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# Association of Dietary Macronutrients and Micronutrients with COVID-19

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**ABSTRACT**

**Introduction:** The Coronavirus Disease 2019 (COVID-19) outbreak is still an ongoing problem affecting people's well-being globally. It is known that malnutrition is an important determinant of immune function, leading to an increased risk of infection and severity of diseases. The aim of this study was to characterize the relationship between macronutrients and micronutrients and this viral infection.

**Methods:** This study was a historical cohort including 6539 subjects (57.2% females, 42.8% males) from the Mashhad stroke and heart atherosclerotic disorder (MASHAD) cohort study. Dietary intakes were assessed using a 65-item validated food frequency questionnaire (FFQ). Data on COVID-19 diagnosis was collected from online health records of patients available in the Sina health information system from the onset of the disease to the end of July 2020. COVID-19 diagnosis has been confirmed using a lung spiral CT scan or PCR laboratory test. SPSS software (Version 20) was used for the analysis of data.

**Results:** A total of 154 subjects including 85 men (55.2%) and women (44.8%) were infected with COVID-19. Body mass index (p=0.03) and waist circumference (p=0.01) of the patients along with the protein (p=0.02), total $N_2$ (p=0.02), calcium (p=0.02) and thiamin (p=0.04) content of their diet was significantly associated with COVID-19. After multivariate analysis, dietary calcium remained the only dietary factor that predicted COVID-19 infection (OR=0.94, 95%CI [0.87-0.99], p value=0.04).

**Conclusion:** Our findings indicated that prevalence of COVID-19 may be affected by dietary macronutrients and micronutrients. According to our data, increased calcium intake can reduce the prevalence of COVID-19.

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## Introduction

The COVID-19 is a global outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The prevalence of this disease reported by 651.918.402 and 6.656.601 confirmed cases and deaths, respectively, in December 25th,2022 (1). COVID-19 mainly affects the respiratory system but may also lead to multi-organ failure and cause mortality in susceptible patients with comorbidities and chronic diseases including cardiovascular disease, diabetes and obesity (2,3).

The nutritional status of populations can be a protective key factor against weakening of the immune system in COVID-19 infection (4). Any infection outcome is influenced by nutritional status, because of its importance role on innate and adaptive immune responses (5). Malnutrition is a well-known risk factor for reduced immunity (6). Vitamins B, C, and E, along with iron, selenium, and zinc, play a supportive role in immunocompetence (7). Somewhat chronic deficiency in these micronutrients may disturb immune function by cellular activation and alternation in signaling, molecule production and gene expression (8). Previous evidence have shown that some micronutrients such as vitamins D, A, and C, selenium, and zinc can characterize the clinical course of COVID-19 patients (9). Whereas there are controversial debates regarding COVID-19 prevention by vitamin D (10), amino acids, polyunsaturated fatty acids (PUFAs), and other micronutrients (11).

Several dietary elements such as vitamins, omega-3 fatty acids and polyphenols perform their immunomodulatory function by affecting the pro-inflammatory genes expression, cytokines production, proliferation and development of immune cells (12-14).

A systematic review has been reported that a balanced diet and proper nutrients supplementation can exert a critical role in prevention, treatment and management of COVID-19 (15). Although, there have been few clinical trials regarding the effect of micronutrient supplementation in patients with COVID-19 (15).

On the other hand, COVID-19 may reduce food intake and absorption (16), In the current study we aimed to assess the association of dietary macronutrients and micronutrients with COVID-19 in North eastern of Iran.

## Materials and Methods

### *Study design and population*

This research was a historical cohort including 6539 subjects (57.2% females, 42.8% males) from the Mashhad Stroke and Heart Atherosclerotic Disorders Study (MASHAD study). Exclusion criteria were: energy consumption of less than of 800 kcal/d or more than 4,200 kcal/d and completion of < 90% of the food frequency questionnaire (FFQ). We have previously reported the Cronbach's alpha by 0.67 (17).

The MASHAD study was initiated in 2010 and concluded in 2020. Subjects were chosen from three areas in the city, using a stratified cluster random sampling method. The details of the study population have been published previously (18). The protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences (MUMS) and participants' written consent were acquired when they entered the cohort study (figure 1).

### *Demographic data*

Demographic characteristics data including age, sex, socioeconomic status, education and lifestyle data of the subjects were documented by Health care professionals and a nurse via interview.

Anthropometric parameters including height, weight and waist circumference (WC) were assessed in all participants. Standing height (cm) and waist circumference (cm) were measured to the nearest millimeter with a tape measure. Weight (kg) was measured to the nearest 0.1 kg using electronic scales. Body mass index (BMI) was calculated by dividing n kilograms by height in meters squared (13).

### *Dietary intake assessment*

We used a previously validated semiquantitative FFQ to evaluate the dietary intake (14), consisting of 65 food items with five consumption frequency groups (daily, weekly, monthly, rarely, and never) for each food item and portion size. The FFQ was filled out by expert nutritionists by face-to-face interviews. In order to evaluate macro and micronutrient contents from FFQ, Diet Plan 6 software (Forestfield Software Ltd., Horsham, West Sussex, UK) was used.

### *Diagnosis of COVID-19*

Data collection started from the disease onset until the end of July 2020. Records of the COVID-19 diagnosis were received from the Sina health information system, that included patients' electronic health profiles from hospitals and health care centers of the country. COVID-19 diagnosis has been confirmed using a lung spiral CT scan or PCR laboratory test.

### *Statistical analysis*

Statistical analysis was performed using SPSS, version 20.0 (SPSS, Chicago, IL, USA). P-value<0.05 was considered statistically significant. Data is described by mean, frequency and standard deviation (SD). Mean±SD was used for normally distributed variables (or as median and IQR for not normally distributed variables). Mann-Whitney and Chi-Square tests were used to compare quantitative and qualitative variables with the outcome, respectively. The subjects were compared based on getting affected by COVID-19 during the time period of the study. The multivariate logistic regression model was used to determine the association of macronutrients and micronutrients with COVID-19.

### *Ethics*

Human Research Ethics Committee of Mashhad University of Medical Sciences has reviewed and approved the study protocol, informed consent form, and other study-related documents. All participants provided informed, written consent.

## Results

In the present study 6539 participants (consisting of 3738 female and 2801 male) were recruited as part of the MASHHAD cohort study. During the collection of the data, 154 participants became infected with COVID-19 including 85 men (55.2%) and women (44.8%).

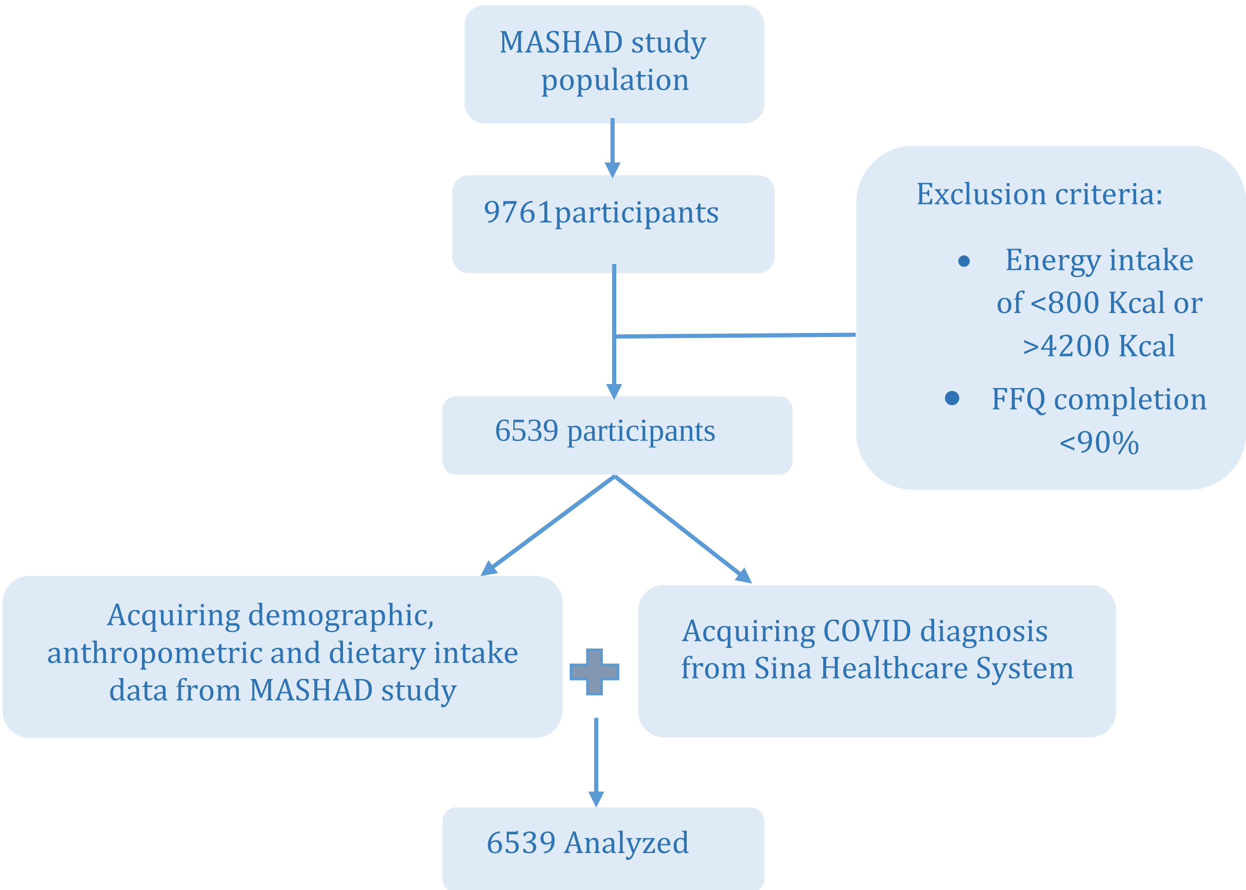


**Figure 1.** The flowchart of study.

The Baseline characteristics of the participants are reported in Table 1. There was a significant higher in the BMI for COVID positive group (27.63±6.04 kg/m2) compared with COVID-19 negative group (28.05±6.70 kg/m2) (P-value=0.03). Furthermore, there was an augmented WC in subjects with COVID-19 (97.00±14.63 cm) compared to subjects without COVID-19 (95.00±15.50 cm) (P-value=0.01). Moreover, 20.8% of each study group were current smokers. We also found that the majority of participants had a moderate to low socioeconomic status.

Table 2 has summarized the association of COVID-19 with macronutrients and micronutrients adjusted for energy in two study groups. A significant association was found between the protein, total N2, and calcium intake with COVID-19 (P-value=0.02 for all variables).

The results of binary logistic regression analysis showed that out of the all significantly related anthropometric measurements and nutrients, only dietary calcium was remarkably associated with reduced risk of COVID-19 (OR=0.94, 95%CI [0.87-0.99], P-value =0.04). For every 100 mg rise in calcium intake, the chance of getting infected by COVID-19 is reduced by 6% (Table 3).

## Discussion

The results showed that there were significant associations between the protein, total N2 and calcium intake with COVID-19. Furthermore, every 100 mg rise in calcium intake can reduce the chance of getting infected with COVID-19, by 6%.

Nutritional status exerts a key role in optimal prognosis in subjects with COVID-19 and can characterize the disease severity (19).

A balanced and sufficient diet is needed for the immune system's cells to function properly. In some conditions with augmented demand (such as stress, infection, and pollution), the immune system is activated, resulting in increased energy demand. An optimal diet can support the immune system not only by creating an efficient response against pathogens, but also via improving infections in a short time and thereby refraining from further chronic inflammation (20, 21).

**Table 1.** Baseline characteristics of participants within the different groups.

| Variables | | Covid-19-(۶۳۸۵) | Covid-19+-(154) | P-value |
|---|---|---|---|---|
| **Sex** | **Female** | 3653(57.2%) | 85(55.2%) | 0.62 |
| | **Male** | 2732(42.8%) | 69(44.8%) | |
| **Age [years]** | | 47.00(12.00) | 49.00(13.00) | 0.15 |
| **Weight [kg]** | | 71.40(16.40) | 73.50(12.88) | 0.06 |
| **BMI [kg/m$^2$]** | | 27.63(6.04) | 28.05(6.70) | **0.03** |
| **WC [cm]** | | 95.00(15.50) | 97.00(14.63) | **0.01** |
| **SBP [mmHg]** | | 120.00(20.00) | 120.00(23.33) | 0.42 |
| **DBP [mmHg]** | | 80.00(16.00) | 80.00(13.33) | 0.82 |
| **Currently Smoker** | | 1327(20.8%) | 32(20.8%) | 0.88 |
| **Socioeconomic status** | **Low** | 1385(50.0%) | 32(45.7%) | 0.66 |
| | **Moderate** | 1238(44.7%) | 35(50.0%) | |
| | **High** | 149(5.4%) | 3(4.3%) | |

**Abbreviations: BMI**: Body mass index; **WC:** Waist Circumference; **FBG**: Fasting Blood Glucose; **SBP:** Systolic blood pressure; **DBP**: Diastolic blood pressure; **PAL:** Physical Activity Level.

- Mann Whitney and Chi-Square tests were used for analysis.

-Values are indicated as Median (Interquartile Range) or Number (%).

**Table 2.** Association of COVID-19 with macronutrients and micronutrients adjusted for energy.

| Parameter[1] | Covid-19-(۶۳۸۵) | Covid-19+-(154) | P-value |
|---|---|---|---|
| **Macronutrients** | | | |
| Total fat (g/day) | 69.73(24.83) | 72.92(24.79) | 0.14 |
| Mono unsaturated fatty acid (g/day) | 19.30(7.40) | 19.85(7.11) | 0.14 |
| Poly unsaturated fatty acid (g/day) | 22.85(13.45) | 23.86(13.99) | 0.09 |
| Cholesterol (mg/day) | 184.01(186.92) | 182.22(203.31) | 0.93 |
| Carbohydrates (g/day) | 240.77(63.30) | 242.86(59.89) | 0.50 |
| Starch (g/day) | 144.49(62.07) | 141.83(60.11) | 0.24 |
| Total sugar (g/day) | 84.48(53.64) | 85.24(51.58) | 0.65 |
| Fiber (g/day) | 16.08(11.01) | 16.31(10.87) | 0.97 |
| Protein (g/day) | 67.96(20.79) | 65.91(21.43) | **0.02** |
| **Micronutrients** | | | |
| Total N2 (mg/day) | 10.59(3.32) | 10.21(3.20) | **0.02** |
| Zinc (mg/day) | 8.95(3.29) | 8.74(2.63) | 0.11 |
| Phosphorus (mg/day) | 1283.02(401.51 | 1230.43(394.23) | 0.10 |
| Potassium (mg/day) | 2746.65(1166.79) | 2696.56(967.42) | 0.77 |
| Calcium (mg/day) | 817.60(419.91) | 722.53(433.72) | **0.02** |
| Magnesium (mg/day) | 236.72(98.16) | 241.34(94.38) | 0.77 |
| Iron (mg/day) | 10.22(6.37) | 9.49(4.77) | 0.23 |
| Manganese (mg/day) | 3.81(1.51) | 3.78(1.53) | 0.81 |
| Selenium (µg/day) | 31.52(21.70) | 31.42(19.14) | 0.95 |
| Iodine (µg/day) | 92.08(106.32) | 87.15(96.55) | 0.51 |
| Sodium (mg/day) | 2100.15(1636.97) | 2110.62(1830.94) | 0.51 |
| Copper (µg/day) | 1.81(0.49) | 1.76(0.45) | 0.26 |
| Retinol (mg/day) | 174.63(163.31) | 174.98(150.64) | 0.94 |
| Carotene (µg/day) | 1354.78(2857.71) | 1345.34(1911.15) | 0.54 |
| Thiamin (mg/day) | 1.71(0.60) | 1.69(0.61) | 0.10 |
| Riboflavin (mg/day) | 1.98(0.72) | 1.84(0.89) | 0.10 |
| Niacin (mg/day) | 15.61(6.87) | 15.52(7.16) | 0.74 |
| Pantothenic acid (mg/day) | 4.99(2.44) | 4.75(2.43) | 0.72 |
| Vitamin B6 (mg/day) | 2.04(0.73) | 1.94(0.63) | 0.42 |
| Biotin (µg/day) | 25.39(13.91) | 24.74(14.40) | 0.61 |
| Folate (µg/day) | 215.65(124.39) | 216.06(143.66) | 0.83 |
| Vitamin B12 (µg/day) | 1.74(2.24) | 1.51(2.20) | 0.34 |
| Vitamin C (mg/day) | 69.54(95.71) | 63.19(109.37) | 0.46 |
| Vitamin D (µg/day) | 1.57(1.06) | 1.49(1.05) | 0.28 |

[1] All parameters were adjusted for energy intake and indicated as Median (Interquartile Range).

Decreased protein intake is associated with stripper collagen and connective tissue that reduces the antibodies numbers in the physical barrier and cause an ideal condition for the aggressor (22). The protein-energy malnutrition is known as a virulence agent for severe COVID-19 and increases the inflammation in the lungs (23). The results of a recent systematic review showed that some nutrients affect the function and strength of the immune response against viral infections including protein, omega-3 fatty acids, vitamin C, vitamin A, vitamin D, vitamin E, thiamine, pyridoxine, cobalamin, iron, zinc, and selenium (24).

**Table 3.** Association of COVID-19 with macronutrients and micronutrients using multivariate logistic regression model.

| Variables | odds ratio | 0.95.CI for odds ratio | P-value |
|---|---|---|---|
| BMI [$kg/m^2$] | 1.02 | 0.95-1.09 | 0.61 |
| Waist circumference[cm] | 1.01 | 0.99-1.04 | 0.43 |
| Protein | 1.04 | 0.93-1.17 | 0.49 |
| Total N2 | 0.74 | 0.37-1.50 | 0.41 |
| Calcium | 0.94 | 0.87-0.99 | 0.04 |

It is indicated that a low amount of protein in the body leads to a low antibody production and also a decline in functional active antibodies and gut-associated lymphoid tissue (GALT) (25). Likewise, the current study revealed that protein intake was significantly associated with COVID-19 infection although this significant relationship did not remain after controlling BMI and WC as confounding factors.

Thiamin is a micronutrient that has previously been proposed to be related to COVID-19 infection when there is a deficiency (24). Thiamin deficiency affects oxygen consumption in various tissues through a reduction in pyruvate dehydrogenase activity. Thiamin deficiency has some influences such as changes in carbohydrates, proteins and fats metabolism, immunosuppression, and nerve and memory disorders (26). We found that there was an association between decreased intake of thiamin and COVID-19, although this relation did not remain after adjustment for confounding variables.

Coronavirus membrane fusion is related to cellular ion conditions. Calcium level affects the fusion of SARS-COV into cells. It has been reported that the entrance of SARS-CoV into some cells has been decreased following the chelation of intracellular calcium (27). It is previously shown that patients with COVID-19 had low calcium in the early stage of the disease; the severe patients had significantly lower calcium concentrations than mild/moderate cases in the early stage. Pro-inflammatory cytokine IL-6 is also associated with serum calcium concentration in patients in any stage of disease (28). Hypocalcemia is prevalent in pneumonia and viral infection. The mechanisms of hypocalcemia include decreased dietary intake, vitamin D deficiency, rise in PTH secretion, increased calcium influx and hypoproteinemia (29, 30). Sun et al., found that low serum calcium level (especially ≤2.0 mmol/L) was related to worse clinical presentation, increased organ damage and septic shock, and more 28-day mortality in patients with confirmed COVID-19 (29). Furthermore, the results of a recent pooled analysis, in line with the current study, indicated that patients with severe COVID-19 significantly had lower serum calcium concentration (weighted mean difference: –0.20 mmol/L [95% CI: –0.25 to –0.20 mmol/L]) (31).

There were a few limitations to the present study. One of the potential limitations of our study is that our data belongs to a single-center study. Therefore it may not be suitable for generalizing to the society. Dietary intake is a factor that may be changed over time due to financial problems or developing a disease that requires special diets; thus, reliance on a food frequency questionnaire and a retrospective dietary assessment may not be sufficient. Moreover, the results might be inconclusive, and the accuracy should be confirmed by large-scale prospective clinical studies.

## Conclusion

Our finding revealed that calcium dietary intake is negatively associated with COVID-19 infection in a way that every 100 mg rise in calcium intake reduces the chance of COVID-19 infection reduces by 6%.

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## Conflict of interest

The authors have no conflict of interest to disclose.

## References

1. World Health Organization. Weekly Epidemiological Record (WER), 13 November 2020;95(46):557–572.

2. Hu L, Chen S, Fu Y, Gao Z, Long H, Ren HW, et al. Risk factors associated with clinical outcomes in 323 coronavirus disease 2019 (COVID-19) hospitalized patients in Wuhan, China. Clinical infectious diseases. 2020 Oct 15;71(16):2089-98.

3. Wu C, Chen X, Cai Y. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China (vol 180, pg 934, 2020). Jama Internal Medicine. 2020:1031-.

4. Alwarawrah Y, Kiernan K, MacIver NJ. Changes in nutritional status impact immune cell metabolism and function. Frontiers in immunology. 2018 May 16;9:1055.
5. Naja F, Hamadeh R. Nutrition amid the COVID-19 pandemic: a multi-level framework for action. European journal of clinical nutrition. 2020 Aug;74(8):1117-21.
6. Bourke CD, Berkley JA, Prendergast AJ. Immune dysfunction as a cause and consequence of malnutrition. Trends in immunology. 2016 Jun 1;37(6):386-98.
7. Gombart AF, Pierre A, Maggini S. A review of micronutrients and the immune system–working in harmony to reduce the risk of infection. Nutrients. 2020 Jan 16;12(1):236.
8. Valdés-Ramos R, Martínez-Carrillo BE, Aranda-González II, Guadarrama AL, Pardo-Morales RV, Tlatempa P, et al. Diet, exercise and gut mucosal immunity. Proceedings of the Nutrition Society. 2010 Nov;69(4):644-50.
9. Beigmohammadi MT, Bitarafan S, Hoseindokht A, Abdollahi A, Amoozadeh L, Mahmoodi Ali Abadi M, et al. Impact of vitamins A, B, C, D, and E supplementation on improvement and mortality rate in ICU patients with coronavirus-19: a structured summary of a study protocol for a randomized controlled trial. Trials. 2020 Dec;21:1-4.
10. Rabbitt L, Slattery E. Vitamin D and Covid-19: a note of caution. Ir Med J. 2020 May 7;113(5):82.
11. Rozga M. The effect of micronutrient and single amino acid supplementation on coronavirus-related outcomes: A scoping review. J. Acad. Nutr. Diet. 2021;121:1354-63.
12. Pecora F, Persico F, Argentiero A, Neglia C, Esposito S. The role of micronutrients in support of the immune response against viral infections. Nutrients. 2020 Oct 20;12(10):3198.
13. Yahfoufi N, Alsadi N, Jambi M, Matar C. The immunomodulatory and anti-inflammatory role of polyphenols. Nutrients. 2018 Nov 2;10(11):1618.
14. Hoseinpour S, Aghaei M, Aghasizadeh M, Hasanzadeh E, Foroughipour M, Ghayour-Mobarhan M. A Case of Possible Motor-Sensory Symptoms Event Associated with SARS-Coronavirus-2. Journal of Cardio-Thoracic Medicine. 2022 Dec 1;10(4).
15. BourBour F, Mirzaei Dahka S, Gholamalizadeh M, Akbari ME, Shadnoush M, Haghighi M, et al. Nutrients in prevention, treatment, and management of viral infections; special focus on Coronavirus. Archives of physiology and biochemistry. 2023 Jan 2;129(1):16-25.
16. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The lancet. 2020 Feb 15;395(10223):507-13.
17. Ahmadnezhad M, Asadi Z, Miri HH, Ebrahimi-Mamaghani M, Ghayour-Mobarhan M, Ferns GA. Validation of a short semi-quantitative food frequency questionnaire for adults: a pilot study. Journal of Nutritional Sciences and Dietetics. 2017 Jun 25:49-55.
18. Ghayour-Mobarhan M, Moohebati M, Esmaily H, Ebrahimi M, Parizadeh SM, Heidari-Bakavoli AR, et al. Mashhad stroke and heart atherosclerotic disorder (MASHAD) study: design, baseline characteristics and 10-year cardiovascular risk estimation. International journal of public health. 2015 Jul;60:561-72.
19. de Faria Coelho-Ravagnani C, Corgosinho FC, Sanches FL, Prado CM, Laviano A, Mota JF. Dietary recommendations during the COVID-19 pandemic. Nutrition reviews. 2021 Apr 1;79(4):382-93.
20. Childs CE, Calder PC, Miles EA. Diet and immune function. Nutrients. 2019 Aug 16;11(8):1933.
21. Chaari A, Bendriss G, Zakaria D, McVeigh C. Importance of dietary changes during the coronavirus pandemic: how to upgrade your immune response. Frontiers in Public Health. 2020 Aug 27;8:476.
22. Aslam F, Muhammad SM, Aslam S, Irfan JA. Vitamins: key role players in boosting up immune response-a mini review. Vitamins & Minerals. 2017;6(01).
23. Ciavarella C, Motta I, Valente S, Pasquinelli G. Pharmacological (or synthetic) and nutritional agonists of PPAR-γ as candidates for cytokine storm modulation in COVID-19 disease. Molecules. 2020 Apr 29;25(9):2076.
24. BourBour F, Mirzaei Dahka S, Gholamalizadeh M, Akbari ME, Shadnoush M, Haghighi M, et al. Nutrients in prevention, treatment, and management of viral infections; special focus on Coronavirus. Archives of physiology and biochemistry. 2023 Jan 2;129(1):16-25.
25. Iddir M, Brito A, Dingeo G, Fernandez Del Campo SS, Samouda H, La Frano MR, et al. Strengthening the immune system and reducing inflammation and oxidative stress through diet and nutrition: considerations during the COVID-19 crisis. Nutrients. 2020 May 27;12(6):1562.
26. Hamada AM. Vitamins, omega-3, magnesium, manganese, and thyme can boost our immunity and protect against COVID-19. European Journal of Biological Research. 2020 Aug 19;10(4):271-95.
27. Taheri M, Bahrami A, Habibi P, Nouri F. A review on the serum electrolytes and trace elements role in the pathophysiology of COVID-19. Biological trace element research. 2021 Jul;199(7):2475-81.

28. Zhou X, Chen D, Wang L, Zhao Y, Wei L, Chen Z, et al. Low serum calcium: a new, important indicator of COVID-19 patients from mild/moderate to severe/critical. Bioscience reports. 2020 Dec;40(12):BSR20202690.

29. Sun JK, Zhang WH, Zou L, Liu Y, Li JJ, Kan XH, et al. Serum calcium as a biomarker of clinical severity and prognosis in patients with coronavirus disease 2019. Aging (albany NY). 2020 Jun 6;12(12):11287.

30. Liu J, Han P, Wu J, Gong J, Tian D. Prevalence and predictive value of hypocalcemia in severe COVID-19 patients. Journal of infection and public health. 2020 Sep 1;13(9):1224-8.

31. Lippi G, South AM, Henry BM. Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). Annals of clinical biochemistry. 2020 May;57(3):262-5.