reproducible genome mutations which are found in two RNA's: influenza as well as in coxsackievirus (foot and mouth disease) which further emphasizes that deficiencies in host nutritional status can effect various viral infections.³ Consumption of high saturated fats, typical of a WD, provoke a lipotoxic state activating the innate immunity and inhibiting T and B lymphocyte function in the adaptive immune system due to an increase in oxidative stress. In animal studies, increased macrophage infiltration to lung tissue, specifically in the alveoli was observed by a high-fat diet.⁴ This can be especially important in COVID-19 patients since these patients suffer from high level of lung alveolar epithelial cells infection, inflamed lung tissues, and damage to alveoli in COVID pathology.⁵

Micronutrients, Macronutrients, and Immunity

While vitamins are essential both for natural and adaptive immunity,⁶ almost all vitamins are essential for producing body's antibodies which help in neutralizing the pathogens. Water soluble B vitamins (B_6 , B_9 , B_{12}) and C vitamin enhance cell-mediated response of the immune system via production of cytokines and T-lymphocytes, whereas fat soluble A, D, and E vitamins, in addition to enhancement of cell-mediated immune system (maintaining the structure of the cells in the gut, respiratory tract, and the skin) also help in improving the barrier function of skin epithelium.⁷⁻⁹ Dietary intake according to recommended dietary allowances (RDAs) is recommended to avoid deficiency of these vitamins which suppresses the overall immunity. Recommended dietary allowances for all these vitamins can be easily met if one has the right knowledge of the source of the vitamin and amount required.

Retinol (vitamin A) is found to be rich in oily fish, egg yolks, meats, dairy products, grains, nuts, and oil seeds, whereas its precursor (beta-carotene) is found to be rich in orange and yellow fruits and vegetables, such as carrot, sweet potato, pumpkin, papaya, and mangoes, as well as in leafy greens, such as turnip greens and spinach. Recommended dietary allowance for Indians for retinol is 600 or 4800 $\mu\text{g/day}$ of beta-carotene.¹⁰

Recommended dietary allowance for vitamin E (ce tocopherol) is 7.5–10 mg/day ¹⁰ and one can easily get this vitamin from food sources, such as wheat germ oil, vegetable oils, nuts, and oil seeds as well as green leafy vegetables.

Research shows that supplementing the diet; especially of deficient individuals, with vitamin D; protected against acute respiratory infections (ARIs).¹¹ Therefore, this can be an important point to note in treatment of corona patients since respiratory failure is one of the major outcomes of this disease.

Skin synthesizes the fat soluble vitamin D (also called sunshine vitamin) in the presence of UV radiations. It is also found in small amounts in some foods, such as fish, eggs, and fortified foods, such as milk and butter, but main source remains the sunshine exposure to skin. In case of deficiency, supplementation is a must. Good physical activity on daily basis also assists the body to produce this vitamin. Recommended dietary allowance for vitamin D is 400 μg or 10 IU/day.¹⁰

Among water soluble vitamins which upgrades cell-mediated immune response, important B vitamins like B_6 RDA is 2 mg/day ¹⁰ and rich sources include meat, liver, soybean, peanuts, whole grains, poultry, fish, and eggs. B_9 (dietary folate) RDA is 200 $\mu\text{g/day}$ ¹⁰ and dietary sources include dark green leafy vegetables, broccoli, liver, dry beans, and pulses, whereas RDA for B_{12} is 1 $\mu\text{g/day}$.¹⁰ It is synthesized by bacteria and is present only in animal foods, such as poultry, fish, eggs, milk, and milk products as well as in fortified breakfast cereals. Vitamin C is richly available in citrus fruits, such as Indian goose berry, oranges, and lemon, and in other fruits, such as guava and melons. Fresh raw vegetables should be eaten as salads since most of the vitamin C is destroyed by heat, by exposure of cut vegetables to air and in stale vegetables. Sprouting of grains also enhances vitamin C. Recommended dietary allowance for normal adults for this vitamin is 40 mg/day .¹⁰

Some minerals, such as iron, zinc, and selenium, play an important role in growth and functioning of immune cells. Iron is required in various enzyme regulation reactions important for recognition and targeting of pathogens. It is an essential element for immune system to be developed normally. Iron, when in excess

in the body, has the tendency to elevate the tumor cell invasion and infection development.¹²

Recommended dietary allowance for iron for adults is 17–21 mg/day ¹⁰ from daily diet. Rich sources of iron include cereals especially "ragi" and bajra, green leafy vegetables, pulses, nuts, and oil seeds. Addition of vitamin C by squeezing some lemon juice in vegetables and pulses enhance the bioavailability of iron from the food.

Zinc and selenium have a pivotal role in maintaining the integrity of the skin and mucous membranes along with an important role of antioxidant for combating oxidative stress. It is an important part of white blood corpuscles (WBC) which are the defense team of our body. Deficiency of this mineral makes people more susceptible to flu, cold, and other viral infections.^{13,14}

Recommended dietary allowance for zinc for adults is between 10 mg/day and 12 mg/day and for selenium is 40 $\mu\text{g/day}$.¹⁰ Rich sources include sea food, dried beans, pulses, and nuts.

No single food is recommended over another. Variety is the key. The immunoprotection of many of these nutrients is based on their antioxidant capacity and consumption of one particular food in excess can result into loss of the same. Micronutrient adequacy is met only if all macronutrients are taken in balanced amount. COVID risk factors are worldwide but the vulnerable group seems the developed and the developing nations where there is an increased intake of western dietary pattern consisting of high saturated fats, low complex carbohydrates, fiber, and micronutrients.¹⁵

Energy intake at the rate of 30–35 kcal/kg body weight for a normal person from complex carbohydrates (whole grains, fruits, and vegetables) as well as good quality fats (avoid trans fats found in bakery items and over the counter food products, add healthy fats in the form of nuts and oil seeds as snacks) should be maintained. Protein intake at the rate of 1 g/kg body weight from varied sources (high biological value sources — animal proteins like milk and milk products, poultry and eggs and plant-based mixed protein sources, such as from cereals, dry beans, pulses, and nuts) is mandatory for good muscle mass and overall health maintenance.

Natural Polyphenols

Hesperidin, a natural polyphenol, has been researched to possess COVID-19 fighting properties since it inhibits protease (Mpro).¹⁶ Hesperidin is mainly found in citrus fruits. These fruits are also rich in vitamin C as discussed earlier. Approximate content of hesperidin ranges from 20 to 40 mg in 100 mL orange juice (depending on the variety) and around 15–20 mg/100 mL of lime and lemon juice, respectively.¹⁷

Rutin also exhibits the same properties of inhibiting COVID-19 main protease (Mpro). It is found in wide variety of plants as well as citrus fruits. Rich sources include buckwheat, asparagus, citrus fruits, olives, plums, etc.

Some Functional Foods Also Help in Supporting Our Immune System

Turmeric (*Curcuma longa*) has a yellowish-orange compound called curcumin (diferuloylmethane). In India, turmeric is commonly used in almost every curry made at home. In addition to be known as an anti-inflammatory agent since times immemorial, for the last 20 years, it has been successfully researched that curcumin possesses immunomodulatory properties as well. It has the potency of modulating the activation of T cells, B cells, neutrophils, dendrites, and macrophages. Therefore, the age old reported benefits of having turmeric in diet for its beneficial effects on asthma

in addition to other ailments (arthritis, allergy, atherosclerosis, cancer, etc.) can be contributed in part to its modulatory effect on immune system.¹⁸ Turmeric has approximately 2% of curcumin. Turmeric also contains curcuminoids, demethoxycurcumin, and bisdemethoxycurcumin. Approximately 140 mg of curcumin is available in 7 g of turmeric powder. When piperine (black pepper) powder is added to curcumin, it increases its bioavailability by 2,000%. A dose ranging from 500 to 12,000 mg of curcumin is excellently tolerated.¹⁹

Garlic (*Allium sativum* L.) contains sulfur polyphenols [allicin (diallylthiosulfinate)] which work as anti-inflammatory and antioxidant agents fighting both inflammation and infection, but garlic supplements are not as potent as 2 to 3 fresh garlic pods taken after crushing/slicing to activate allicin.²⁰ Research has proved that garlic treats colds and flu and decreases the chances of becoming sick in the first place as well as lengthening the healthy state of body. It also has the ability to alleviate the symptoms.²¹ Another study confirmed that the severity and duration of cold was reduced significantly in subjects who consumed 2.56 g/day of garlic extract compared to placebo group.²²

Ginger is known to soothe the sore throat and promote wellness since ages but now its antimicrobial, anti-inflammatory, as well as antioxidant properties are backed up by scientific evidence. Science had attributed all these properties to the presence of alpha, beta-unsaturated ketone moiety.²³ There has been wide exploration of the antioxidative properties of ginger and its components in various *in vitro* and *in vivo* tests. Animal studies suggest ginger to be as potent antioxidant as vitamin C.²⁴ Ginger has the potential to treat various diseases through its immune nutrition and anti-inflammatory responses. When body's defense is strengthened via elevating its antioxidant status, it creates a protection against many diseases.²⁵ It is best to take ginger in fresh form in morning cup of hot water/lemon tea or can be grated in a meal or had thinly sliced as a part of salad. One to three grams of ginger/day are well tolerated. Taking ginger in fresh form has an edge over dry ginger since studies have shown its effectiveness in blocking viral attachment and internalization against plaque formation on epithelium of airway prompted by human respiratory syncytial virus (HRSV).²⁶

European Society for Clinical Nutrition and Metabolism (ESPEN) Nutritional Considerations in Individuals at Risk or Infected with SARS-CoV-2

Evaluation of nutritional status before starting the general treatment is mandatory.²⁷ Nutritional guidelines for patients at risk/infected with coronavirus are that first and foremost they have to be checked for malnutrition. Research has highlighted that 55% and more of the geriatric patients admitted in hospitals are malnourished. Malnutrition is a major indicator of the survival of medically and surgically treated patients in intensive care units (ICUs) and is an independent risk factor of increased risk of 28-day mortality in critically ill patients.

Therefore, objective and subjective measurements, such as current weight and height, body mass index (BMI), unplanned weight loss, acute disease effect (which means that the person is acutely ill and has no nutritional intake or likelihood of no intake for more than 5 days) are of importance. This can be performed through MUST criteria or NRS-2002 criteria.^{28,29}

Obese patients should also be screened with similar criteria for underweight individuals since they may be unable to preserve

skeletal muscle mass and balanced body composition. Variation in morbidity and mortality age due to influenza is mainly dependent on response of cellular and humoral immune system, on genetics and nutrition.³⁰ Polymorbidity, i.e., presence of two chronic diseases (e.g., diabetes and heart disease) in an individual, is a typical indication of high nutritional risk. That is why obese persons with chronic disease as well as advanced age are at risk of lower muscle mass as well as function. These individuals must be included for malnutrition check.

Second, optimization of nutritional status through professional dietary counseling is a must.

Energy intake of 30 kcal/kg body weight for severely underweight poly-morbid patients as well as for older patients should be built up gradually from their present nutritional status and physical activity. This energy will come from major sources, such as carbohydrates and fats, at the ratio of 70:30 when there is no respiratory deficiency and 50:50 for ventilated patients, respectively.

Protein intake of 1–1.2 g/kg body weight per day but individually adjusted according to age, physical activity, disease status, and tolerance should be emphasized to preserve and prevent muscle mass, weight loss, minimize hospital stay, and improve functional outcome.^{31–33}

For macronutrient adequacy, oral nutrition supplements (ONS) need to be used when patient is not able to fulfil the requirements from kitchen diet. Reaching the nutritional goal is very important for recovery. Calculated doses of the supplement can be administered as a snack or main meal to optimize the energy and protein intake.

Vitamin and mineral supplementation becomes a must in case of malnutrition and deficiencies. Therefore, calculated doses of vitamin A, D, E, B complex, C, zinc, iron, and selenium should be administered to the corona patients. Supplementation with omega 3 has also shown beneficial results.

European Society for Clinical Nutrition and Metabolism experts suggest that optimizing the micronutrient and micronutrient intake through diet and/or supplementation maximizes general anti-infection nutritional defense.^{27,31}

For non-intubated ICU patients to fulfil the targeted macronutrient goals, ONS can be considered first and then enteral nutrition (EN) if ONS are not successful in being tolerated or accepted. If there are difficulties in administering nutrition through EN, then peripheral parenteral nutrition is advised. Ignoring adequacy of calorie protein optimization may result in deterioration of nutritional status and further complications. Assessment for nutritional adequacy when the patient is on ONS or EN is a must.

For Intubated ICU Patients I

Nasogastric (NG) EN should be started; for patients with gastric intolerance/after prokinetic treatment/at high-risk for aspiration, post-pyloric feeding should be there. Target should be not more than 70% of energy expended should be administered in the early phase of acute illness. This is called hypocaloric nutrition. Gradually, it may be increased to 80–100% after 3 days. Protein at the rate of 1.3 g/kg/day can be administered progressively during critical illness.

For Intubated ICU Patients II

Enteral nutrition should be delayed in case of uncontrolled shock and unmet goals of tissue perfusion and hemodynamic situations, uncontrolled acidosis, hypoxemia. Low doses of EN may be started with 30% of the measured energy expenditure as soon as the above-mentioned issues are start resolving and then increased to

50–70% as the parameters progresses and finally to 100%. Targeted protein intake is 1.3 g/kg/day which should be achieved by day 3–5. Administering omega 3 fatty acids via EN may improve oxygenation. Vigilance about electrolyte (sodium, potassium, phosphorus, and magnesium) as well as triglyceride monitoring is a must.³⁴

Positive correlation between nutritional adequacy and long-term outcome in critically ill patients requiring lengthy mechanical ventilation has been proved and patients receiving more than 80% of targeted energy have shown a significant lower mortality.³⁵

Long-term Nutrition-dependent COVID-19 Effects

Recovered COVID-19 patients may lead to an upthrust of medical conditions which are chronic in nature and a chronic disease onset due to faulty dietary habits of a consuming imbalanced macronutrients (high fat, simple carbohydrate, low protein) devoid of essential micronutrients and antioxidants. Long-term effects even after COVID-19 recovery are warned, as data suggest that past viral pandemics, such as influenza, have triggered dementia in the elderly population since inflammatory events may provoke a constant neuroinflammatory response in vulnerable group of population.³⁶ Long-term lung damage can also occur. Therefore, optimum intake of all nutrients is a must and should be monitored to boost immunity and to combat the challenges of the immune system, such as COVID-19.

DISCUSSION

COVID-19 seems to be a replica of pandemic outbreaks of SARS in 2002 to 2004 and Middle East respiratory syndrome (MERS) from 2012 until now which also presented with early symptoms of cough and fever leading to mortality significantly in vulnerable population, i.e., in individuals with compromised immune system, with comorbidities and the older population.³⁷

Intake of micronutrients backed by balanced macronutrients can boost immunity. Vitamins and minerals aid as immune boosters for the body and help in defense against virus. Water soluble vitamin B and C helps to repair tissues as well as makes lower respiratory tract less susceptible to infections^{38,39} as well as enhance cell-mediated immune response. Rich sources of vitamin C are also rich in polyphenols, such as hesperidin and rutin.

Fat soluble vitamins, such as A (retinol, retinoic acid and beta carotene), D, and E, boost resistance to viral infections. In cattle study, supplementing with vitamin D and E boosted resistance to COVID-19.⁴⁰ In another study, it was proven that supplementing with oral or intravenous vitamin E may support both the resistance and recovery from SARS-CoV-2, SARS, and MERS infections.³⁷

Any malnutrition in the form of over/undernutrition of important nutrients have to be checked for and is of utmost importance both in prevention and cure of COVID-19 symptoms. Optimizing macronutrient intake in the form of energy (carbohydrates and fats) and proteins to RDA's adjusting according to the nutrition status of the individual is a must. Micronutrients like vitamin and minerals which form a defense of our body against infections and diseases have to be ingested in age and nutritional status appropriate amounts according to RDA. If required intake of all these macronutrients and micronutrients can be optimized via nutraceuticals and supplements to improve nutritional status of the patient and help in fighting the disease and boost the immunity. Refrain from consuming western dietary pattern loaded with saturated fats, sugars, and devoid of fiber and essential vitamins and

minerals, since this type of diet leads to obesity as well as essential nutrient deficiencies. In one of the studies, assessment of food perceptions which led to unhealthy eating among obese adults was surveyed and it was found out that wrong perceptions about what is healthy and what is believed to be healthy and consumed may be a major contributing factor toward overweight and obesity.⁴¹ Therefore, right nutritional knowledge and awareness about the quality of food one is feeding his body is a must and an important step in nutritional assessment. Different nutritional societies like American Society of Parenteral and Enteral Nutrition (ASPEN), European Society of Parenteral and Enteral Nutrition (ESPEN), and Indian dietetic association (IDA) are emphasizing on the need for optimum and timely nutrition support at every stage of the disease for COVID-19 patients. Therefore, nutritional status as well as care is pivotal in determining both short-term and long-term outcomes of COVID-19 patients.

CONCLUSION

Nutrition knowledge and research has widened the horizons of prevention and cure of dreaded virus threats, such as COVID-19. It identifies further progress in basic and clinical research for incorporating the type of foods which can make our immune system strong enough to resist the infections. Enhancement of public health is of utmost concern and this has to be from natural things rather than artificially incorporated. Therefore, an age old saying "we are what we eat" held true and will hold true in nutrition research. The comprehensive resources of research will be indispensable for further nutrition and disease relation investigations.

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