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Balanced nutrition is needed in times of COVID19 epidemic in India: A call for action for all nutritionists and physicians

Diabetes (India), National Diabetes Obesity and Cholesterol Foundation (NDOC), and Nutrition Expert Group, India

1. Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) epidemic has resulted in significant morbidity and mortality worldwide [1]. A particularly intriguing question is why some individuals get severe coronavirus-19 infection (COVID19) disease while others do not. Further, mortality is high in some countries and ethnicities and not in others [1]. It is now known that old age, presence of comorbidities (diabetes, obesity, hypertension, coronary heart disease, immunocompromised states, etc), lend increased predisposition to severe disease and mortality [2–4]. However, an individual's own physiological status in context of COVID19 remains poorly researched. Could 'low' immunity status of an individual not known to have immunosuppressive disease cause COVID19? Could dietary factors play an important role to increase immunity and resist such infections? The latter is the most debated and least understood issue. In the following sections we discuss these issues in detail, provide a summary of pertinent knowledge in the table, and request all nutritionists and physicians to proactively discuss these issues with the patients.

Dietary intake in urban India has been repeatedly shown to be erratic and imbalanced, influenced by commercial and market forces, easy availability of energy dense and processed foods, and socio-economic factors [5,6]. As a consequence, diets are high in carbohydrates, simple sugars, saturated fats, trans fats, and low in fibre, protein, fruits and vegetables [5–8]. This has led to a rapid increase in obesity and type 2 diabetes mellitus [9–11], two prime risk factors leading to high mortality due to COVID19. It is important to note that during the National lockdown throughout COVID19 epidemic, some lifestyle habits have changed majorly, particularly increased consumption of poor-quality diets [12]. During this time, poor quality diets and decrease in physical activity have caused weight gain [12] and increased predisposition to type 2 diabetes [13].

Much attention has been paid to drugs and vaccine development for COVID19, however, research about diets is far from

satisfactory [14]. Research in this area has lagged during COVID19 epidemic since it is difficult to carry out randomised controlled trials keeping diet as a primary intervention, and due to presence of multiple and fast changing confounders, including use of multiple drugs in COVID19 patients. The discussion below is evidence based. It is to be noted that much of studies on diets in context of infections and immunity has been done preceding current SARS-CoV-2 pandemic. Discussion regarding nutrition during times of COVID19 is being presented in following four groups of individuals/patients; in population not inflicted with COVID19, in patients with mild COVID19, in patients with co-morbidities and COVID19, and in severely sick patients with COVID19 (Table 1).

Diet in patients not infected with COVID19 infection, having mild COVID19 as well as those who have recovered from COVID19 infection should be balanced. It is reasonable to suggest that all individuals should continue to follow principles of healthy diets, and specific recommendations about consumption of sugar, salt, refined carbohydrates, edible oils, saturated fats and trans fatty acids, total dietary fibre, processed and canned foods [15–17]. Diets which require major changes in macro- and micronutrients and prolonged fasting (e.g. ketogenic diets, intermittent fasting) must be avoided during this time. There is some research which supports that specific foods and dietary nutrients may decrease risk of viral infections. In this context proteins, vitamins, minerals, trace elements, prebiotics, probiotics, omega-3 polyunsaturated fatty acids and other specific nutrients have been researched, but direct research on COVID19 patients are lacking. In the following paragraph we summarise the role of some specific nutrients vis-a-vis immunity.

Intake of certain nutrients may be the reason behind variations to susceptibility of individuals or populations to COVID19. In this respect, the effect of some nutrients on angiotensin-converting enzyme (ACE2) receptor, which facilitates entry of SARS-Coronavirus-2 to human cells, needs further discussion. Theoretically, any inhibition of ACE enzyme would lead to changed metabolic pathways which has potential for lung protection. Broccoli protein hydrolysate has shown to have angiotensin-converting enzyme (ACE) inhibitory activity *in vitro* and hypotensive effect *in vivo* [18]. Some dairy products, eggs etc. may also have capacity for ACE inhibition [19], while saturated fat increases ACE levels [20]. Cabbage contains precursors of sulforaphane, which is an active natural

Corresponding author. Anoop Misra, National Diabetes, Obesity and Cholesterol Foundation (N-DOC), Diabetes Foundation (India), and Fortis CDOC Hospital for Diabetes, Metabolic Diseases and Endocrinology New Delhi, India.

Table 1
Key nutrition recommendations according to category of patients.

Category of patients	General Food groups	Macronutrients	Micronutrients/Vitamins
Individuals not inflicted with COVID-19/patients with mild COVID-19	<p>Recommended:</p> <ul style="list-style-type: none"> Fruits, vegetables, legumes (e.g. lentils, beans), nuts and whole grains e.g. unprocessed maize, millet, oats, wheat, brown rice or starchy tubers or roots such as potato, and foods from animal sources (e.g. fish, eggs, milk meat). Daily: 2 cups of fruit (4 servings), 2.5 cups of vegetables (5 servings), 180 g of grains, and 160 g of non-vegetarian foods (fish, lean meats, and poultry) Snacks: choose raw vegetables and fresh fruits rather than foods that are high in sugar, fats, or salt. Increase foods with probiotics (e.g. curds) Choose healthy oils with high monounsaturated fatty acids and polyunsaturated fatty acids (e.g. olive, canola, mustard, soybean, etc.) Adequate energy intake to maintain ideal body weight. Increase hydration particularly when fever or gastrointestinal upset occurs. <p>Avoid:</p> <ul style="list-style-type: none"> Saturated fats (choose healthy oils) and sugar rich foods. Processed foods. Extreme diets (like ketogenic diets, intermittent fasting, religious fasting etc.) <p>Inadequate Research:</p> <ul style="list-style-type: none"> Fermented foods Low purine diets Fish oils Dietary magnesium 	<p>Proteins:</p> <ul style="list-style-type: none"> High-quality sources of protein include red meat, poultry, and dairy products eggs, chicken, fish, quinoa, soybean 1 g protein per kg body weight per day in older persons; the amount should be individually adjusted with regard to nutritional status, physical activity level, disease status and tolerance. <p>Other macronutrients: As per guidelines and underlying disease status (e.g. diabetes)</p>	<ul style="list-style-type: none"> Zinc: <ul style="list-style-type: none"> Seeds: pumpkin (<i>kaddu</i>), flaxseeds (<i>Alsi</i>), chia seeds, Other foods: yoghurt (<i>dahi</i>), kidney beans (<i>rajmah</i>), oats, nuts like almonds (<i>badam</i>), egg, lentils (<i>dals</i> like <i>moong/masoor</i>) etc. Selenium: whole wheat flour, green gram dal (<i>moong dal</i>), eggs, chia seeds, nuts and seeds, mushrooms, sardines, cottage cheese (<i>paneer</i>), brown rice (long grain). Vitamin C: Indian gooseberry (<i>amla</i>), citrus fruits, such as, limes (<i>mausambi</i>), oranges and lemons, guava, green chillies, tomatoes, green vegetables like broccoli etc. Vitamin A: Spinach, carrot, red peppers, papaya, mangoes, broccoli, apricots (<i>khubani</i>) etc. Vitamin D: Mainly derived through sunlight exposure for 15–20 min between 11 and 2 PM with good body part exposure, and also available as supplement.
Severely sick patients with COVID-19/patients with co-morbidities and COVID-19/Hospitalized patients with COVID-19	<ul style="list-style-type: none"> If patient can take orally, and taking organ functions in consideration, diets outlined as above. Oral nutritional supplements (ONS): Should be used whenever possible to meet patient's needs, when food fortification is not sufficient to reach nutritional goals, In intubated and ventilated ICU patients, enteral nutrition (EN) should be started through a nasogastric tube. In ICU patients who do not tolerate full dose enteral nutrition (EN) during the first week in the ICU, initiating parenteral nutrition (PN) should be weighed on a case-by-case basis. PN should not be started until all strategies to maximize EN tolerance have been attempted. 	<p>Oral Nutritional Supplements:</p> <p>ONS should provide at least 400 kcal/day including 30 g or more of protein/day and should be continued for at least one month.</p> <p>Enteral Feeding:</p> <ul style="list-style-type: none"> For non-obese critically ill patients, the recommended amount of energy target of 25–30 kcal per day/day. Low dose feeding is recommended initially reaching the target over 3–7 days. <p>Other macronutrients in critical illness:</p> <ul style="list-style-type: none"> 1.3 g/kg body weight protein equivalents per day should be delivered progressively Fat: carbohydrate ratio should be between 50:50 for ventilated patients. 	<ul style="list-style-type: none"> Micronutrients should be replaced whenever possible through oral nutritional supplements, enteral and parenteral nutrition. Inadequate research: <ul style="list-style-type: none"> High dose intravenous Vitamin C supplementation. Fish oils/omega-3 polyunsaturated fatty acid lipid emulsion infusion

Adapted from Refs. [15,16,30,36,41,42]. For details, please see text.

These are general guidelines, and must be adapted to locally available nutrients, supplements, and availability of hyperalimentation formulas. All diets must be individualised based on physical, biochemical, and disease types and severity. For detailed recommendations on each nutrients or ICU-based nutrition above references would be useful. Many of these food groups and nutrients have not been adequately researched in patients with COVID19.

activator of nuclear factor (erythroid-derived 2)-like 2 (Nrf2), which influences angiotensin II receptor type 1 axis. Fermented vegetables contain many lactobacilli, which are also potent Nrf2 activators [21]. These authors point out that populations in Eastern Asia, Central Europe or the Balkans eat large quantities of fermented foods, which has implications to COVID19 related mortality [21]. Clinical benefits of these foods in context of COVID19 are yet to be proved.

There is no doubt that protein deficiency must be avoided. Protein

undernutrition can cause anaemia, vascular dysfunction, and impaired immunity. Protein intake must be adequate even in healthy elderly since low albumin levels predict increased mortality [22]. Research on micronutrients and minerals regarding immunity is a continuing area of interest. Vitamin C has been shown to be severely depleted in critically ill patients at admission, and more so in patients with sepsis. In such patients mega doses (in grams) are required [23]. Importantly, pneumonia and other respiratory infections are commonly seen in

severe vitamin C deficiency [24]. There is some evidence that Vitamin C may reduce infections, vascular injury and inflammation in acute respiratory distress syndrome [24, 25]. It is possible, but not proven, that vitamin C status is severely low in COVID19 associated pneumonia, however, more research is needed. Probiotics have been shown to decrease growth of pathogenic bacteria, decrease inflammation and enhance immunity. In a Cochrane review [26], and other studies [27] probiotics were shown to decrease upper respiratory infections through their effect on the gut lung axis [28]

Role of several other nutrients and food constituents like Vitamins (E, B) Carotenoids, minerals (Fe, Zn, Mg, Cu, Se), and polyphenols in immunity have been suggested because of their effects on inflammatory cascade, antioxidant activities and effects on nitrous oxide signalling pathways [25] (Table 1). Recent data on status of vitamins B₁, B₆, B₁₂, D (25-hydroxyvitamin D), folate, selenium, and zinc levels are available in 50 hospitalized Korean patients with COVID-19. Among these, 76% patients were vitamin D and 42% were selenium deficient, while other vitamin and mineral deficiencies were not present [29]. In an comprehensive review of 662 studies, Jayawardena et al. [30] concluded that vitamins A and D showed a potential benefit in viral diseases, particularly in people who are deficient. Vitamin D has a role in immunomodulation, and its deficiency has been shown to be correlated to mortality in COVID19 [31], however, there are currently no intervention trials. Among trace elements, selenium and zinc have also shown favourable immunomodulatory effects in viral respiratory infections [30]. Regarding the former, sodium selenite, a most common water soluble selenium compound, can oxidize thiol groups in the virus protein disulfide isomerase resulting in its inability to penetrate the healthy cell membrane [32]. In this context, it is important to note that selenium deficiency was shown to be associated with increased mortality in patients with COVID19 [33]. Zinc deficiency is common worldwide, and such individuals have an increased risk of acquiring viral infections such as human immunodeficiency virus and hepatitis C virus [34]. In Vero-E6 cells, zinc inhibited SARS- coronavirus RdRp template binding and elongation [35]. However, its role in adult pneumonias or COVID19 has not been proven. Fish oils have some role in boosting immune functions, and decreasing inflammation and thrombotic events [36,37] Interestingly infusion of omega-3 fatty acid lipid emulsion in critically sick patients with sepsis was associated with improved survival [38] but research on patients with COVID19 is lacking. A few researchers have suggested that coronaviruses use purine nucleotides which could promote RNA synthesis [39], hence low purine diets may be beneficial [27]. Interestingly, curcumin has been shown to bind to target on the SARS-CoV-2 receptor [40].

When individuals have severe COVID19 infections, marked nutritional deficiencies may rapidly occur due to increased energy expenditure (fever, mechanical ventilation), decreased intake (loss of appetite, nausea, vomiting, diarrhoea), accelerated metabolism and reduced synthesis of nutrients (e.g. proteins). It is important that such malnutrition is recognised quickly (one can resort to screening scores for malnutrition risk), particularly in vulnerable populations (e.g. elderly, those with multiple co-morbidities, cancer etc.) and given adequate importance and treated [36]. This could be achieved by oral nutritional supplements, enteral feeding with nasogastric tube, and parenteral nutrition (Table 1) [15, 16, 30, 36, 41, 42]. Medical nutrition therapy should be instituted as soon as possible after intensive care unit (ICU) admission [42]. It is important that feeding formulas contain balance of macro- and micro-nutrients. Details of intake of energy, protein and other nutrients are beyond purview of this article and other reviews should be referred [36][41, 42]. In hospitalized patients, maintaining good protein intake is important to avoid hypoalbuminemia. Specifically, albumin levels may decrease rapidly due to pre-existing poor nutritional status; inflammation, decreased production by liver, and acute severe catabolic state. Several studies show

that low albumin levels in hospitalized patients lead to increase in mortality [43–45], morbidity, ICU stay and resource utilisation [44]. Acute kidney injury, a known complication in patients with COVID19, when complicated with hypoalbuminemia, may further increase mortality as shown in a meta-analysis [46]. Controlled trials also show reduced complications when serum albumin level is adequate [44]. In a recent scoping review (four studies in patients with ventilator-related pneumonia and acute respiratory distress syndrome, and the other 4 in patients with ventilator-associated pneumonia), intravenous ascorbic acid, intramuscular cholecalciferol, enteral and intramuscular vitamin E, enteral zinc sulphate, and oral and parenteral glutamine were given as interventions. Most (6/8) studies did not have baseline status of the nutrient of interest. The authors state it was not possible to evaluate efficacy of such interventions because of inadequate baseline data [47].

In the absence of clear and robust evidence showing efficacy of specific nutrients and minerals, it is best practice to rely on traditional dietary advice with enhanced servings of proteins, local and seasonal fruits and vegetables, overall rounding off to have a balanced diet [47]. (Table 1). We believe that the above knowledge and discussion on nutrition in COVID19 will enable physicians and physicians to disseminate this knowledge effectively. Finally, a *call for action* by the nutritionist and physician community to proactively discuss and implement healthy dietary practices and appropriate nutrition in all individuals and admitted patients with COVID19 is crucial at this time.

Steering committee: SR Aravind, Banshi Saboo, and Anoop Misra.

Conceptualisation, drafting, editing and finalisation: Anoop Misra.

Coordination, drafting of table, editing and finalisation of draft: Mrs. Bhavya Arora.

National Advisory Committee (Surnames in alphabetical order): Agarwala Anuja (New Delhi), Bajaj Meenakshi (Chennai), Deshpande Neeta (Belgaun), Gulati Seema (New Delhi), Joshi Shilpa (Mumbai), Nambiar Vanisha (Vadodara), Madan Jagmeet (Mumbai), Puri Seema (New Delhi), Salis Sheryl (Mumbai), Sharma Rekha (New Delhi).

Review of draft and editing (surnames in alphabetical order): Atrey Shubhra (New Delhi), Bhardwaj Shruti (Ahmedabad), Bhanot Shubhda (New Delhi), Bati Diya (New Delhi), Chawla, Purvi Shroff (Mumbai) Bansal Chetna (New Delhi), Chakravarti Ipsita (Kolkata), Canday Eileen (Mumbai), Dharmatti Geeta (Pune), Datta Rupali (New Delhi), Dutta Koel (New Delhi), Gupta Kavita (Nagpur), Gupta Megha (New Delhi), Guglani Ritika (Chandigarh), Gupta Shipra (New Delhi), Garg Neha (New Delhi), Gulyani Purva (Melbourne, Australia), Gupta Aanchal (New Delhi), Goel Chavi (Falna), Jatana Anita (New Delhi), Jain Gupta Sonal (New Delhi), Kehar Sugandha (New Delhi), Kumar Ramani (Bengaluru), Krishnan Dharaini (Chennai), Krishnaswamy Sheela (Goa), Kundu Moumita (Kolkata), Lahiry Priyangee (Kolkata), Mishra Mitali (New Delhi), Mittal Juhi (New Delhi), Mukhija Megha (New Delhi), Paralkar Bhatte Sukhada (Mumbai), Rohtagi Priyanka (Bengaluru), Singh Seema (New Delhi), Shetty Zankhana (Mumbai), Saudagar Deepti (Mumbai), Sudhakar Ritu (Ludhiana), Soni Shalvi (New Delhi), Sinha Shruti (Chennai), Singhal Shalini (New Delhi), Shah Priyali (Pune), Singh Neelanjana (New Delhi), Shukla Preeti (Indore), Samaddar Ritika (New Delhi), Srivastava Richa (New Delhi), Sarna Tejinder Kaur (Ethiopia), Singh Shweta (New Delhi), Singhal Prachi (Dubai), Tyagi Kanika (New Delhi), Tambekar Amita (Surat), Tandon Aparna (New Delhi).

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Declaration of competing interest

None.

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