

Covid-19 and Nutrition: Review of Available Evidence

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Abstract

Review Article

To our best knowledge, no rigorously designed clinical trials have evaluated the relation between nutrition and the large family of Coronaviruses. Drawing on experience from prior zoonotic Coronaviruses outbreaks, public health specialists have initiated preparedness and response activities to define and collect all the required knowledge about this pandemic. In this review, the authors try to introduce the most reliable scientific evidence that connects the nutrition and COVID-19. This review will summarize the nutritional management in ICU patients infected with COVID-19, vitamin supplements and COVID-19, and pre-existing diseases and COVID-19.

Keywords: Coronavirus, Covid, Nutrition, Supplement, Diseases.

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INTRODUCTION

Currently, there are insufficient data to propose the optimum interaction between nutrition and COVID-19. Thus, it is appropriate to collect all available data in one piece as a door for more cohort studies and experimental research. Coronaviruses (CoVs) are large family viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). A novel coronavirus (nCoV) is a new strain that has not been previously identified in humans. Nutrition is one of the host factors that correlated with variations in influenza morbidity and mortality [1]. The adaptive immune response to infection is multi-faceted and complex, and it involves a variety of cell types and factors such as chemokines, cytokines, enzymes, and hormones [1-3]. The effect of vitamin supplements on immunity not only is difficult to measure but can also involve affecting one component of the immune system but not another. The main way to boost immunity against infections is to maintain personal hygiene, adequate nutritional intake, and a healthy lifestyle [6, 7]. By the time the very first cases of COVID-19 were identified in many countries, it was already clear that certain groups were at greater risk of serious illness, and possibly death, than others. The most susceptible people include subjects with chronic lung diseases, immunocompromised people, heart diseases, diabetes, liver diseases, chronic kidney disease, obesity, and neurological disorders. COVID-19 is a new disease and there is limited evidence regarding risk factors for

severe disease. Based on currently available knowledge and clinical expertise; there is no clear picture of this virus. The aim of this paper is to review the latest scientific evidence on the interaction between COVID-19 and nutrition.

METHODOLOGY

Google Scholar search engine was used to gather information relating to Coronavirus, COVID-19, nutrition, vitamin supplements, pre-existing diseases, and nutritional care management. The studies were written in English. The period of literature age has extended from the inception of the search engine to the mid of April 2020. The search generated about 319 sources, of which 70 sources were used. These 70 articles were considered relevant because they answered the objectives of the review. The library databases such as PubMed and MEDLINE were also used during the study.

DISCUSSION

Coronavirus disease 2019 (COVID-19)

COVID-19 appeared in Wuhan in December 2019, the capital of Hubei province, China. COVID-19 is an RNA caused by an newly emerged zoonotic coronavirus [1]. A positive-sense wrapped single-stranded RNA virus; named Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has been isolated from a patient with pneumonia, and attached to the cluster of acute respiratory illness cases from Wuhan. COVID-19 is spread from human to human by droplets coughed or respired by infected persons and by

touching droplet-contaminated surfaces or objects and then touching the eyes, nose or mouth [2]. The probable causes of the occurrence the unexplained mass pneumonia cases in Wuhan were leave out one by one, including influenza, avian flu, adenovirus, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). Epidemiological surveys indicate that the case infection may be linked to the South China seafood market in Wuhan [3, 4]. According to the European, United State Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO), the COVID-19 disease is considered a deadly disease and highly contagious disease is now spreading across the world and through European Economic Area, European Union Member States, with increasing in the number of affected countries, important case, confirmed cases and infection-related deaths [5]. A new study from China has been done by Nan-Shan, on 1099 confirmed cases establish that the most common clinical appearances included; fever (88.7% of the patients), cough (> 80%), weakness (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), muscle ache (11%), and headache (13.6%). Furthermore, certain patients appeared with gastrointestinal symptoms like, diarrhea (3.8%) and vomiting (5.0%) [6]. Fever and cough were the major symptoms, on the other hand upper respiratory symptoms and gastrointestinal symptoms were not common, suggesting the differences in viral tropism as compared with SARS-CoV, MERS-CoV, and influenza. Among elderly and those with chronic diseases, such as hypertension, chronic obstructive pulmonary disease, diabetes, and cardiovascular disease, the new crowns grown quickly into acute respiratory distress syndrome, septic shock, even leading to the death [7-9].

Nutritional management in ICU patients infected with COVID-19

Retrospective analysis of data available on the 1918 influenza pandemic showed that disease severity

rest on viral and host factors. Amongst the host factors correlated with variations in influenza morbidity and mortality age, cellular and humoral immune responses, genetics and nutrition [10]. Malnutrition and famine were associated with high disease severity and was related to mortality also in the younger population. Under-nutrition remains a problem for viral pandemics of the twenty-first century and beyond. Indeed, chronic malnutrition was thought to have contributed to the high morbidity and mortality seen in Guatemalan children during the 2009 influenza pandemic [11]. According to the recent European Society Parenteral and Enteral Nutrition ((ESPEN)) guidelines on nutritional therapy in Intensive Care Unit (ICU) and the respiratory therapy stages; the nutritional management is guided by the patient's condition [12]. The nutritional management should consider the respiratory support allocated to the ICU patients to prevent the occurrence of malnutrition. As it is know not all the COVID-19 patients admitted to ICU need to intubated to ensure the successful oxygenation, some patients will placed on Non Invasive Ventilator ((NIV)) or Flow Nasal Cannula ((FNC)) / High Flow Nasal Cannula ((HFNC)) to monitoring their thermodynamical state especially oxygen statues [11]. Limited studies described the implementation of nutritional support when NIV or FNC / HFNC techniques are used. Nevertheless, limited evidence indicated that the amount of calories and proteins intakes may be inadequate to achieve the patients' requirements and will not prevent malnutrition occurrence [13, 14]. comparing to patients whose intubated and ventilated on Mechanical Ventilator, most studies confirmed that the importance implementation of nutritional support when patient on intubation, and this is in agreement with ESPEN guidelines in ICU. ESPEN also has critical care nutrition specific guidelines and just produced a new paper that does address COVID-19 (not yet published) [15, 16]. Table-1 shows the possible nutrition intervention according to oxygen support therapy and ICU setting.

Table-1: Nutrition intervention according to oxygen support therapy and ICU setting

Setting	ICU	
	1ST Day	> 2Day
O2 therapy and M.V	FNC followed by M.V	Minute Volume “MV”
Nutrition Intervention	-Screening to detection malnutrition. -Define energy and protein target -In case of FNC or NIV, administer energy/protein orally or enterally and if not possible parenterally	-Prefer early enteral feeding. -No response with GIT disorders start parenterally

The enteral nutrition Orogastric feeding / Nasogastric feeding should be started during the first 24-48 hours of admission. For highly inadequate implementation of enteral nutrition which may result in patient starvation particularly in the first 24 hours of ICU stay and higher risk of malnutrition and associated complications; the peripheral parenteral nutrition may be therefore used under these conditions [17]. Overlooking administration of adequate calorie-protein

may result in worsening of nutritional status with malnutrition and related complications. Adequate nutrient intake assessment is recommended during treatment for monitoring oral nutrition supplements, enteral nutrition and to detect if oral route is insufficient. Most of studies that have been conducted on SARS-CoV and MERS-CoV new crown viruses recommended the importance of applying a nutritional assessment protocol according to ESPEN guidelines to

decrease the possibility of malnutrition in ICU settings. Although no specific guidance for COVID-19 disease has been identified, the ESPEN guideline have recommended using the nutritional management to any other ICU patient admitted with pulmonary compromise [18, 19]. In a recent review about potential interventions for novel coronavirus based on the Chinese experience authors suggested that the nutritional status of each infected patient should be screened and evaluated before the administration of general treatments [20]. Currently, there is no specific nutrition intervention strategy for COVID-19 has been fully tested for efficacy, but as authors recommend following the previously guidelines.

At present, the first stage, of nutritional intervention for COVID-19 case include nutritional risk screening Nutrition Risk Screening 2002 (NRS-2002) [21], nutritional risk score for critically ill patients (NUTRIC score), or extra tools such as Malnutrition Universal Screening Tool ((MUST) for patients affected with COVID-19 to prevent and management the malnutrition. Therefore, an early enteral nutritional support should commence within 24 to 48 hours. Post-pyloric feeding will be favored when aspiration risk is high, age more than 70 years, consciousness level affected, prone position, gastroesophageal reflux and a single load of enteral nutrition. The most important macronutrients requirements for COVID-19 patients in ICU are energy and proteins. The energy expenditure (EE) should be determined to evaluate energy needs by using indirect calorimetry when available. Isocaloric nutrition rather than hypocaloric nutrition can then be progressively implemented after the early phase of acute illness. If calorimetry is not available, VO₂ (oxygen consumption) from pulmonary arterial catheter or VCO₂ (carbon dioxide production) derived from the ventilator will give a better evaluation on EE than predictive equations. If predictive equation cannot be used for any cause the indirect method should be conduct 15-20 kcal/kg actual body weight (ABW)/day (70-80% of needs). In state, the refeeding syndrome risk is present suspect to start at 25% of caloric goal with slow increase, with frequent monitoring of serum phosphate, magnesium and potassium levels [22]. Hypocaloric nutrition should be administered in the early phase of inflammatory (acute illness) with raises up to 80–100% after three days. If predictive equations are used to estimate the energy need, hypocaloric nutrition (below 80% estimated needs) should be preferred over isocaloric nutrition for the first week of ICU stay due to reports of overestimation of energy needs [23]. During critical illness the protein requirement starting from 1.3 g/kg ABW/day and it can be increased progressively according to health statuses. Considering the importance of preserving skeletal muscle mass and function and the highly catabolic conditions related to disease and ICU stay. Additional strategies may be considered to enhance skeletal muscle anabolism. In particular, controlled physical activity

and mobilization may improve the beneficial effects of nutritional therapy [22]. Several studies have been done about the role of carbohydrate and fat in accelerate the weaning time form mechanical ventilator for patients with respiratory diseases [24-26]. In 2014 Sabour Faramawy [27] concluded that, the combustion of 1000 calories of the high fat formula result in the production of 173.6 liters of CO₂, in contrasts with the 186 liters of CO₂ produced from 1000 calories of the standard feed mainly carbohydrate. Another study has been done in 1989 by Al-Saady showed that, the patients who received high fat formula spent 62 hours less time on ventilator than those receive high carbohydrate formula. It seems that the high fat, low carbohydrate enteral formula appears to be beneficial with COVID-19 patients undergoing artificial ventilation. According to Society of Critical Care Medicine and ASPEN and North American societal guidelines [28, 12, 30]; it should be that start with a standard EN isotonic, high protein formula (1 kcal/ml or 1.5 kcal/ml) and the flow rate started slowly 10-20 ml/h by using continuous route in medical stability. Maintain trophic rate with worsening hemodynamics case during 5 to 7 days and if patient unable to progress during this period start parenteral nutrition earlier. If parenteral nutrition is advised by dietitian in the first week of ICU stay during the acute inflammatory phase of COVID-19, important step should be taken with pure soybean lipid emulsions and check the serum triglyceride after 24 hours of starting lipid emulsion containing formula. Nutrition intervention and management needs to be set as an essential part of the COVID-19 patients' treatment plan [31, 32].

Vitamins Supplements and COVID-19

Immunological response to an infection is not static; initial stages of antigenic stimulation to the later stages of disease development can undergo changes in the characteristics of the response [4, 33]. Therefore the effect of supplements on immunity not only is difficult to measure but can also involve affecting one component of the immune system but not another [34]. Some protective measures can effectively prevent SARS-CoV-2 infection, such as improving personal hygiene, wearing medical masks when needed, good ventilation and adequate rest [35]. However, patients with current diseases, especially chronic diseases such as diabetes, hypertension, coronary heart disease and cancer, are more prone to SARS-CoV-2 infection and its poor prognosis, disease status and sometimes ongoing treatment by these vulnerable group leads to having a lower systemic immunity, "therefore, it is particularly important to enhance self-resistance" Studies have reported that vitamin C; under certain conditions, may lower the susceptibility of lower respiratory tract infection COVID-19 may cause lower respiratory tract infection. Therefore, a moderate amount of vitamin C supplementation has been suggested as a method to prevent COVID-19 [36-39]. Though no conclusive evidence are available and safety

is questionable, high-dose of intravenous vitamin C has been recommended for treatment of early stages COVID-19 pneumonia [40]. Vitamin D and E have been suggested to enhance resistance to SARS-CoV-2, backed by the relationship found between vitamin D and vitamin E deficiency in cattle and their susceptibility toward the infection from bovine coronavirus [41]. However, due to the complexity of innate and adaptive immune responses to antigenic stimulation, it is difficult to pinpoint the overall effect of vitamin D during infection. This complexity sometimes results in different results in vitro compared with in vivo studies [42]. In several observational studies, lower 25(OH) D serum levels were associated with increased risk of respiratory infection in adults, 25(OH) D deficiency has also been connected to increased severity of acute lower respiratory infection in children and mortality from pneumonia in adults [43, 44]. Vitamin D is believed to reduce risk of infection through multiple mechanisms, including inducing defenses and cathelicidins that reduce viral replication rates and lower pro-inflammatory cytokines concentrations, which produce the inflammation induced pneumonia, as well as increasing concentrations of anti-inflammatory cytokines. Several clinical trials and observational studies reported that vitamin D supplementation reduced the influenza risk [45-47], while others did not [48, 49]. Available evidence supporting the role of vitamin D in reducing risk of COVID-19 includes 1-that the outbreak occurred in winter, during which 25-hydroxyvitamin D (25(OH)D) concentrations are lowest [50]. The number of cases near the end of summer in the Southern Hemisphere are low, 3- deficiency of vitamin D was found to contribute to acute respiratory distress syndrome, and 4- case fatality rates increase with chronic disease comorbidity and with age, both of which are associated with lower 25(OH)D concentration. To reduce the risk of infection, Grant and colleagues recommend that people at risk of influenza and/or COVID-19 consider taking 10,000 IU/d of vitamin D3 for a few weeks to rapidly raise 25(OH)D concentrations, followed by 5000 IU/d [51-53]. Aiming to raise 25(OH)D concentrations above 40-60 ng/mL (100-150 nmol/L). For treatment of people who become infected with COVID-19, the authors recommend higher vitamin D3 doses. Large population studies and randomized controlled trials should be conducted to evaluate these recommendations [54, 55].

Existing co-morbidities and covid-19

The presence of existing co-morbidities is associated with poorer clinical outcome in patients with COVID-19 [56]. In a study of 1099 COVID-19 laboratory confirmed patients, 261(23.7%) patients reported having at least one comorbidity, most commonly are diabetes, hypertension and coronary heart disease, in addition 223 (2.1%) of these patients had hepatitis B infection [57]. Those with severe case presentations were more likely to have hepatitis B infection (2.4% versus 0.6%). Abnormal liver function

tests, including elevated alanine aminotransferase, aspartate aminotransferase, and total bilirubin were noted [57]. Possible explanations to liver abnormalities in patients with COVID-19 are viral infection in liver cells [1], systemic inflammation and drug toxicity [58]. Cancer patients infected with COVID-19 were observed to have a higher risk of severe events [59]. Patients with cancer are considered more susceptible to infection as a result of their immunocompromised status resulting from anticancer treatments and malignancy.

Malnutrition in critically ill patients is associated with poor outcomes, including impaired wound healing, higher rates of nosocomial infections, and all-cause mortality. Nutritional status of patients admitted to the intensive care unit (ICU) is influenced by both chronic and acute starvation, but also by the severity of the underlying pathophysiological processes leading to ICU admission. This typically induces a marked catabolic response leading to rapid loss of lean body mass, varying from 5% in single-organ failure to 25% in multi organ dysfunction syndrome (MODS), during the first 10 days after ICU admission. Nutritional therapy can improve outcomes associated with malnutrition in critically ill patients. To identify ICU patients most likely to benefit from nutritional support, validated tools are required. Food safety and hygiene is a significant component during food preparation and serving to Covid-19 patients. It is required to use personal hygiene practices against contamination of food, food-contact surfaces, and food packaging and serving [31]. Malnutrition and weight loss is a frequently occurring complication in patients' pulmonary disease and it is a determining factor of functional capacity, health status and mortality. Malnutrition is a consequence of increased energy requirements that are not balanced by dietary intake. Both metabolic and mechanical inefficiency contribute to elevated total daily energy expenditure. Alterations in anabolic and catabolic mediators resulting in an imbalance between protein synthesis and protein breakdown may cause a disproportionate depletion of fat-free mass in some patients. Nutritional support is indicated for depleted patients with respiratory diseases because it provides not only supportive care, but direct intervention through improvement in respiratory and peripheral skeletal muscle function and in exercise performance. A combination of oral nutritional supplements and exercise or anabolic stimulus appears to be the best approach to obtaining significant functional improvement. Patients responding to this treatment even demonstrated a decreased mortality. Furthermore, weight loss and malnutrition opens the door of infection reoccurrence Poor response was related to the effects of systemic inflammation on dietary intake and catabolism [30-32].

Dietary management of pre-existing diseases has been suggested as a strategy to minimise the potential risk of SARS-CoV-2 infection in conditions

such as irritable bowel syndrome, Crohn's and Colitis [60-62]. World Health Organizations, dietetic associations and dietitians have been calling for patients with pre-existing conditions to continue abiding to their dietary advice and nutritional therapy steps received from their dietician if tested positive for COVID-19 [63-66] and ASPEN has released a nutritional guideline for patients covering at home [67-69].

Competing interests: Authors have declared that no competing interests exist.

CONCLUSION

Nutritional management in ICU patients infected with COVID-19, vitamin supplements and COVID-1, and the comorbidity spectrum of nutrition related conditions and their impact on outcome of COVID-19 and treatment remains largely unknown. More data need to be analysed on the impact of nutritional status and dietary modification on COVID-19. In order to more precisely ascertain the risk of SARS-CoV-2 infection in patients with existing comorbidities, and to predict their prognosis.

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