

Dear Editor,

Thank you for your letter and the reviewers' comments concerning our manuscript entitled "Medical Nutritional Therapy for Renal Transplantation in the COVID-19 Pandemic". Those comments are all valuable and very helpful for revising and improving our paper. We have studied the comments carefully and have made some corrections. For the convenience of the reviewers, we have highlighted the main changes to the previous manuscript by using colored texts in the revised paper. Also, thank reviewers for all of the positive comments and we answered to comments, that were seen lack of information about the manuscript, in this letter.

Reviewer 1

The reviewed manuscript is supposed to be a mini-review on nutrition in patients with kidney transplantation in COVID-19 pandemic. This information is on high-demand and would attract attention of the readers. Although the main aspects of nutrition for patients in the waiting list and after kidney transplantation are given, there are some concerns that require author's attention. Although it is clear that the authors faced the problem of lacking evidence-based information on the association of nutrition and kidney disease flow and outcomes in SARS-CoV2 infected persons, in the current state the paper seems too general. I would suggest that general trends in change of nutrition in the era of COVID-19 outbreak would be added, in view of their influence on chronic kidney disease (CKD) and kidney transplantation (factors that currently supposed to be associated with higher chances to acquire infection, those associated with the severity of COVID manifestations, and recovery). The title of the paper contains "medical nutritional therapy". Could you please explain the term in the text? Are there any concerns related to provision of medical nutrition to patients before and after kidney transplantation in COVID era? What about the use of the specialized products (availability? products for nutritional support of patients with CKD and respiratory insufficiency? the influence of products enriched with PUFAs on kidney function?)? What is the role of enteral and parenteral nutrition in the management of patients with CKD or after kidney transplantation in case they are infected with SARS-CoV-2? Whether it is possible to assess the efficacy of the published guidelines for nutritional management of individuals with SARS-CoV-2 infection (for example, <https://doi.org/10.1016/j.clnu.2020.03.022>) on CKD and peri-transplantation period?

Answer to Reviewer 1

Thank you for your contribution. The full text was rearranged by light of your comments. Also, the important information was added as follow.

1. Medical nutritional therapy is defined as follows in the text.

"Nutritional diagnostic, therapy, and counseling services for the purpose of disease management, which are furnished by a registered dietitian or nutrition professional"

2. ESPEN guideline the recommendations are included in the manuscript. Physical activity recommendations have been added to "other recommendations" section. A new nutritional

support subtitle has been added in the text. In this subtitle, conditions that require nutritional support, nutritional route, formula selection and the effects of omega-3 are mentioned.

“Nutritional support

Nutritional support is recommended for patients who cannot or are predicted to be unable to meet their energy and nutrient requirements sufficiently before and after transplantation. In the posttransplantation period, oral food intake and enteral nutrition are recommended as early as possible. The use of standard enteral formulas is generally recommended for the patients. However, the use of renal enteral formulas comes to the fore in patients with electrolyte disturbances in the early period after transplantation. Similarly, in polymorbid intensive care patients with COVID-19, oral nutritional supplements are recommended in patients who are not intubated. If the patient is intubated, post-pyloric nasogastric tube feeding can be suggested. Parenteral nutrition is recommended for patients whose energy and nutrient intake is insufficient through oral nutritional supplements and tube enteral nutrition or who are contraindicated for enteral nutrition. It is observed that enteral formulas with moderately high protein are generally recommended for patients with COVID-19. This recommendation seems more applicable in patients who received dialysis treatment before renal transplantation. If there is no electrolyte disorder in patients with COVID-19 in the posttransplantation, it may be more appropriate to use standard isoosmolar polymeric enteral formulas. In addition, it is thought that products enriched with omega-3 fatty acids, which have a positive effect on kidney functions, can both improve oxygenation and help reduce especially cardiovascular complications of COVID-19.”

Reviewer 2

Overall, this is an interesting and relevant brief review, which is well written and instructive. I have several comments on additional information and citations I deem worth including. Supplements are briefly mentioned. Could the author elaborate a little bit more on that topic? What is known about their role in boosting the immune response against COVID-19? Are there any data available specifically in patients after renal transplantation? The following article could be interesting for that matter. https://www.frontiersin.org/articles/10.3389/fimmu.2020.01548/full?fbclid=IwAR33z_j5ndzi_smgWBK5Po_egVkecQGWZhxBg-u7go35ytchTUE8JWFUC64. The importance of vitamin D is stressed in the article for a good reason. Can the author elaborate a little more on the biological mechanisms of its beneficial effects in kidney transplantation and protection against viral infection? As vitamin C is a subject of a long-standing discussion in the treatment of viral infections in general and recently COVID-19 in particular, can the author include a paragraph on its role in combating the SARS-CoV-2 virus? Is there any empirical data available for patients with renal disease in particular? (See also [https://www.jrnjournal.org/article/S1051-2276\(20\)30083-2/fulltext](https://www.jrnjournal.org/article/S1051-2276(20)30083-2/fulltext) and https://helda.helsinki.fi/bitstream/handle/10138/317374/ic_52_222.pdf?sequence=1) Another thematic complex touched upon in the manuscript is minerals. Can the author elaborate in greater detail on the specific roles of particular micronutrients? As iron deficiency is a notorious problem in patients after kidney transplantation (<https://pubmed.ncbi.nlm.nih.gov/19076330/>) I'd be particularly interested in the part of iron deficiency and supplementation strategies in the context of kidney transplantation and viral

infection. Another interesting aspect is melatonin's potential roles, which have been attributed to kidney-protective effects in sepsis and probiotic supplements. E.g., mentioned in this review: <https://www.sciencedirect.com/science/article/pii/S2405844021001134#bib152> . Can the author discuss these topics briefly and cite available evidence in transplanted patients (or otherwise point out that evidence is lacking).

Answer to Reviewer 2

1 Thank you for your contribution. The vitamins and minerals title has been expanded. In this title, especially Vitamins D, C, iron, and nutraceuticals are detailed. The below information was added.

“Principally, low levels of some micronutrients have been associated with negative clinical outcomes during viral infections. Vitamins A, D, B, C, omega-3, as well as selenium, zinc and iron should be advised in the assessment of micronutrients in COVID-19 patients.”

“In response to COVID-19 infection, vitamin D can prevent disease progression through the production of antimicrobial peptides in the respiratory epithelium and help reduce inflammatory response”

“Vitamin C is an important antioxidant nutrient, specifically for white blood cells to fight infections. Vitamin C contributes to immunity by supporting both the innate and adaptive immune system, modulating inflammatory mediators, and influencing epithelial barriers. It has important benefits such as preventing common cold and upper respiratory tract infections, reducing the duration and severity of the disease and supporting respiratory defense mechanisms. In addition, it is thought that vitamin C may have a positive effect against COVID-19, as many upper respiratory tract infections are caused by endemic coronaviruses. In excessive intake of Vitamin C, accumulation of oxalose, which is a metabolic byproduct of ascorbic acid, can be seen in kidney patients. Therefore, dietary vitamin C intake appears to be safer than supplementation. Consumption of fresh vegetables and fruits with high vitamin C contributes to increasing the intake of not only vitamin C but also other antioxidant vitamins. However, it should not be forgotten that the potassium contents of vitamin C sources are generally high. Therefore, it is important to offer these recommendations by monitoring serum potassium levels in patients”

“Iron deficiency and related anemia are frequently seen in renal transplantation patients due to insufficient iron stores, intraoperative blood loss and frequent phlebotomy after transplantation. During the first 12 weeks after transplantation, blood and iron losses are important and may require intravenous iron administration. Although iron supplementation offers immune-boosting benefits in individuals with iron deficiency, it can exacerbate infections and inflammation. Given that iron is important for viral replication, the safety and effectiveness of iron supplementation during the COVID-19 pandemic is controversial.”

“Nutraceuticals can increase the immune responses of people infected with encapsulated RNA viruses such as influenza and coronavirus. Because of the immune-modulating effects of nutraceuticals such as beta-glucans, melatonin and probiotics, it might be valuable for efficient clinical outcomes for COVID-19 patients. However, there are insufficient data and strong evidence for these components.”

Science Editor

1 Scientific quality: The manuscript describes a review of the medical nutritional therapy for renal transplantation in the COVID-19 pandemic. The topic is within the scope of the WJT. (1) Classification: Grade C and Grade D; (2) Summary of the Peer-Review Report: The authors found an interesting and relevant brief review, which is well written and instructive. However, the additional information and citations need to be added. The questions raised by the reviewers should be answered; and (3) Format: There are 2 figures. (4) References: A total of 31 references are cited, including 26 references published in the last 3 years; (5) Self-cited references: There are no self-cited references; and (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B and Grade B. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJT. 5 Issues raised: (1) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (2) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout; (3) Please obtain permission for the use of picture(s). If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable; and (4) The column should be minireviews. 6 Recommendation: Conditional acceptance.

Answer to Science Editor

Thank you for your attention. Original figures have been added as an editable PowerPoint file. The references have been updated including all authors' names, PMID and DOI numbers.

