Editorial: Nutraceuticals for the recovery of COVID-19 patients

Tilakavati Karupaiah¹ and Kuo-Cheng Lu²,³*

¹Faculty of Health and Medical Sciences, School of BioSciences, Taylor’s University, Subang Jaya, Selangor, Malaysia, ²Division of Nephrology, Department of Medicine, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei City, Taiwan, ³Division of Nephrology, Department of Medicine, School of Medicine, Fu Jen Catholic University Hospital, Fu Jen Catholic University, New Taipei City, Taiwan

KEYWORDS
COVID-19, dietary patterns, nutraceuticals, vegetarian diet, vitamin D

The novel coronavirus disease (COVID-19) unleashed sudden and unprecedented mortality on global populations and fosters a lingering health burden. In our call for papers on the theme Nutraceuticals for the recovery of COVID-19 patients, we purposively invited topics on the immunomodulatory effects of nutrients and bioactive compounds falling into the narrow definition of nutraceuticals and functional foods (1–3) as well as dietary supplements and designed diets (4), given the knowledge gaps in adjunctive therapy management for the post-infection stages of COVID-19. Falling within this research theme are 10 papers covering dietary protein (Hashemi et al.), melatonin (Su et al.), curcumin (Yang et al.), herbal tea (Hsiesh et al.), dietary supplements (Hashemi et al.), and dietary patterns (Ebrahimzadeh et al.; Hou et al.; Vajargah et al.) as well as vitamin D (Bogliolo et al.; Chiang et al.) (Figure 1).

Malnutrition is prevalent in COVID-19-infected patients, particularly in those with a greater severity of the disease and who are critically ill (1). A major complication associated with the initiation of feeding in malnourished patients is refeeding syndrome (2). In a prospective cohort study, Shariatpanahi et al. assessed patients for their risk of developing refeeding syndrome and those who did develop it. They found the incidence of refeeding syndrome was relatively high in the majority of critically ill COVID-19 patients, but increased protein intake was associated with reduced occurrence of refeeding syndrome.

The protective role of vitamin D in COVID-19 sufferers (3) is commonly researched for its immunomodulatory and anti-inflammatory action at the level of endothelial function (4–6), and is highly recommended as an adjuvant therapy for COVID-19 (7). In this special issue, a prospective observational multicenter study by Bogliolo et al. showed that very low 25(OH) vitamin D levels were highly prevalent in patients with severe COVID-19, but low 25(OH) vitamin D levels were not associated with high mortality outcomes in moderate to severe cases of COVID-19. This finding is contrary to a meta-analysis of seven systematic reviews (7) that showed that vitamin D supplementation reduces the risk of mortality, need for intensive care, and mechanical
ventilation requirements in COVID-19 patients. Another
direction in vitamin D adjuvant therapy is in kidney
disease, given the concern that COVID-19 patients who
are asymptomatic or have mild symptoms show dynamic
changes in renal function (8), whilst patients with chronic
kidney disease (CKD) frequently have vitamin D deficiency
and increased susceptibility to infection. In their review article,
Chiang et al. highlight the double burden of increased risk for
vitamin D deficiency in CKD patients due to the coexistence
of immune activation and immune deficiency, and proposed
mechanisms by which vitamin D administration could modulate
the immune system and alleviate the pathological consequences
of COVID-19. A further benefit of vitamin D supplementation
would be to reduce the severity of acute kidney injury in
COVID-19 patients via reducing soluble urokinase-type
plasminogen activator receptor levels.

Factors such as age, sex, and comorbidities are key
determinants of illness severity and progression of COVID-
19. The review article by Su et al. centers attention on the
decline in melatonin levels exacerbated by aging, with a strong
implication of compromised mitochondrial redox activities
which could explain the higher death rate of COVID-19
in older age groups. Declining melatonin levels are closely
related to mitochondrial dysfunction, and its reversal with
melatonin supplementation could limit virus-related diseases.
Hence, melatonin in elderly people may be warranted in the
treatment of COVID-19.

The special edition introduces curcumol as a common
traditional Chinese medicine (TCM), isolated from Rhizoma
Curcumae with well-documented anti-viral activity (9). By
using network pharmacology and systematic bioinformatics
analysis, Yang et al. identified seven core targets of curcumol
therapy for lung adenocarcinoma (LUAD) patients infected
with COVID-19. These targets influence cell-signaling
associated with the Warburg effect, which supports SARS-
CoV-2 replication and inflammatory response. Comparative
transcriptomic analysis specified the effects of curcumol
through control of cell cycle, DNA damage response, and
cell apoptosis. The combination of TCM and standard
management in treating patients with COVID-19 in Taiwan
was examined using Jing Si Herbal Tea (JSHT). A prospective
cohort study by Hsieh et al. that recruited patients with
mild to moderate COVID-19 suggests JSHT combined
with standard management may prevent critical status and
mortality. Effective improvements in measured outcomes
such as reverse transcription–polymerase chain reaction cycle
threshold value, C-reactive protein level, and Brixia score
occurred in male and older patients (≥60 years), suggesting
that three main pathophysiological pathways, anti-infective,
anti-inflammation, and anti-thrombosis, were potentially
targeted (10).

The ability of purposive dietary patterns to protect
against respiratory viral infections and reduce associated
inflammation and oxidative stress is also examined in this
special edition. A retrospective evaluation of COVID-19
patients by Hou et al. found COVID-19 symptom severity
was significantly and inversely associated with adherence to
a self-reported vegetarian diet compared to those consuming
a non-vegetarian diet, with the latter group having a higher
risk in contracting critically severe COVID-19. A cross-
sectional study of COVID-19 hospitalized patients by Vajargah
et al. showed higher consumption of fruits, vegetables, and
fiber was inversely linked with COVID-19 severity, clinical
symptoms, hospitalization, and convalescence duration,
and concentrations of inflammatory markers. Fruits and
vegetables are rich in fiber and a good source of anti-
inflammatory and immune-boosting vitamins, minerals,
and antioxidants (11). In contrast, the pre-COVID-19
status of habitual food intake could be an environmental
factor affecting inflammation status in the body (12) and
potentially outcome response to COVID-19 infection (13).
Ebrahimzadeh et al. retrospectively evaluated 250 recovered
COVID-19 cases to explore diet pattern effects using a
self-reported web-based food questionnaire. They found
cases reporting a higher adherence to a healthy diet pattern
were associated with lower inflammatory markers levels
and lower risk of COVID-19 severity, hospitalization, and
convalescence duration.

Was consumption of immune-boosting supplementation
critical to offering protection during the COVID-19 pandemic?
Hashemi et al. in a cross-sectional study involving 300
adult men and women with COVID-19, probed recent and
long-term supplement intakes using a questionnaire. Short-
term use (∼2 months) saw improvements in blood urea
nitrogen and higher serum 25(OH)D levels whilst long-term
use achieved significantly lower invasive oxygen support, lactate
dehydrogenase (LDH), fewer days of fever, and higher serum
25(OH)D levels.

The papers included under the theme of Nutraceuticals for
the recovery of COVID-19 patients are highly relevant to the
emergence of long COVID symptoms as a health burden and the need for encouraging more research in this area.

Author contributions

KC-L wrote the introduction and the conclusion. TK wrote the central part with comments on the cited papers and references. Both authors contributed to the article and approved the submitted version.

Acknowledgments

We thank the staff of the medical research center of Taipei Tzu Chi Hospital for technical support.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher’s note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Shahbazi S, Hajimohammadebrahim-Ketabforoush M, Vahdat Shariatpanahi M, Shahbazi E, Vahdat Shariatpanahi Z. The validity of the global leadership initiative on malnutrition criteria for diagnosing malnutrition in critically ill patients with COVID-19: A prospective cohort study. Clin Nutr ESPEN. (2021) 43:377N.mo doi: 10.1016/j.clnesp.2021.03.020
2. da Silva JSV, Seres DS, Sabino K, Adams SC, Berdahl GI, Citty SW, et al. ASPEN consensus recommendations for refeeding syndrome. Nutr Clin Pract. (2020) 35:178–95. doi: 10.1002/ncp.10474
3. Teshome A, Adane A, Girma B, Mekonnen ZA. The impact of vitamin D level on COVID-19 infection: systematic review and meta-analysis. Front Public Health. (2021) 9:624559. doi: 10.3389/fpubh.2021.624559
4. Rhodes JM, Subramanian S, Laird E, Griffin G, Kenny RA. Perspective: Vitamin D deficiency and COVID-19 severity - plausibly linked by latitude, ethnicity, impacts on cytokines, ACE2 and thrombosis. J Intern Med. (2021) 289:97raman doi: 10.1111/joim.13149
5. Peng MY, Liu WC, Zheng JQ, Lu CL, Hou YC, Zheng CM, et al. Immunological aspects of SARS-CoV-2 infection and the putative beneficial role of vitamin-D. Int J Mol Sci. (2021) 22:10. doi: 10.3390/ijms22105251
6. Ho P, Zheng JQ, Wu CC, Hou YC, Liu WC, Lu CL, et al. Perspective adjunctive therapies for COVID-19: beyond antiviral therapy. Int J Med Sci. (2021) 18:314, Wu doi: 10.7150/ijms.51935
7. Shah K, V PV, Sharma U, Mavalankar D. Does vitamin D supplementation reduce COVID-19 severity? - a systematic review. QJM. (2022) hca178. doi: 10.1093/qjmed/hca178
8. Chang YC, Tsai PH, Chou YC, Lu KC, Chang FY, Wu CC. Biomarkers linked with dynamic changes of renal function in asymptomatic and mildly symptomatic COVID-19 patients. J Pers Med. (2021) 11:5. doi: 10.3390/jpm11050432
9. Jennings MR, Parks RJ. Curcumin as an antiviral agent. Viruses. (2020) 12:11. doi: 10.3390/v121111242
10. Shibu MA, Lin YJ, Chiang CY, Lu CY, Goswami D, Sundhar N, et al. Novel anti-aging herbal formulation Jing Si displays pleiotropic effects against aging associated disorders. Biomed Pharmacother. (2022) 146:112427. doi: 10.1016/j.biopha.2021.112427
11. Alkhateb A. Antiviral functional foods and exercise lifestyle prevention of coronavirus. Nutrients. (2020) 12:2633. doi: 10.3390/nu12092633
12. Saghafi-Asl M, Mirmajidi S, Asghari Jafarabadi M, Vahid E, Shivappa N, Hebert JR, et al. The association of dietary patterns with dietary inflammatory index, systemic inflammation, and insulin resistance, in apparently healthy individuals with obesity. Sci Rep. (2021) 11:7515. doi: 10.1038/s41598-021-86993-7
13. Salazar Robles E, Kalantar Zadeh K, Radillo H, Calderon-Juaréz M, Garcia-Barcenas CA, Ledesma-Perez PD, et al. Association between severity of COVID-19 symptoms and habitual food intake in adult outpatients. BMJ Nutr Prev Health. (2021) 4:469 Hea doi: 10.1136/bmjnpb-2021-000348