

## Nutritional management and support in COVID-19: Emerging nutravigilance

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### Abstract

Corona virus disease (COVID-19) emerged as an epidemic from China, with quick spread globally. The disease can lead to serious problems, like pneumonia or even death especially among vulnerable people with existing health conditions. Its treatment and management require huge efforts from medical professionals often at the cost of their own health and life. Nutrition is the epicenter for the management of such diseases which works synergistically with the medical treatment for quick and better recovery. It has been associated with great human and economic toll and it is still not contained. Currently over two million people are affected and over 300,000 deaths globally. However, due to its newness and unfamiliarity, the understanding of this novel virus is still evolving. This viral infection poses numerous metabolic challenges to those severely affected and addressing them is a key to better outcomes. Medical nutritional therapy is thus among the mainstay of core components of comprehensive treatment measures for patients with COVID-19. This manuscript therefore aims to highlight the role of nutritional management and support in covid-19 disease.

**Keywords:** Corona virus, covid-19 disease, nutritional management, medical nutrition therapy, nutritional support, food safety, recommendations, diabetes, hypertension.

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### Introduction

Corona virus disease (COVID-19), an infectious disease, is a global pandemic. It spreads through contaminated air-droplets of infected persons. The survival of virus is dependent on the surface and favourable environmental conditions keeping it alive from a few hours to a few days.<sup>1,2</sup> Most people have mild disease and recover well. In understanding the course of the disease, we aim to

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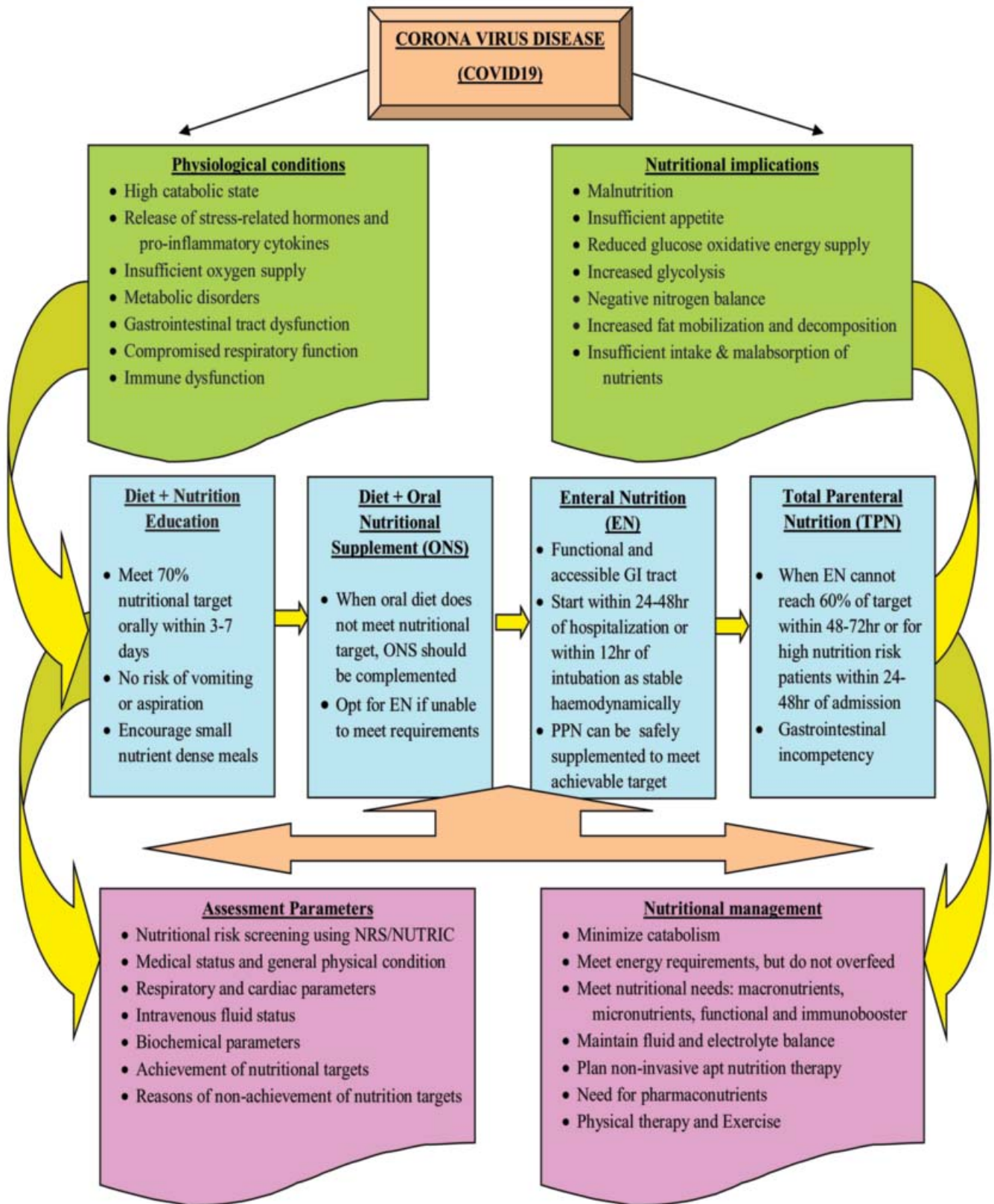
elaborate the role of nutritional management and support in COVID-19 disease.

### Clinical presentation, classification and progression

The disease of COVID-19 may occur asymptomatic and pre-symptomatic but the risk of transmission persists in both.<sup>3</sup> People generally develop respiratory illness with signs and symptoms such as a cough, nasal secretions, dyspnoea, fever, myalgia, and in more severe cases, difficulty breathing after the mean incubation period of 3-7 days (range 2-14 days). In a few conditions, gastrointestinal symptoms such as diarrhoea and nausea may also occur.<sup>4</sup>

It can be classified as stage 1 (early infection) wherein virus enters, multiplies and starts affecting the lungs in human body. It is a viral response phase. It is characterized with mild to moderate clinical signs (lymphopenia, increased prothrombin time, increased D-dimer and mild LDH) and symptoms (fever, dry cough, diarrhoea, headache), pneumonia). Stage 2 (Pulmonary phase) and 3 (Hyper-inflammation phase) are both marked by hyper-inflammation in the host, cytokine storm and death if uncontrolled. These both are host inflammatory response phase which may be severe or critical on the basis of illness severity. Stage 2 is particularly characterized by clinical symptoms of shortness of breath, hypoxia and signs of abnormal chest imaging, transaminitis, low-normal procalcitonin while stage 3 is particularly characterized by clinical symptoms of ARDS, SIRS/shock, cardiac failure or multi-organ system dysfunction and signs of elevated inflammatory markers such as CRP, LDH, IL-6, D-dimer, ferritin; troponin and NT-proBNP elevation etc.<sup>4,5</sup> Depending on few considerations such as disease severity, burden and spread of the infection to self as well as others, it is decided to be treated at either indoor (hospital-quarantined) and outdoor (home-quarantined).

There is potential for some patients requiring hospitalization to intensive care unit (ICU) for intensive medical equipment, services and observation.<sup>6</sup> The older persons, particularly those with frailty or co-morbidity or people with declined immune function,<sup>7</sup> underlying medical conditions have all been associated with



**Figure-1:** Physiological conditions, nutritional implications and care management algorithm associated with COVID-19.<sup>6,8,12-21</sup>

increased illness severity and adverse outcomes.<sup>6</sup> Persons with severe COVID-19 disease are in a highly inflammatory and catabolic state. There is significant mortality in malnourished patients.<sup>8,9</sup> On the extreme end one has to be cautious with patients on invasive mechanical ventilation as they may develop persistent inflammation-immuno-suppression and catabolism syndrome, often ensuing in secondary infections and/or viral reactivation associated with increased morbidity and mortality.<sup>10,11</sup> Even then, adequate nutrition strategies have a preventive role for COVID-19 on one hand and is also associated with better chances of survival on the other hand.

### **Medical Nutrition Therapy (MNT) for nutritional support**

Supportive care provided to patients with COVID 19 involves a variety of therapies that have been used or proposed before for the treatment of other CoVs such as SARS-CoV, MERS-CoV and other viral diseases including antiviral drugs, immune-suppressants, steroids, plasma from recovered patients and psychological support while research for antibodies and vaccines against the virus is still evolving.<sup>12</sup>

The systematic levels of prevention in MNT are primordial (no risk), primary (at risk but no infection), secondary (early stages of infection but no complication) and tertiary levels (infection along with complications) running in parallel with infection severity. Optimal nutritional support based on MNT is an important key for disease prevention, management, achieving positive clinical outcomes and sustainable recovery. Compared to healthy people, patients with COVID-19 are affected by higher energy expenditure, thereby their energy requirements and risk of malnutrition is increased.<sup>12</sup> Underfeeding may increase hospital length of stay, incidence of complications such as infections and organ failure, and risk of mortality while on the other hand, overfeeding has been associated with complications such as hyperglycaemia, hypertriglyceridaemia, hepatic steatosis, azotemia, and hypercapnia, and increased rate of mortality among patients.<sup>13</sup>

The assessment parameters are mandatory to be performed frequently including nutritional risk screening [done using nutrition risk score (NRS) while in conditions where body weight and diet history cannot be obtained, a modified NUTRIC score is used or hospital admission of more than 48 hours in the ICU], general physical condition, respiratory and cardiac parameter (including rising pCO<sub>2</sub> levels, increasing minute ventilation, FiO<sub>2</sub>, pulmonary oedema and arrhythmias etc.), intravenous

fluid status, biochemical parameters (including CBC, LFT, KFT, lipid profile, dyselectrolytemia or hyperglycaemia due to sepsis, antibiotic therapy and other medical conditions, achievement of nutritional targets and reasons of non-achievement of nutritional targets (including multiple feed interruptions, malabsorption, deteriorating medical condition, body weight loss, muscle/fat store depletion etc).<sup>14</sup> It is a very useful parameter and can be done frequently, to decide the kind of nutritional support required to provide nutrition intervention (Figure-1).<sup>15</sup>

Mode of nutrient delivery is next most crucial decision regarding nutrition support for dieticians and doctors. It can be (1) diet + nutrition education, (2) diet + oral nutritional supplement (ONS), (3) total enteral nutrition (TEN), (4) partial enteral nutrition (PEN) + partial parenteral nutrition (PPN), (5) total parenteral nutrition (TPN) planned according to clinical reality.<sup>15,16</sup> For the outdoor patients being treated at home-quarantined environment, diet rich in protein, carbohydrates and micronutrients is recommended to be consumed orally and may be combined with ONS to meet nutritional targets for early recovery. Those patients who cannot eat, usually treated indoor at hospital-quarantined setting, should be given enteral nutrition as soon as possible. For the patients incompatible with enteral nutrition, parenteral nutrition should be given timely to meet energy requirement. The individualized patient specific care plan is practiced inline with assessment parameters for invasive mode of delivery (Figure-1).

### **Nutritional Recommendations**

Nutritional recommendations are planned to meet nutritional needs and are targeted to improve the effectiveness of nutritional treatment, combined with medical treatment, coinciding with physiological needs, metabolism conditions, nutritional screening, and treatment targets of optimum recovery and reduce mortality.<sup>16</sup> The nutritional need of the patients is estimated according to body weight or BMI, physiological needs and severity of infection.<sup>17</sup>

At the primordial level, general advice is to increase the intake of antioxidant and associated nutrients to support immune function to meet nutritional requirements including consumption of 4-5 servings of coloured fruits and vegetables enhancing diet diversity. For patients with mild to moderate infection, MNT comprises the beneficial role of primary and secondary levels of prevention while for critically ill patients, the beneficial role of tertiary levels of prevention are adequately considered.

**Energy:** For patients with mild to moderate infection (home quarantined or hospital ward quarantined), MNT comprises the beneficial role of primary, secondary and early tertiary levels of prevention with the recommended amount of energy target is 25-30 kcal/ kg/ day while for critically ill patients, MNT comprises the beneficial role of late tertiary levels of prevention for patients admitted in critical care with the recommended amount of energy target shall be reached to 30 kcal/ kg/ day planned ideally and well distributed throughout the day.<sup>18-20</sup> Meeting such a target gets difficult to achieve in severe conditions which may require infusion of glucose-containing liquids (such as dextrose: 3.4 kcal/g, glycerol/glycerol: 4.3 kcal/g) and fat-containing liquids (such as propofol: 1.1 kcal/ml) etc. Standard ICU feeds are planned hypocaloric (0.8kcal/ml) for initiation, progressing to isocaloric (1kcal/ml) and hypercaloric (up to 1.5kcal/ml) once well tolerated along with the monitoring of gastric residual volumes (GRVs). More specialized feeds are considered, as clinically indicated, such as a renal feed for patients with acute kidney injury (AKI) and chronic kidney injury (CKD) that have electrolyte abnormalities as well.<sup>21,22</sup>

**Protein:** For patients with mild to moderate infection (primary and secondary levels of prevention), the recommended amount of protein target is 20-25% of the calories while for critically ill patients (tertiary levels of prevention), 25-30% is ideally planned and well distributed throughout the day considering protein sparing action. It can also be estimated as 1.2-1.3 g/kg/day and 1.3-1.5 g/kg/day for mild to moderate and critically ill patients respectively (calculated from ideal body weight).<sup>18-22</sup> In South Asian diet, the amount of protein is less. Also in current scenario of lockdown, availability can be an issue. Patients with impaired renal function and not receiving continuous renal replacement therapy (CRRT) should appropriately reduce protein intake to 0.8-1.0 g/kg/day while for patients undergoing CRRT, protein intake should be increased with a target amount of 1.5-2.0 g / kg/day. Good protein quality with branched chain amino acids (BCAA) supplements, whey protein and other animal proteins should be included to prevent muscle loss, enhance the strength of respiratory muscles and early recovery. It is recommended to reduce the non-protein thermal energy / nitrogen ratio.<sup>23</sup> To meet such a target gets difficult to achieve in severe conditions which may require supplemental intravenous amino acid infusions also to sustain positive protein balance.

**Fat:** For both patients with mild to moderate infection (primary and secondary levels of prevention) and critically ill patients (tertiary levels of prevention), the

recommended amount of fat target is 25-30% of the total energy, ideally planned considering fat absorption and metabolism.<sup>18-20</sup> To meet such a target, a variety of cooking vegetable oils, especially monounsaturated fatty acid vegetable oils can be used while the use of medium and long chain fatty acids is preferred to improve oxidative utilization of fatty acids.<sup>21,22</sup> Fat-containing liquids such as propofol are also used purposefully. Imbalance of intravenous injection of fat can lead to lipid overload and toxicity causing hypertriglyceridemia and abnormal liver function. Glycerol concentration levels are associated with improved survival. Therefore, it is recommended that the daily intravenous lipid (including non-nutritional lipid sources) of fat is 1g/kg, and the maximum is not more than 1.5 g / kg, and it needs to be adjusted according to individual tolerance. In addition, the use of omega-3 fatty acids in critically ill patients has a lower risk of infection and death with faster recovery. Omega-9 fatty acids have immune-neutral effects and have less interference with haemodynamics, endothelial cell function, immune function and liver function, so it is recommended to increase the proportion of olive oil (mainly omega-9 fatty acids).<sup>18-22</sup>

**Glycolipid ratio:** Endogenous glucose production is increased in critically ill patients and insulin resistance is present. Too much glucose can lead to high blood glucose, increase CO<sub>2</sub> production, increase fat synthesis, and increase insulin requirements. In addition, compared with fat-based energy supply, glucose-based energy supply has no advantage in saving protein. The minimum carbohydrate requirement is 2 g / kg of glucose per day with continuous dynamic monitoring and optimizing blood glucose levels. In case of hyperglycaemia, patient's risk of mortality and infection complications may increase requiring insulin management. An energy ratio from fat and carbohydrates between 30:70 (for subjects with no respiratory deficiency) to 50:50 (for ventilated patients) is further encouraged to meet the nutritional needs.<sup>18,19</sup>

**Electrolytes and Fluids:** Fluid and electrolyte imbalances (Sodium, calcium, potassium, chloride, phosphate, and magnesium) are associated with increased morbidity and mortality among critically ill patients. The "Four-Anti and Two-Balance" strategy defined as antiviral, anti-shock, anti-hypoxaemia, anti-secondary infection, and maintaining of water, electrolyte and acid base balance and microecological balance is an effective treatment strategy.<sup>24</sup> Follow the general principles of fluid therapy, which is to stabilize patients at 30 to 40 ml/ kg/day adjusted with respect to body temperature, pulmonary oedema, renal dysfunction and fluid accumulation.<sup>18-21</sup> While maintaining fluid balance, it is even more necessary

to prevent excess fluid, especially intravenous fluid volume. In such conditions, use of Furosemide may be initiated as well.

**Micronutrients:** A conventional multiple-micronutrient supplementation, besides vitamins A and D, B vitamins, vitamin C, omega-3 polyunsaturated fatty acids, as well as selenium, zinc and iron are recommended during all levels of prevention (primordial, primary, secondary and tertiary) in COVID-19 patients to meet recommended daily allowances (RDA) is beneficial and meet additional needs associated with underlying patient's condition.<sup>18,19,22</sup> For instance, vitamin D deficiency has been associated with a number of different viral diseases, while low levels or micronutrients intake such as vitamins A, E, B6 and B12, Zn and Se have been associated with adverse clinical outcomes during viral infections.<sup>25</sup> Vitamin A has been named as "anti-infective" vitamin for its potential to defense against infection. Hence, the recommendations of vitamins D, B and C, omega-3 polyunsaturated fatty acids, as well as selenium, zinc and iron should be adequately considered in the assessment of micronutrients in COVID-19 patients. Limited evidence shows that high-dose vitamin C (3~10 g/d) intravenous injection may be useful to significantly reduce mortality in critically ill patients, shorten the use of booster drugs and mechanical ventilation time, and integrate acute respiratory distress. While for patients with impaired liver and kidney function, increased gastrointestinal loss, refeeding syndrome or electrolyte disorders etc., it should be adjusted according to the actual situation.<sup>26,27</sup> However, there is paucity of experimental doses of such micronutrients with regard to its effects to prevent or improve clinical outcomes of COVID-19 but anti-oxidants and related nutrients do enhance T-cell and B-cell immunity in human studies.

**Supplements:** The various nutritional supplements are available with pharmaceutical companies for high calorie, high protein and rich in micronutrients such as Maxvida, Ensure Plus, Hinex HP, Prohance HP, Frezubin Plus. It can be safely combined with oral diet as well as used in EN. RTH (Read- to-hang) is liquid formula available for EN. While ready to use and easily accessible bags of TPN such as Kabiven, TNA (Total Nutrition Admixture, given via central line) and TNA Peri (given via peripheral route) etc. are also readily available which can be used to meet the daily nutritional needs of the patients. Additionally, Aminoven and SMOF lipid are used as IV infusions. These supplements are all calorie-nutrient dense formulations, designed specifically for meeting nutritional needs of critically ill patients.

**Probiotics:** There is no scientific rationale of using

probiotics to protect, prevent or treat COVID-19 infection specifically. Nutritional support complemented with prebiotics or probiotics helps regulate the balance of intestinal microbiota, improve gastrointestinal function and reduce the risk of secondary infection due to bacterial translocation thereby boosting immunity.<sup>28</sup> Combining a healthy and balanced diet together with prebiotics, probiotics, vitamin supplementation may reinforce the immune system during the COVID-19 outbreak. Because several COVID-19 patients present microbial dysbiosis, it is possible that the use of prebiotics or probiotics (in food supplements with a type of strains) could prevent secondary infections due to bacterial translocation.<sup>29,30</sup>

**Special medical conditions of Obesity, Diabetes and Hypertension:** Currently there is no evidence that people with obesity, diabetes and HTN are vulnerable to acquire the infection unless they have other accompanying risk factor or poor control of their existing condition. Such conditions pose a risk of causing adverse outcomes for them similar to any immuno-compromised condition such as AIDS, cancer, malnutrition, and certain genetic disorders including people with special needs.<sup>31</sup> Morbid obesity is positively associated with sleep-apnoea syndrome, impaired ventilator function, surfactant dysfunction and deteriorated glycaemic control. It was evidenced in earlier similar disease of middle east respiratory syndrome (MERS)-CoV which showed an association of diabetes with greater weight loss and greater pulmonary inflammation, with macrophage infiltrates.<sup>21</sup> Secondly, persons with hypertension and diabetes mellitus are at increased risk possibly due to alterations in the angiotensin converting enzyme 2 (ACE 2) receptor produced by ACE 1inhibitors.<sup>7</sup> Hence, these conditions require specific recommendations such as maintaining optimum targets of BGLs, follow sick day rules, keep adequate stock of medications and diabetes utilities at home, monitor their blood glucose levels (BGLs), ketone bodies (if BGLs are high >250mg/dl) and blood pressures, continue prescribed medications with no alterations without consultation, maintain healthy eating schedules, keep hydrated, minimize intake of salt and sugar (called twin white herrings in diabetes and endocrinopathies) follow home-based exercises for fitness to help reduce risk of infection, modulate severity of clinical expression of disease, counteract increased risk of the COVID-19 flu and heart complication.<sup>31-34</sup> Chronic uncontrolled hyperglycaemia negatively affects immune function and increases the risk of diabetic complications such as ketoacidosis, infections, more severe complications, morbidity and mortality. Majorly nutritional requirements remain same as that for people without diabetes. It is advisable to eat low glycaemic

index diet rich in immunonutrients at frequent intervals to prevent fluctuations in blood glucose levels.

**Physical activity:** Being physically active at home quarantined environment using various simple and easily implementable exercises is very much recommended to avoid the airborne coronavirus, preserve muscle mass and maintain fitness levels. Thus quarantine can cause lower energy expenditure, improper eating schedule, weight gain, loss of skeletal muscle mass and strength, worsening of pre-existing health conditions and possibly also loss of immune competence. Addition of dietary fiber and nutrients regulating the energy metabolism may help in weight management as well as reduction of glycaemic spikes.<sup>35</sup>

**Food safety and health hygiene:** Primary prevention requires strict guidance for food hygiene, food packaging

**Table-1:** Food safety and health hygiene with COVID-19.<sup>36-38</sup>

<b>During purchasing</b>
<ul style="list-style-type: none"> <li>◆ Take precautions while grocery shopping                             <ul style="list-style-type: none"> <li>✓ Maintain a distance of at-least 1 meter from others</li> <li>✓ Don't touch face after coming in contact with outside objects</li> <li>✓ Limit the number of trips to the store</li> </ul> </li> <li>◆ Keep food safety in mind while buying essential items                             <ul style="list-style-type: none"> <li>✓ Wash fruits and vegetables, milk packets before use</li> <li>✓ Clean packets of food items before storing</li> <li>✓ Use a cloth bag and avoid plastic bag</li> <li>✓ Carry your own clean shopping bag and wash it thoroughly with soap, disinfectant and clean water</li> <li>✓ Immediately wash hands after coming from outside without touching other objects</li> </ul> </li> <li>◆ Limit highly processed foods</li> <li>◆ Plan what to buy and avoid panic buying behaviour that cause increase in food prices, overconsumption of food, unequal distribution of products and food wastage</li> </ul>
<b>During cooking</b>
<ul style="list-style-type: none"> <li>◆ Ensure safe cooking practices at home                             <ul style="list-style-type: none"> <li>✓ Wash hands frequently with soap and water specially before handling raw, cooked or ready-to-eat food items and after handling kitchen waste</li> <li>✓ Keep hair neatly combed and tied</li> <li>✓ Keep nails short and clean</li> <li>✓ Wear clean clothes</li> </ul> </li> <li>◆ Use fresh ingredients that have a shorter shelf life first over non-perishables.</li> <li>◆ Wash raw vegetables and fruits thoroughly to remove all visible dirt under running water.</li> <li>◆ Packaging like cans can be wiped with a disinfectant before being opened or stored.</li> <li>◆ Always wash utensils and plates before use</li> <li>◆ Avoid handling food if you are ill</li> <li>◆ Keep your gadgets (phones, laptops, mouse etc) clean</li> </ul>
<b>During storing</b>
<ul style="list-style-type: none"> <li>◆ Refrigerate left-over food immediately</li> <li>◆ Clean refrigerator thoroughly inside out</li> <li>◆ Keep food safe in times of social distancing</li> <li>◆ Keep food safety in mind while storing food</li> </ul>

hygiene and water hygiene. Food Safety and Standards Authority of India (FSSAI) has put up the most accessible efforts to ensure easy, affordable, safe and wholesome food for the country and prevent further transmission of COVID-19 during this public health crisis.<sup>36-38</sup> It has been tabulated systematically in Table-1. While at present there is no evidence of food or food packaging being associated with the transmission of coronavirus disease (COVID-19), it may be possible that people can become infected by touching a surface or object contaminated by the virus and then touching their face.

**Recovery phase:** It is equally important to continue good food and health care practices, firstly to overcome the challenges of decreased immunity, cardio-respiratory dysfunction and vasculo metabolic dysfunction, and secondly to promote sustainable healthy body.

### Conclusion

During this period of global crisis, nutritional risk screening and optimizing MNT targets of both outdoor as well as indoor quarantined patients, is indispensable component for disease prevention and treatment. The focus is to adequately address nutritional needs and offer nutritional support as it works synergistically for faster recovery at all the stages of infection. Social distancing, avoiding close contact with those who are sick, food security and recommended hygiene practices are essential keys to overcome this infection. During such pandemics, vulnerable populations should take extra precautions. With appropriate medical nutrition therapies and approaches, it is expected that the COVID-19 pandemic will be successfully beaten preventing unexpected human, healthcare and materialistic loss.

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