Impact of Nutrition and Diet on COVID-19 Infection and Implications for Kidney Health and Kidney Disease Management

IT IS NO exaggeration to say that since early 2020, the world has radically changed because of the pandemic caused by the novel coronavirus, also known as COVID-19. Drastic preventative measures including social distancing have overshadowed our day-to-day dynamics. An urgent quest has ensued to find effective strategies against COVID-19 by using traditional and novel pharmacotherapy and developing vaccines if possible. Because COVID-19 virus invades human cells through the angiotensin-converting enzyme 2 (ACE2) receptors, heated discussions abound as to whether prior use of ACE inhibitors or angiotensin receptor blockers (ARB) can cause ACE2 receptor upregulation that would in turn lead to worse COVID-19 infection. However, it has also been argued that, if these same patients contract COVID-19 infection, their prior ARB therapy should not be discontinued because a resulting cytokine storm could lead to worse outcomes. Thus, paradoxically, even more judicious ARB therapy may be beneficial during the active infection.[1] This is similar to the obesity paradox hypothesis that was commented about in a 2016 article in *NATURE* magazine[2]: It's like "that guy who led you to prison, becomes your friend in prison." The challenge is even greater in patients with diabetic and hypertensive kidney disorders or proteinuric patients because many of them have received ACE inhibitors or ARB agents. In addition, emerging data suggest that derivatives of the antimalarial agent quinine such as chloroquine and hydroxychloroquine may help against COVID-19 infection; some of these drugs are actively used in infected dialysis patients.[1] Although clinical trials are underway to test these and other agents and related hypotheses, an important question for the nutrition community is whether there are certain nutrients and food patterns that can prevent the viral infection or mitigate its severity.

The COVID-19 epidemic started at wintertime in regions of the world where consumption of wildlife is not unusual. Coronavirus is one of the viruses causing the common cold, a disease that has never had a cure nor any effective prevention or vaccine. Yet, there are relatively consistent data suggesting that the risk of contracting the common cold is high under inadequate sleep, psychosocial or physical stress including exposure to cold temperatures, inadequate nutrition, and any condition that compromises the body's immune system. There are mixed data on nutritional and dietary approaches to prevent the common cold, including by coronaviruses. Dr. Linus Pauling, the only person who ever won two unshared Nobel prizes, believed that higher intake of ascorbic acid, also known as vitamin C, is an effective way to prevent and treat the common cold. While many studies on the efficacy of vitamin C supplementation in preventing the common cold were inconclusive or negative, meta-analyses suggest a consistent and statistically significant benefit of vitamin C to prevent the common cold or to reduce its duration and severity and support respiratory defense mechanisms,[3] including data suggesting a role for vitamin C in persons exposed to brief periods of severe physical exercise[4] or cold environment,[3] not to mention the potential role of vitamin C in the management of anemia in chronic kidney disease (CKD).[5] If so, and given that COVID-19 is a coronavirus and given the low cost and high safety of natural foods rich in vitamin C, it may be worthwhile to be diligent regarding adequate vitamin C in our daily foods during the COVID-19 pandemic. Notwithstanding emerging quackery on immune-boosting and magic foods to prevent or cure COVID-19 infection as a result of global desperation and anxiety, it is reasonable to ensure adequate consumption of citrus fruits (e.g., oranges, nectarine, tangerines, grapefruit, lemons, limes) as well as tomatoes, broccoli, cauliflower, cantaloupe, kale, kiwi, sweet potato, strawberries, papaya, and all those fruits and vegetables rich in vitamin C. Indeed, we should remember to eat good amounts of fresh fruits and vegetables to ensure needed supply of not only vitamin C but also other antioxidant vitamins.[6,7]

Are there other foods and nutrients that can protect us against COVID-19? Fava beans contain chemical compounds similar to quinine-based antimalarial medications, some of which are being used in COVID-19 infected persons such as hydroxychloroquine.[1] Interestingly, a case-control study showed that persons with certain hemoglobin subtypes, who ate fava beans, were significantly protected against *Plasmodium falciparum* malaria in Thailand.[8] However, persons with favism should avoid fava beans given risk of hemolytic anemia. Whether higher consumption of such natural foods as citrus fruits, fava

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beans, and other fruits, vegetables, and legumes can be beneficial against COVID-19 infection deserves well-designed and well-conducted studies, while in between, it is important to remain well-nourished and enforce all practices that are traditionally used against the common cold.[9]

Are there nutritional recommendations to protect persons with CKD including patients who are dialysis-dependent or have acute kidney injury (AKI) against the ravages of COVID-19? Data suggest that a prior history of cardiovascular comorbidities including hypertension is associated with a more severe respiratory disease upon COVID-19 infection.[1,10] As to whether such CKD-specific risk factors as protein-energy wasting (PEW) are linked to worse COVID-19 outcomes, this and other important questions remain to be addressed in upcoming epidemiologic studies of COVID-19-infected patients with kidney diseases. Some studies suggest a high rate of AKI events on COVID-19 infection, whereas a recent study from Wuhan, China, reported that AKI happened in none of the hospitalized patients with this viral infection.[11] As more studies are underway, it is prudent that during an active COVID-19, we ensure the mitigation of PEW risk and immediate correction of PEW in all patients with kidney diseases including transplant recipients. We encourage adequate protein and calorie intake, be it enterally or parenterally, so that any occurrence of hypokalemia or hypophosphatemia can be avoided and that PEW, sarcopenia, and cachexia can be prevented or immediately corrected.[12] In the midst of this serious infection, there is no role for delaying nutrition support or for low protein, low phosphorus, or low potassium regimens if the patient has COVID-19 infection.[13] Therefore, the need to supervise the nutrition regimens of patients with kidney diseases may be enhanced during this period and should not be ignored while focusing on other, seemingly more urgent, matters.

This issue of the *Journal of Renal Nutrition* (JREN) encompasses a diverse array of topics in renal nutrition. Chewcharat et al[14] presented the results of a meta-analysis on the effects of restricted protein diet supplemented with keto-analogues on several clinical outcomes in 1,459 persons with CKD, who participated in 17 randomized, controlled trials. The authors showed that this dietary intervention could effectively improve kidney endpoints including preserving kidney function and diminishing proteinuria, blood pressure levels, and CKD-mineral bone disorder parameters without causing malnutrition.[14] In another meta-analysis of 8 randomized controlled trials comprising 371 patients on hemodialysis by Dezfouli et al,[15] omega-3 supplementation was found to decrease serum C-reactive protein concentration in these patients.

In a 24-week nonblinded randomized controlled trial by Liao et al,[16] the antiproteinuric effect of calcitriol was examined in 60 patients with CKD who had vitamin D deficiency. The investigators found that the urine protein/creatinine ratio was significantly lower than the baseline values in the calcitriol group compared with the control group.[16] In another randomized, double-blind, placebo-controlled trial by Ostadmohammadi et al,[17] in 60 patients with diabetes and chronic hemodialysis, melatonin supplementation for 12 weeks exhibited beneficial effects on mental health, glycemic control, cardiometabolic risk, and oxidative stress.

Hill et al[18] conducted a 20-week, nonrandomized, single-center, pretest-posttest study to investigate the feasibility of consuming an oat beta-glucan supplement for 12 weeks and assessed its effects on selected uremic toxins in 28 patients with CKD. Their report indicated that a diet supplemented with beta-glucan was safe and potentially efficacious in lowering serum concentrations of trimethylamine N-oxide. Trimethylamine N-oxide is related to intake of animal-based proteins including red meat and associated with worse kidney and cardiovascular outcomes.[19] La Scola et al[20] evaluated the association of body mass index with estimated glomerular filtration rate in children with congenital solitary kidney in a multicenter cross-sectional study and found a lower estimated glomerular filtration rate was associated with a higher body mass index–related standard deviation score and the duration of overweight or obesity. They concluded that prevention strategies should be considered to counteract overweight and obesity in persons with a solitary kidney.[20] Gomez-Garcia et al[21] evaluated diet quality and interleukin (IL)-6 genotypes and their association with metabolic and kidney function measures in 219 Mexican patients with type 2 diabetes mellitus and found that interactions between diet quality and IL-6 genotypes/haplotypes were associated with the main metabolic and kidney function parameters. They concluded that genetic profiling can be useful in designing dietary portfolios and nutritional interventions for the management of diabetes.[21] Olvera-Soto et al[22] studied the effect of resistance exercise in addition to nutritional vitamin D3 (cholecalciferol) on nutritional status measures in 39 patients with CKD stage 4 not on dialysis and found improved muscle function as measured by handgrip strength. Finally, Martinez-Pineda et al[23] analyzed the effect of culinary treatments on the reduction in potassium content in potatoes and reported that the potassium content of potatoes is reduced to an acceptable limit using these methods.

Although the COVID-19 pandemic is expected to continue to overshadow many aspects of patient care as well as education and research in nutrition and kidney disease, JREN will continue to cover both COVID-19 developments and other important priorities in our field.[24,25] We wish all of our readers and the patients to be well during this pandemic and to remember to take care to protect yourself: wash your hands often with soap and water, avoid touching your eyes, nose, and mouth with unwashed

hands, avoid close contact (6-feet apart), follow the guidelines of the Centers for Disease Control and Prevention,[26] and eat healthy foods with abundant amounts of fruits and vegetables as discussed previously.

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References

1. Ferrey A, Choi G, Hanna RM, et al. A case of COVID-19 in a chronic hemodialysis patient presenting with gastroenteritis and developing severe pulmonary disease. *Am J Nephrol*. 2020:1-5. https://doi.org/10.1159/000507417 [In press].

2. Gupta S. Obesity: the fat advantage. *Nature*. 2016;537:S100-S102.

3. Douglas RM, Hemila H, D'Souza R, Chalker EB, Treacy B. Vitamin C for preventing and treating the common cold. *Cochrane Database Syst Rev*. 2004:CD000980.

4. Hemila H, Chalker E. Vitamin C for preventing and treating the common cold. *Cochrane Database Syst Rev*. 2013:CD000980.

5. Handelman GJ. New insight on vitamin C in patients with chronic kidney disease. *J Ren Nutr*. 2011;21:110-112.

6. Chen J, Wu J, Kong D, et al. The effect of antioxidant vitamins on patients with diabetes and albuminuria: a meta-analysis of randomized controlled trials. *J Ren Nutr*. 2020;30:101-110.

7. Abbasi M, Daneshpour MS, Hedayati M, Mottaghi A, Pourvali K, Azizi F. Dietary total antioxidant capacity and the risk of chronic kidney disease in patients with type 2 diabetes: a nested case-control study in the Tehran Lipid Glucose study. *J Ren Nutr*. 2019;29:394-398.

8. Kitayaporn D, Nelson KE, Charoenlarp P, Pholpothi T. Haemoglobin-E in the presence of oxidative substances from fava bean may be protective against Plasmodium falciparum malaria. *Trans R Soc Trop Med Hyg*. 1992;86:240-244.

9. Joshi S, Shah S, Kalantar-Zadeh K. Adequacy of plant-based proteins in chronic kidney disease. *J Ren Nutr*. 2019;29:112-117.

10. Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically Ill patients with COVID-19 in Washington state. *JAMA*. 2020; https://doi.org/10.1001/jama.2020.4326.

11. Wang L, Li X, Chen H, et al. Coronavirus disease 19 infection does not result in acute kidney injury: an analysis of 116 hospitalized patients from Wuhan, China. *Am J Nephrol*. 2020 [In press].

12. Kalantar-Zadeh K, Moore LW. Improving muscle strength and preventing sarcopenia and cachexia in chronic kidney disease and transplanted patients by physical activity and exercise. *J Ren Nutr*. 2019;29:465-466.

13. Kalantar-Zadeh K, Moore LW. Why the nutritional management of acute versus chronic kidney disease should differ. *J Ren Nutr*. 2019;29:265-268.

14. Chewcharat A, Takkavatakarn K, Wongrattanagorn S, et al. The effects of restricted protein diet supplemented with ketoanalogue on renal function, blood pressure, nutritional status, and chronic kidney disease-mineral and bone disorder in chronic kidney disease patients: a systematic review and meta-analysis. *J Ren Nutr*. 2020;30:189-199.

15. Dezfouli M, Moeinzadeh F, Taheri S, Feizi A. The effect of omega-3 supplementation on serum levels of inflammatory biomarkers and albumin in hemodialysis patients: a systematic review and meta-analysis. *J Ren Nutr*. 2020;30:182-188.

16. Wu CC, Liao MT, Hsiao PJ, et al. Antiproteinuria effect of calcitriol in patients with chronic kidney disease and vitamin D deficiency: a randomized controlled study. *J Ren Nutr*. 2020;30:200-207.

17. Ostadmohammadi V, Soleimani A, Bahmani F, et al. The effects of melatonin supplementation on parameters of mental health, glycemic control, Markers of cardiometabolic risk, and oxidative stress in diabetic hemodialysis patients: a randomized, double-blind, placebo-controlled trial. *J Ren Nutr*. 2020;30:242-250.

18. Hill E, Sapa H, Negrea L, et al. Effect of oat beta-glucan supplementation on chronic kidney disease: a feasibility study. *J Ren Nutr*. 2020;30:208-215.

19. Kalantar-Zadeh K, Moore LW. Does kidney longevity mean healthy vegan food and less meat or is any low-protein diet good enough? *J Ren Nutr*. 2019;29:79-81.

20. La Scola C, Guarino S, Pasini A, et al. Effect of body mass index on estimated glomerular filtration rate levels in children with congenital solitary kidney: a cross-sectional multicenter study. *J Ren Nutr*. 2020;30:261-267.

21. Gomez-Garcia EF, Cortes-Sanabria L, Cueto-Manzano AM, et al. Interactions between diet quality and interleukin-6 genotypes are associated with metabolic and renal function parameters in Mexican patients with type 2 diabetes mellitus. *J Ren Nutr*. 2020;30:223-231.

22. Olvera-Soto MG, Ruiz Medina VL, Medeiros M, et al. Effect of resistance exercise plus cholecalciferol on nutritional status indicators in adults with stage 4 chronic kidney disease. *J Ren Nutr*. 2020;30:232-241.

23. Martinez-Pineda M, Yague-Ruiz C, Vercet-Tormo A. Is it possible to include potato in the diet of chronic kidney disease patients? New culinary alternatives for limiting potassium content. *J Ren Nutr*. 2020;30:251-260.

24. Moore LW, Kalantar-Zadeh K. Opportunities for renal nutrition and metabolism at the dawn of 2020s: an inauguration message from the new JREN editors-in-chief. *J Ren Nutr*. 2019;29:1.

25. Moore LW, Kalantar-Zadeh K. Promoting clinical nutrition science in chronic kidney disease. *J Ren Nutr*. 2020;30:1-3.

26. How to protect yourself. Coronavirus disease 2019 (COVID-19). Centers for disease control and prevention. Available at: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fprepare%2Fprevention.html. Accessed March 28, 2020.