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Coronavirus Pandemic

Effects of dietary supplement use during COVID-19 treatment on post-COVID academic motivation: a sample of college students

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Abstract

Introduction: Although few studies have emphasized the preventive and therapeutic efficacy of dietary supplements in COVID-19, their efficacy in the postinfection period has not been focused. The aim of the current study was to examine the effects of therapeutic use of dietary supplements during COVID-19 treatment on post-COVID academic motivation in college students

Methodology: The study was conducted with 1584 college students studying at Karamanoğlu Mehmetbey University. Three-day food consumption was recorded and anthropometric measurements (height and body weight) were taken to assess nutritional status. The Academic Motivation Scale (AMS), a 28-item 7-point Likert scale consisting of three subdimensions (amotivation, intrinsic motivation, and extrinsic motivation), was used to assess the motivational status of participants.

Results: The rate of participants who survived COVID-19 was 35.9% (n = 568). There was no significant difference in AMS subscores between participants who routinely used dietary supplements and those who did not. Participants who used dietary supplements preventively had higher intrinsic motivation scores than those who did not. Lastly, all AMS subscores of COVID-19 survivors who used dietary supplements therapeutically during treatment were found to be more favorable than those who did not. However, there was no significant difference in AMS subscores between the types of dietary supplements most frequently used therapeutically.

Conclusions: The finding of higher post-COVID academic motivation in COVID-19 survivors who used dietary supplements as an adjunct to treatment will make an important contribution to the literature. However, longitudinal intervention studies examining the effectiveness of specific dietary supplements in COVID-19 will undoubtedly provide more valuable results.

Key words: Food supplement; COVID-19; amotivation; university students.

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Introduction

Coronavirus disease 2019 (COVID-19), caused by the spread of the novel severe acute respiratory syndrome-associated coronavirus 2 (SARS-CoV-2), is an infectious disease leading to a global pandemic [1]. The World Health Organization (WHO) COVID-19 bulletin reported more than 762 million confirmed cases and more than 6.9 million confirmed deaths worldwide as of April 19, 2023 [2]. The Turkish Ministry of Health reported more than 17 million COVID-19 cases in the country as of November 27, 2022. On the same date, the number of deaths due to the disease was determined to be 101 492 [3]. These numbers have made COVID-19 the deadliest coronavirus outbreak to date [4].

The virus gains cellular entry via the ACE2 receptor, primarily localized in the lungs and intestines. The clinical manifestations of the virus, which is spread through respiratory droplets, include a wide range of symptoms such as fever, chills, cough, shortness of breath, loss of taste or smell, headache, and myalgia [5]. Infection with SARS-CoV-2 induces a T-cell-mediated adaptive immune response that is essential for viral clearance. Although this immune response initially plays a protective role, exacerbating the inflammatory response can rapidly worsen patients' condition [1]. Normally, SARS-CoV-2 infection is detected by macrophages or dendritic cells, and viral-derived peptides are presented to CD4+ Th0 cells. In a healthy immune environment, there is a balance between T-cell subsets that secrete cytokines and those that trigger humoral responses. Disruption of this balance leads to chronic inflammation, increased inflammatory cytokine production, and T-cell exhaustion. A steady increase in inflammatory cytokine levels triggers a cytokine storm resulting in alveolar damage, systemic organ failure, and death [6]. Chronic inflammation-related comorbidities, such as obesity, diabetes, and cardiovascular diseases, may increase susceptibility to cytokine storm. Therefore, it is hypothesized that healthy dietary patterns containing adequate antioxidant and anti-inflammatory components may provide preventive and therapeutic support against COVID-19 [1].

Although healthy eating strategies may be effective in preventing or treating COVID-19, the available evidence is not clear to support the preventive and therapeutic efficacy of dietary supplements in COVID-19 [7]. Nevertheless, societies have sought additional protection through the use of various dietary supplements and nutraceuticals that they believe provide beneficial effects to prevent or mitigate COVID-19 [8]. During the COVID-19 pandemic, the sales of dietary supplements increased in many countries due to the belief that they protect against infection and are immune boosters [9]. Despite the lack of evidence on their safety and efficacy, some dietary supplements have shown potential prophylactic effects. Potential candidate micronutrients that target various aspects of COVID-19 viral pathology or are thought to boost the host immune system have been highlighted in the literature. Vitamins and minerals involved in antioxidant defense mechanisms are the main candidates [8]. In a randomized controlled trial conducted early in the COVID-19 pandemic, healthy individuals received a combined dietary supplement consisting of vitamins C, D3 and E, zinc, L-lysine, quercetin and quina daily for 20 weeks. At the end of the study, the rate of diagnosis of SARS-CoV-2 infection in the control group was 15%, while this rate was 0% in the intervention group [10]. In another randomized controlled trial on hospitalized COVID-19 patients, high-dose vitamin C supplementation was associated with improved cardiac injury and microbial damage and was shown to reduce inflammatory markers such as CRP, IL-6, IL-8, and tumor necrosis factors [11].

Although few studies have emphasized the preventive and therapeutic efficacy of vitamin and mineral supplementation for COVID-19, the efficacy of dietary supplements during the postinfection period has not been investigated. However, the vast majority of COVID-19 survivors report long-lasting clinical sequelae even months after the treatment process is completed. Known as postacute COVID-19 syndrome or long COVID-19, this condition encompasses symptoms such as dyspnea, fatigue, dysrhythmias, heartburn, and memory and attention difficulties (brain fog) and has a significant impact on quality of life [12]. Few studies have reported the efficacy of dietary supplements for the long COVID-19 treatment. These studies have mostly focused on post-COVID fatigue [12,13]. However, neurological and psychiatric disorders are also among the most important sequelae of long COVID-19. For example, brain fog and difficulty concentrating as collateral damage from COVID-19 have severely affected students who are still studying [14]. Brain fog is predicted to directly affect students' desire to learn and motivation [15]. Therefore, the main aim of the current study was to examine the effects of surviving COVID-19 and the therapeutic use of dietary supplements on post-COVID academic motivation in college students.

Methodology

Subjects and ethics

The study was conducted with undergraduate students studying at Karamanoğlu Mehmetbey University. No sample size was calculated, all faculties were visited and students who agreed to participate were included in the study. In addition to demographic data such as age and gender, routine (since before the COVID-19 pandemic), preventive (during the COVID-19 pandemic), and therapeutic (at least seven days during COVID-19 treatment) dietary supplement use data were collected with a general questionnaire. For participants who survived COVID-19 more than once, the use of dietary supplements during the first disease was taken into account. To assess nutritional status, three-day food consumption records were taken retrospectively, height and body weight measurements were recorded, and body mass index (BMI) values were calculated. The Academic Motivation Scale (AMS) was used to assess academic motivation.

Before the study, ethical approval was obtained from the Karamanoğlu Mehmetbey University Scientific Research Ethics Committee (Approval number: 303-305, Date: 12/26/2022).

Data acquisition

All undergraduate schools within the university were visited between December 2022 and March 2023. The 1667 students who agreed to participate were provided with clear explanations about the purpose and methodology of the study and were asked to sign a voluntary participation form. Eighty-three participants who provided incomplete or contradictory data were excluded, and the data of 1584 participants were analyzed within the scope of the study. All procedures were conducted following the Declaration of Helsinki (World Medical Association). A face-to-face interview method was used for data collection.

Dietary assessment and body mass index (BMI)

The three-day food consumption record method was used to assess nutritional status. Portion sizes were determined using the "Food and meal photo catalog: measures and quantities", a photographic atlas of Turkish foods and meals [16]. The data obtained were analyzed using BEBIS v.8.0, a food analysis software.

The participants' height and body weight measurements were performed per the methods. A portable stadiometer with 0.1 cm sensitivity was used to measure height, and a calibrated digital scale with 0.1 kg sensitivity was used to measure body weight. During the height measurement, care was taken to ensure that the individual stood upright and that the head was in the Frankfort horizontal plane. In addition, the individuals were shoeless and dressed in thin clothes during the measurements. Body mass index (BMI) was calculated by dividing body weight by height squared (kilograms/meter^2).

Academic motivation

The Academic Motivation Scale (AMS) was used to assess the motivational status of the participants. The AMS, a 28-item 7-point Likert scale developed by Vallerand, Pelletier, Blais, Brière, Senécal, and Vallières [17], consists of three subdimensions: intrinsic motivation (12 items), extrinsic motivation (12 items), and amotivation (4 items). Each item is scored between 0 and 6 points. Therefore, the intrinsic and extrinsic motivation subdimensions are scored between 0 and 72 points, and the amotivation subdimension is scored between 0 and 24 points. High scores on the intrinsic and extrinsic motivation subscales indicate greater motivation, while high scores on the amotivation subscales indicate less motivation. A study of the validity and reliability of the scale in the Turkish population was conducted by Karataş and Erden [18]. The Cronbach's alpha reliability coefficients were 0.857 (intrinsic motivation), 0.841 (extrinsic motivation), and 0.802 (amotivation).

Table 1. General characteristics.

Characteristics	**n (%)**
Gender	
Male	609 (38.4%)
Female	975 (61.6%)
Nutritional parameters	**Mean ± SD**
Weight (kg)	64.3 ± 13.5
BMI (kg/m^2)	22.3 ± 3.5
Energy (kcal)	2446.6 ± 1304.0
Protein (g)	92.8 ± 43.3
Vitamin A (µg RAE*)	940.6 ± 625.4
Vitamin C (mg)	93.5 ± 69.0
Vitamin D (µg)	5.5 ± 8.2
Vitamin E (mg)	14.4 ± 11.4
Iron (mg)	16.0 ± 11.2
Zinc (mg)	12.6 ± 6.5
COVID-19 history	**n (%)**
Yes	568 (35.9%)
No	1016 (64.1%)
Time since recovering from COVID-19**	**Mean ± SD**
Time (months)	12.8 ± 6.8
AMS subscores	**Mean ± SD**
Amotivation	11.3 ± 6.7
Intrinsic motivation	57.5 ± 15.9
Extrinsic motivation	59.0 ± 14.1

*RAE: retinol activity equivalent; **COVID-19 survivors; SD: standard deviation.

Statistical analysis

Statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) v. 26.0. In the evaluation of normality, the Shapiro-Wilk test was used. Both skewness-kurtosis values (skewness/standard error and kurtosis/standard error) and histogram graphs were considered for the data that did not have a normal distribution according to the Shapiro-Wilk test. Skewness-kurtosis values between -1 and +1 were accepted as indicators of a normal distribution. The homogeneity of the data was evaluated using Levene's test. According to Levene's test, $p > 0.05$ indicates that there is no difference between the homogeneity of variances. For quantitative variables, Student's t test was used to compare two groups, and one-way analysis of variance (one-way ANOVA) was used to compare more than two groups. In addition, Pearson's chi-square test was used to evaluate categorical data. The confidence interval for type I error was accepted as 95% ($p < 0.05$).

Results

Table 1 presents general characteristics regarding gender, nutritional parameters, COVID-19 history, and AMS subscores. Of the participants, 38.4% were male and 61.6% were female. The mean weight and BMI were 64.3 ± 13.5 kg and 22.3 ± 3.5 kg/m^2, respectively. In addition, the mean dietary energy and protein intakes were 2446.6 ± 1304.0 kcal and 92.8 ± 43.3 g, respectively. Apart from these parameters, the mean intake levels of some antioxidant/anti-inflammatory vitamins and minerals were also analyzed. The mean intakes of vitamins A, C, D, and E, iron, and zinc were 940.6±625.4 µg, 93.5 ± 69.0 mg, 5.5 ± 8.2 µg, 14.4 ± 11.4 mg, 16.0 ± 11.2 mg, and 12.6 ± 6.5 mg, respectively. The percentage of participants who survived COVID-19 was 35.9%. Participants who survived COVID-19 reported that they had recovered from the disease 12.8 ± 6.8 months before the interview. Finally, the mean AMS scores were 11.3 ± 6.7 (amotivation), 57.5 ± 15.9 (intrinsic motivation), and 59.0 ± 14.1 (extrinsic motivation).

Table 2. Comparison of nutritional parameters (body weight, BMI and dietary intake) and AMS subscores in COVID-19 survivors and non-infected participants.

	COVID-19 survivors (Mean ± SD)	Non-infected participants (Mean ± SD)	t*	*p*
Nutritional parameters				
Body weight (kg)	64.8 ± 13.6	64.0 ± 13.5	0.785	0.433
BMI (kg/m^2)	22.6 ± 3.5	22.1 ± 3.5	1.652	0.099
Energy (kcal)	2358.3 ± 1002.6	2496.8 ± 1439.0	-1.326	0.185
Protein (g)	90.9 ± 42.0	93.9 ± 44.0	-0.869	0.385
Vitamin A (µg RAE***)	961.2 ± 703.0	928.9 ± 577.4	0.644	0.520
Vitamin C (mg)	89.0 ± 63.7	96.1 ± 77.7	-1.171	0.242
Vitamin D (µg)	4.7 ± 6.2	5.8 ± 9.9	-1.053	0.293
Vitamin E (mg)	13.1 ± 7.3	15.0 ± 12.5	-2.118	**0.035****
Iron (mg)	16.3 ± 12.8	15.8 ± 10.4	1.094	0.275
Zinc (mg)	12.4 ± 7.2	12.6 ± 6.1	-0.595	0.552
AMS subscores				
Amotivation	13.9 ± 6.6	9.9 ± 6.3	8.118	**< 0.001****
Intrinsic motivation	56.7 ± 15.4	57.9 ± 16.1	-0.914	0.361
Extrinsic motivation	56.1 ± 13.3	60.5 ± 14.3	-4.107	**< 0.001****

*Student's t test; ***p* < 0.05; ***RAE: retinol activity equivalent; SD: standard deviation.

As shown in Table 2, the nutritional parameters and AMS subscores of COVID-19 survivors and non-infected individuals were compared. No significant difference was found between these two gr oups regarding nutritional parameters other than vitamin E intake ($p > 0.05$). Vitamin E intake levels were significantly greater in non-infected participants ($p < 0.05$). On the other hand, significant differences were found between the groups in terms of the AMS subscores for amotivation and extrinsic motivation. COVID-19 survivors had higher amotivation and lower extrinsic motivation scores ($p < 0.05$).

The rates of routine, preventive, and therapeutic use of dietary supplements are presented in Table 3. In addition, the types of dietary supplements the participants prefer are presented in Table 4. Of the participants, 7.3% reported using dietary supplements routinely. There was no significant difference in the use of dietary supplements between COVID-19 survivors and non-infected participants ($p > 0.05$, Table 3). The most preferred supplements were vitamin B_{12} (24.3%), multivitamin (22.6%), vitamin D (19.1%), omega-3 polyunsaturated fatty acids (PUFAs) (17.4%), and vitamin C (16.5%) (Table 4). The rate of dietary supplement use to prevent COVID-19 was 10.0%.

Table 4. Dietary supplements used routinely, preventively, and therapeutically.

Dietary supplements used routinely	**n (%)**
Multivitamin	26 (22.6)
Vitamin B_{12}	28 (24.3)
Vitamin C	19 (16.5)
Vitamin D	22 (19.1)
Zinc	8 (7.0)
Iron	9 (7.8)
Magnesium	5 (4.3)
Probiotic	6 (5.2)
Omega-3 PUFAs	20 (17.4)
Whey protein	11 (9.6)
Creatine	9 (7.8)
Branched-chain amino acids (BCAA)	7 (6.1)
Dietary supplements used as a preventive against COVID-19	
Multivitamin	42 (26.4)
Vitamin B_{12}	11 (6.9)
Vitamin C	59 (37.1)
Vitamin D	24 (15.1)
Zinc	20 (12.6)
Iron	5 (3.1)
Probiotic	5 (3.1)
Omega-3 PUFAs	9 (5.7)
Dietary supplements used therapeutically during COVID-19 treatment*	
Multivitamin	22 (21.2)
Vitamin B_{12}	4 (3.8)
Vitamin C	55 (52.9)
Vitamin D	15 (14.4)
Zinc	12 (11.5)
Iron	5 (4.8)
Magnesium	4 (3.8)
Probiotic	3 (2.9)
Propolis	3 (2.9)

*COVID-19 survivors.

Table 3. Use of dietary supplements by participants according to their experience of COVID-19 disease.

	COVID-19 survivors	Non-infected participants	Total	χ^2*	*p*
Routine use of dietary supplements					
Yes	44 (7.7%)	71 (7.0%)	115 (7.3%)	0.167	0.683
No	524 (92.3%)	945 (93.0%)	1469 (92.7%)		
Use of dietary supplements to prevent COVID-19					
Yes	49 (8.6%)	110 (10.8%)	159 (10.0%)	0.308	0.428
No	519 (91.4%)	906 (89.2%)	1425 (90.0%)		
Use of dietary supplements during the COVID-19 treatment**					
Yes	104 (18.3%)	-			
No	464 (81.7%)	-			

*Chi-square test; **COVID-19 survivors.

Table 5. Comparison of AMS subscores of participants according to dietary supplement use.

	AMS subscores		
	Amotivation	**Intrinsic motivation**	**Extrinsic motivation**
Routine use of dietary supplements			
Yes (Mean ± SD)	10.3 ± 6.1	60.7 ± 20.0	56.7 ± 14.2
No (Mean ± SD)	11.4 ± 6.8	57.2 ± 15.5	59.2 ± 14.1
t*	-1.134	1.526	-1.709
p-value	0.257	0.127	0.075
Preventive use of dietary supplements against COVID-19			
Yes (Mean ± SD)	10.9 ± 6.7	61.5 ± 15.2	59.9 ± 12.9
No (Mean ± SD)	11.4 ± 6.7	56.8 ± 15.4	58.0 ± 14.2
t*	-0.611	2.401	1.087
p-value	0.541	**0.017****	0.277
Therapeutic use of dietary supplements during the COVID-19 treatment***			
Yes (Mean ± SD)	11.9 ± 6.9	61.5 ± 16.4	59.8 ± 14.1
No (Mean ± SD)	14.3 ± 6.6	55.7 ± 13.7	55.3 ± 13.0
t*	-2.164	2.324	2.073
p-value	**0.031****	**0.021****	**0.039****

*Student's t test; ***p* < 0.05; *** Only COVID-19 survivors were compared; SD: standard deviation.

There was no significant difference in the rate of preventive use of dietary supplements between COVID-19 survivors and non-infected participants ($p > 0.05$, Table 3). The most preferred dietary supplements to prevent disease were vitamin C (37.1%), multivitamin (26.4%), vitamin D (15.1%), and zinc (12.6%) (Table 4). On the other hand, the rate of dietary supplement use during the treatment period was 18.3% among the COVID-19 survivors (Table 3). The most preferred dietary supplements for therapeutic purposes were vitamin C (52.9%), multivitamin (21.2%), vitamin D (14.4%), and zinc (11.5%) (Table 4).

The AMS subscores according to dietary supplement use are shown in Table 5. There was no significant difference in any of the AMS subscores between participants who routinely used dietary supplements and those who did not ($p > 0.05$). Participants who used dietary supplements to prevent disease had significantly higher intrinsic motivation scores than those who did not ($p < 0.05$). There was no significant difference in amotivation or extrinsic motivation scores between participants who used dietary supplements preventively and those who did not ($p > 0.05$). The situation is quite different when COVID-19 survivors are compared in terms of the therapeutic use of dietary supplements. COVID-19 survivors who used dietary supplements during treatment had significantly lower amotivation scores and significantly higher intrinsic and extrinsic motivation scores ($p < 0.05$).

Table 6 shows the AMS subscores according to the most preferred dietary supplement types during treatment in COVID-19 survivors. Multivitamins, vitamin C (alone), vitamin D (alone), combined vitamin C and D, and zinc (alone) were the most commonly preferred dietary supplements in COVID-19 survivors. There was no significant difference between these five groups regarding any of the AMS subscores ($p > 0.05$).

Discussion

With the onset of the COVID-19 pandemic, interest in preventive and supportive therapies against the disease has also increased. In particular, some vitamin and mineral supplements have been suggested to be effective against SARS-CoV-2 infection, and their use has become widespread [19]. The lack of safe and effective treatments against COVID-19 and the fact that some nutrients are known to be effective in maintaining and strengthening the immune system have played a fundamental role in this behavior of societies [4]. It is suggested that vitamins A, B-group, C, and D may provide prophylactic and therapeutic benefits against lung infection in patients with COVID-19. Nutrients such as zinc, selenium, iron, and omega-3 PUFAs are also known to strengthen the immune system against disease [20]. Societies in general have sought additional

Table 6. Comparison of AMS subscores of COVID-19 survivors according to the most preferred dietary supplements.

AMS subscores	The most used dietary supplements by COVID-19 survivors during treatment*					**F****	***p***
	Multivitamin (Mean ± SD)	**Vitamin C alone** (Mean ± SD)	**Vitamin D alone** (Mean ± SD)	**Vitamin C and D** (Mean ± SD)	**Zinc alone** (Mean ± SD)		
Amotivation	12.5 ± 8.0	8.7 ± 5.6	11.5 ± 4.1	7.3 ± 2.7	11.2 ± 6.4	1.907	0.121
Intrinsic motivation	55.0 ± 18.7	65.4 ± 15.2	55.8 ± 11.8	66.0 ± 10.0	59.2 ± 14.7	1.472	0.223
Extrinsic motivation	57.4 ± 11.5	61.1 ± 12.5	58.4 ± 14.6	65.9 ± 8.8	61.6 ± 12.8	0.931	0.452

*Only COVID-19 survivors who used dietary supplements therapeutically were compared; **One-Way ANOVA test; SD: standard deviation.

protection via the consumption of vitamins, minerals, and nutraceuticals with antioxidant, anti-inflammatory, and immunomodulatory properties [8].

Alkharashi [21] reported that during the COVID-19 pandemic, more than 45% of the Saudi Arabian population (45.5% men, 64.3% women) regularly or irregularly used dietary supplements or herbal products. In an older report from the same country, the use rate of dietary supplements and herbal products was 22.1% [22]. Norton *et al.* [23] reported a 21.9% rate of preventive or therapeutic use of dietary supplements in the first four months of the COVID-19 pandemic in Arkansas State, USA. In a multinational study conducted by Mukattash *et al.* [24] in Middle Eastern populations, the rate of preventive use of dietary supplements during the COVID-19 pandemic was reported to be 46.6%. Chiba and Tanemura [25] determined that the rate of preventive use of dietary supplements was 8.3% in a population of 48,925 people in Japan during the pandemic period. On the other hand, the current study showed that the rate of routine use of dietary supplements was 7.7%, while the rate of preventive use of dietary supplements was 8.6% during the COVID-19 outbreak. Among participants who had recovered from COVID-19, the rate of therapeutic use of dietary supplements was 18.3%. There are major differences between studies in terms of the rates of preventive use of dietary supplements. The use of herbal remedies as dietary supplements may increase the prevalence of supplement use. The cultural use of herbal products is more common in Middle Eastern and South Asian countries than in other countries [26].

Vitamin C was the most commonly used dietary supplement for preventing and treating COVID-19 in the present study. The preventive and therapeutic use rates of vitamin C were 37.1% and 52.9%, respectively. Many studies have also reported that vitamin C is the most widely used dietary supplement during the COVID-19 pandemic [24,27]. Vitamin C supports immune functions and protects against infection thanks to its antiviral and immunomodulatory properties [28]. Inflammation is triggered, and the levels of oxidative stress markers increase in patients with COVID-19. Therefore, the hypothesis that vitamin C may support cellular defense against SARS-CoV-2 infection has gained wide acceptance. In addition, the finding that high-dose vitamin C alters oxidative stress pathways in patients with sepsis suggests that it may be effective against cytokine storm [29,30]. Due to the vast literature supporting its anti-infective properties, many studies have suggested its therapeutic potential for COVID-19 [31].

The use of vitamin D, another dietary supplement, has increased during the COVID-19 pandemic. In the current sample, the rates of preventive and therapeutic use of vitamin D were 15.1% and 14.4%, respectively. Chiba and Tanemura [25] reported that 20.5% of participants who used dietary supplements to prevent COVID-19 preferred vitamin D, and similar to our findings, vitamins C and D were the most commonly used dietary supplements. The effect of vitamin D on immunity is due to the interaction between the biologically active form of vitamin D and the nuclear vitamin D receptor located on immune components such as monocytes, macrophages, and dendritic cells [32]. Vitamin D contributes to the immune system by stimulating the production of antimicrobial peptides such as cathelicidins and defensins that fight against a wide range of pathogens [33]. It suppresses the production of proinflammatory cytokines, and is therefore thought to have the potential to reduce cytokine storm [4]. It also contributes to the first line of defense by protecting cellular barriers such as tight junctions, gap junctions, and adherens junctions [34]. COVID-19 susceptibility is also increased in groups with widespread vitamin D deficiency, such as older adults, individuals with hyperpigmentation, obese individuals, and smokers [4]. A meta-analysis reported that vitamin D may help prevent respiratory tract infections, possibly by stimulating the production of antimicrobial peptides [35]. Some recent reports have justified the use of vitamin D preventively or therapeutically for the treatment of COVID-19. In a systematic review, it was emphasized that vitamin D reduces the risk of mortality and the need for intensive care and mechanical ventilation in hospitalized COVID-19 patients [36]. In an umbrella review reported by Petrelli *et al.* [37], vitamin D_3 supplementation was stated to be associated with a significant reduction in infection severity and mortality in COVID-19 patients.

Zinc is one of the micronutrients known for its effectiveness in combating various viral infections and has been suggested to be useful against COVID-19. It is important for developing and functioning components of innate and adaptive immunity [38]. It is found in the structure of every metalloenzyme in the body and involved in more than 300 reactions. Due to the large number of enzymes involved and the number of molecular pathways affected, zinc deficiency is associated with a wide range of diseases, including hypogonadism, skin diseases, cognitive dysfunction, anemia, and impaired immune function [39]. It also contributes to the regulation of tight junction proteins.

Therefore, infectious diseases such as pneumonia have been reported to be associated with zinc deficiency [40]. Due to these properties, zinc has been one of the most frequently used dietary supplements in the fight against COVID-19. Chiba and Tanemura [25] emphasized that zinc is the most commonly used mineral to prevent COVID-19 in the Japanese population. In a study by Borzoee *et al.* [41] investigating self-medication-related factors to prevent COVID-19 in pregnant women, the rate of zinc supplementation was reported to be 13.3%. Similarly, in the present study, the rates of preventive and therapeutic use of zinc supplements were 12.6% and 11.5%, respectively.

Other supplements commonly preferred in the fight against COVID-19 are selenium, omega-3 PUFAs, B vitamins, and probiotics. Selenium, which has been shown to improve the antiviral immune response against the deadly H1N1 influenza virus [42], may also be effective in the fight against COVID-19 [43]. The ability of omega-3 PUFAs to affect antigen presentation and CD4+ Th1 cell production suggests that they may modulate the immune response, and their potential as precursor molecules for specialized proresolving mediators (SPMs), such as protectins and resolvins suggests that they may be effective against COVID-19-related cytokine storm and pulmonary inflammation [8]. The nonrespiratory symptoms of COVID-19 have been likened to pellegra in many ways. It is thought that NAD+ depletion caused by SARS-CoV-2 infection may be the cause of the pellegra-like phenotype characterized by vitamin B_3 deficiency [44]. In addition, ameliorating COVID-19-induced intestinal dysbiosis may be protective and curative against disease symptoms by supporting innate and adaptive immunity in the gut. For this purpose, probiotics with antiviral properties may be good adjunctive treatment options in the fight against COVID-19 [45].

As mentioned earlier, the vast majority of COVID-19 survivors reported long-term clinical sequelae after the course of treatment. This period, called long COVID-19, is characterized by symptoms such as fatigue, dyspnea, cough, palpitations, dysrhythmias, myalgia, heartburn, and brain fog, which have a direct impact on quality of life in adults [12,46]. In children and adolescents, fatigue, headache, sleep disturbance, nausea, abdominal pain, diarrhea, weight loss, anosmia, incomplete bladder emptying, emotional lability, peripheral neuropathy, and impaired concentration are the most commonly reported long COVID-19 manifestations [47]. However, it is noteworthy that neurological/neuropsychiatric symptoms and brain sequelae accompany long-term respiratory and gastrointestinal symptoms. Approximately 25% of COVID-19 survivors suffer from neurological disorders [48]. SARS-CoV-2 has been reported to trigger neurological symptoms after entering the central nervous system via hematogenous spread. This stimulates neuroinflammation and triggers a coagulation cascade involving changes in neurotransmitters, NMDA receptors, and glutamate [47]. In addition to brain fog, a common symptom, some patients experience anxiety, depression, and psychosis [49]. A review revealed that symptoms such as tremor, confusion, and stiff limbs are common neurological disorders associated with long COVID-19 [50]. Between 20% and 70% of young adult patients in Germany and the UK developed neuropsychiatric symptoms even months after COVID-19-related respiratory symptoms resolved [49]. Buonsenso *et al.* [51] reported that 10% of Italian children who survived COVID-19 experienced a lack of concentration during the posttreatment period. In another study, depression, anhedonia, executive function deficits, and perceived stress were found to be more prevalent in individuals who recovered from COVID-19 1-4 months after the treatment period than in healthy controls without a history of COVID-19 [52].

The present study examined the effect of using dietary supplements during COVID-19 treatment on posttreatment motivational state, which is known to be associated with neuropsychiatric features. The fact that amotivation scores were significantly greater and extrinsic motivation scores were significantly lower in COVID-19 survivors (Table 2) indicates a lack of motivation during the long COVID-19 period. There was no significant difference in all AMS subscores between participants who routinely used dietary supplements and those who did not (Table 5). In contrast, intrinsic motivation scores were significantly greater for participants who used dietary supplements to prevent disease (Table 5). Moreover, it is worth noting that there was no significant difference in the rates of routine or preventive use of dietary supplements between participants with and without a history of COVID-19 (Table 3). Significant differences were found in all AMS subscores between COVID-19 survivors who used dietary supplements therapeutically and those who did not. COVID-19 survivors who used dietary supplements during treatment had significantly lower amotivation scores and significantly higher intrinsic and extrinsic motivation scores (Table 5). Interestingly, these findings highlight that therapeutic use of dietary supplements may maintain high levels of academic motivation during the posttreatment period. Several studies have examined the effects of certain dietary supplements on long COVID-19 symptoms [13,53]. However, these studies mostly focused on fatigue, muscle strength, sleep disturbances, pain, and anosmia. No study has reported on the effect of dietary supplement use on neurological and neuropsychiatric symptoms of long COVID-19. Therefore, we did not expect to find a study focusing on the effect of the therapeutic use of dietary supplements on post-COVID academic motivation. In addition, it is surprising that there is no study comparing SARS-CoV-2-infected and non-infected school-age children in terms of academic motivation. Instead of examining the relationship between COVID-19 disease and academic motivation in infected individuals, studies have focused on the relationship between COVID-19 pandemic and academic motivation in students. The effects of isolation, lockdown, online learning, and various stressors associated with the pandemic on academic motivation have been examined in several studies [54-57]. It is thought that the finding that post-COVID academic motivation was higher among COVID-19 survivors who used dietary supplements during COVID-19 treatment will make an important contribution to the literature. However, the AMS subscores were compared according to the most commonly used dietary supplements, and no significant difference was found (Table 6). The retrospective nature of the study and the lack of information about the content of the multivitamin supplements used were limitations.

Conclusions

The current results indicate that using dietary supplements as adjunctive therapy during COVID-19 treatment may positively affect post-COVID academic motivation. This study presents a remarkable finding in this respect. However, it is difficult to state that preventive use of dietary supplements provides an advantage in terms of post-COVID academic motivation.

Some limitations regarding the methodology of the study should be acknowledged. COVID-19 has posed unusual challenges for response efforts around the world. For example, SARS-CoV-2 infection requires strict home quarantine, making recruiting infected individuals for studies impossible. In addition, intervention studies in Turkey require ethics committee approval from the Turkish Ministry of Health, which was almost impossible to obtain for studies on infected patients during the COVID-19 pandemic. Nonetheless, it is obvious that examining the effects of specific dietary supplements in COVID-19 patients with longitudinal intervention studies rather than retrospective studies would provide clearer results. Although large literature gap still exists, approaches based on vitamins, minerals, and other dietary supplements may be as beneficial as pharmaceutical interventions.

It is also important to emphasize the possible risk factors associated with using dietary supplements. The Food and Drug Administration (FDA) treats dietary supplements differently from prescription drugs. Dietary supplements do not need FDA approval before they can be marketed [58]. They are also easily accessible in Turkey, as they are sold over the counter [59,60]. It is therefore possible to administer very high doses of one or more products. The use of dietary supplements by vulnerable groups such as pregnant/nursing women, older adults, and individuals with a history of cancer or those who are receiving cancer treatment may pose a risk. In addition, the uncontrolled use of irrational supplements can jeopardize people's health and safety. The abuse of dietary supplements can cause an unseen parallel and hidden epidemic [9]. Therefore, the efficacy of dietary supplements should be explained well in dietary guidelines regarding COVID-19 to increase public awareness.

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References

1. Singh B, Eshaghian E, Chuang J, Covasa M (2022) Do diet and dietary supplements mitigate clinical outcomes in COVID-19?. Nutrients 14: 1909. doi: 10.3390/nu14091909.
2. World Health Organization (2023) Coronavirus (COVID-19) dashboard. Available: https://covid19.who.int/. Accessed: 30 March 2023.
3. Republic of Turkey Ministry of Health (2023) COVID-19 information platform. Available: https://covid19.saglik.gov.tr/TR-66935/genel-koronavirus-tablosu.html. Accessed: 30 March 2023.
4. Bogan-Brown K, Nkrumah-Elie Y, Ishtiaq Y, Redpath P, Shao A (2022) Potential efficacy of nutrient supplements for treatment or prevention of COVID-19. J Diet Suppl 19: 336-65. doi: 10.1080/19390211.2021.1881686.
5. Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R (2023) Features, evaluation, and treatment of coronavirus (COVID-19). Florida: StatPearls Publishing.
6. Ragab D, Salah Eldin H, Taeimah M, Khattab R, Salem R (2020) The COVID-19 cytokine storm; what we know so far. Front Immunol 1446. doi: 10.3389/fimmu.2020.01446.

7. National Institutes of Health (2023) Dietary supplements in the time of COVID-19 - health professional fact sheet. Available: https://ods.od.nih.gov/factsheets/COVID19-HealthProfessional/. Accessed: 31 March 2023.
8. Lordan R, Rando HM, Consortium CR, Greene CS (2021) Dietary supplements and nutraceuticals under investigation for COVID-19 prevention and treatment. mSystems 6. doi: 10.1128/mSystems.00122-21.
9. Radwan H, Hasan H, Jaafar Z, Abbas N, Rashed Saif E, Al Kitbi M, Al Hilali M, Naja F (2022) Diets and dietary supplements used during the COVID-19 pandemic in the United Arab Emirates: a cross-sectional survey. Saudi Pharm J 30: 421-32. doi: 10.1016/j.jsps.2022.01.019.
10. Margolin L, Luchins J, Margolin D, Margolin M, Lefkowitz S (2021) 20-week study of clinical outcomes of over-the-counter COVID-19 prophylaxis and treatment. J Evid Based Integr Med 26: 2515690X211026193. doi: 10.1177/2515690X211026193.
11. Xia G, Qin B, Ma C, Zhu Y, Zheng Q (2021) High-dose vitamin C ameliorates cardiac injury in COVID-19 pandemic: a retrospective cohort study. Aging (Albany NY) 13: 20906-14. doi: 10.18632/aging.203503.
12. Tosato M, Calvani R, Picca A, Ciciarello F, Galluzzo V, Coelho-Junior HJ, Di Giorgio A, Di Mario C, Gervasoni J, Gremese E, Leone PM, Nesci A, Paglionico AM, Santoliquido A, Santoro L, Santucci L, Tolusso B, Urbani A, Marini F, Marzetti E, Landi F (2022) Effects of l-arginine plus vitamin c supplementation on physical performance, endothelial function, and persistent fatigue in adults with long COVID: a single-blind randomized controlled trial. Nutrients 14. doi: 10.3390/nu14234984.
13. Galluzzo V, Zazzara MB, Ciciarello F, Savera G, Pais C, Calvani R, Picca A, Marzetti E, Landi F, Tosato M (2022) Fatigue in COVID-19 survivors: the potential impact of a nutritional supplement on muscle strength and function. Clin Nutr ESPEN 51: 215-21. doi: 10.1016/j.clnesp.2022.08.029.
14. Aftab M, Abadi AM, Nahar S, Ahmed RA, Mahmood SE, Madaan M, Ahmad A (2021) COVID-19 pandemic affects the medical students' learning process and assaults their psychological wellbeing. Int J Environ Res Public Health 18: 5792.
15. Kavanagh E (2022) Long COVID brain fog: a neuroinflammation phenomenon? Oxf Open Immunol 3: iqac007. doi: 10.1093/oxfimm/iqac007.
16. Rakıcıoğlu N, Acar-Tek N, Ayaz A, Pekcan G (2016) Food and meal photo catalog: dimensions and quantities. Ankara, Ata Ofset Typography. [Book in Turkish].
17. Vallerand RJ, Pelletier LG, Blais MR, Brière NM, Senécal CB, Vallières ÉF (1993) Academic motivation scale (AMS-C 28), college (CEGEP) version. Educ Psychol Meas 52: 1992-3. doi: 10.1177/0013164492052004025.
18. Karataş H, Erden M (2012) Bilingual equivalence, validity and reliability of academic motivation scale. Education Sciences 7: 983-1003. [Article in Turkish].
19. Balboni E, Zagnoli F, Filippini T, Fairweather-Tait SJ, Vinceti M (2022) Zinc and selenium supplementation in COVID-19 prevention and treatment: a systematic review of the experimental studies. J Trace Elem Med Biol 71: 126956. doi: 10.1016/j.jtemb.2022.126956.
20. Zhang L, Liu Y (2020) Potential interventions for novel coronavirus in China: A systematic review. J Med Virol 92: 479-90. doi: 10.1002/jmv.25707.
21. Alkharashi N (2021) The consumption of nutritional supplements and herbal products for the prevention and treatment of COVID-19 infection among the Saudi population in Riyadh. Clin Nutr Open Sci 39: 11-20. doi: 10.1016/j.nutos.2021.09.001.
22. Alyami HS, Orabi MA, Aldhabbah FM, Alturki HN, Aburas WI, Alfayez AI, Alharbi AS, Almasuood RA, Alsuhaibani NA (2020) Knowledge about COVID-19 and beliefs about and use of herbal products during the COVID-19 pandemic: a cross-sectional study in Saudi Arabia. Saudi Pharm J 28: 1326-32. doi: 10.1016/j.jsps.2020.08.023.
23. Norton JC, Politis MD, Bimali M, Vyas KS, Bircan E, Nembhard WN, Amick BC, Koturbash I (2023) Analysis of COVID-19 pandemic on supplement usage and its combination with self-medication within the state of Arkansas. J Diet Suppl 20: 171-98. doi: 10.1080/19390211.2022.2128500.
24. Mukattash TL, Alkhalidy H, Alzu'bi B, Abu-Farha R, Itani R, Karout S, Khojah HMJ, Khdour M, El-Dahiyat F, Jarab A (2022) Dietary supplements intake during the second wave of COVID-19 pandemic: a multinational Middle Eastern study. Eur J Integr Med 49: 102102. doi: 10.1016/j.eujim.2022.102102.
25. Chiba T, Tanemura N (2022) The prevalence of dietary supplement use for the purpose of COVID-19 prevention in Japan. Nutrients 14. doi: 10.3390/nu14153215.
26. Paudyal V, Sun S, Hussain R, Abutaleb MH, Hedima EW (2022) Complementary and alternative medicines use in COVID-19: a global perspective on practice, policy and research. Res Social Adm Pharm 18: 2524-8. doi: 10.1016/j.sapharm.2021.05.004.
27. Francis TV, Sooriyaarachchi P, Jayawardena R (2022) Usage of nutritional supplements to improve immunity during the COVID-19 pandemic: an online survey. Clin Nutr Open Sci 43:6-19. doi: 10.1016/j.nutos.2022.04.003.
28. Hemila H (2003) Vitamin C and SARS coronavirus. J Antimicrob Chemother 52: 1049-50. doi: 10.1093/jac/dkh002.
29. Li J (2018) Evidence is stronger than you think: a meta-analysis of vitamin C use in patients with sepsis. Crit Care 22: 258. doi: 10.1186/s13054-018-2191-x.
30. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, Deng Y, Wei S (2020) Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Zhonghua Jie He He Hu Xi Za Zhi 43: 203-8. doi: 10.3760/cma.j.issn.1001-0939.2020.03.013. [Article in Chinese].
31. Cheng RZ (2020) Can early and high intravenous dose of vitamin C prevent and treat coronavirus disease 2019 (COVID-19)? Med Drug Discov 5: 100028. doi: 10.1016/j.medidd.2020.100028.
32. Di Rosa M, Malaguarnera M, Nicoletti F, Malaguarnera L (2011) Vitamin D3: a helpful immuno-modulator. Immunology 134: 123-39. doi: 10.1111/j.1365-2567.2011.03482.x.
33. Laaksi I (2012) Vitamin D and respiratory infection in adults. Proc Nutr Soc 71: 90-7. doi: 10.1017/S0029665111003351.
34. Schwalfenberg GK (2011) A review of the critical role of vitamin D in the functioning of the immune system and the clinical implications of vitamin D deficiency. Mol Nutr Food Res 55: 96-108. doi: 10.1002/mnfr.201000174.
35. Bergman P, Lindh AU, Bjorkhem-Bergman L, Lindh JD (2013) Vitamin D and respiratory tract infections: a systematic review and meta-analysis of randomized controlled trials PLoS One 8: e65835. doi: 10.1371/journal.pone.0065835.

36. Shah K, Varna V, Sharma U, Mavalankar D (2022) Does vitamin D supplementation reduce COVID-19 severity?: a systematic review. QJM 115: 665-72. doi: 10.1093/qjmed/hcac040.
37. Petrelli F, Oldani S, Borgonovo K, Cabiddu M, Dognini G, Ghilardi M, Parati MC, Petro' D, Dottorini L, Rea C (2023) Vitamin D3 and COVID-19 outcomes: an umbrella review of systematic reviews and meta-analyses. Antioxidants 12: 247. doi: 10.3390/antiox12020247.
38. McCarty MF, DiNicolantonio JJ (2020) Nutraceuticals have potential for boosting the type 1 interferon response to RNA viruses including influenza and coronavirus. Prog Cardiovasc Dis 63: 383. doi: 10.1016/j.pcad.2020.02.007.
39. Prasad AS (2013) Discovery of human zinc deficiency: its impact on human health and disease. Advances in Nutrition 4: 176-90. doi: 10.3945/an.112.003210.
40. Hess SY, Lönnerdal B, Hotz C, Rivera JA, Brown KH (2009) Recent advances in knowledge of zinc nutrition and human health. Food Nutr Bull 30: S5-S11. doi: 10.1177/15648265090301S102.
41. Borzoee F, Hashmatifar N, Mohamadzadeh Tabrizi Z, Rastaghi S, Davarinia Motlagh Quchan A (2022) Prevalence rate and factors related to self- medication in preventing COVID-19 disease in pregnant women. Sci J Iranshahr Univ Med Sci 1: 157-62. doi: 10.32598/sija.16.1.2983.1.
42. Yu L, Sun L, Nan Y, Zhu LY (2011) Protection from H1N1 influenza virus infections in mice by supplementation with selenium: a comparison with selenium-deficient mice. Biol Trace Elem Res 141: 254-61. doi: 10.1007/s12011-010-8726-x.
43. Kieliszek M, Lipinski B (2020) Selenium supplementation in the prevention of coronavirus infections (COVID-19). Med Hypotheses 143: 109878. doi: 10.1016/j.mehy.2020.109878.
44. Novak Kujundžić R (2022) COVID-19: are we facing secondary pellagra which cannot simply be cured by vitamin B3? Int J Mol Sci 23: 4309. doi: 10.3390/ijms23084309.
45. Nguyen QV, Chong LC, Hor YY, Lew LC, Rather IA, Choi SB (2022) Role of probiotics in the management of COVID-19: a computational perspective. Nutrients 14. doi: 10.3390/nu14020274.
46. Raveendran AV, Jayadevan R, Sashidharan S (2021) Long COVID: an overview. Diabetes Metab Syndr 15: 869-75. doi: 10.1016/j.dsx.2021.04.007.
47. Thallapureddy K, Thallapureddy K, Zerda E, Suresh N, Kamat D, Rajasekaran K, Moreira A (2022) Long-term complications of COVID-19 infection in adolescents and children. Curr Pediatr Rep 10: 11-7. doi: 10.1007/s40124-021-00260-x.
48. Machhi J, Herskovitz J, Senan AM, Dutta D, Nath B, Oleynikov MD, Blomberg WR, Meigs DD, Hasan M, Patel M, Kline P, Chang RC, Chang L, Gendelman HE, Kevadiya BD (2020) The natural history, pathobiology, and clinical manifestations of SARS-CoV-2 infections. J Neuroimmune Pharmacol 15: 359-86. doi: 10.1007/s11481-020-09944-5.
49. Woo MS, Malsy J, Pottgen J, Seddiq Zai S, Ufer F, Hadjilaou A, Schmiedel S, Addo MM, Gerloff C, Heesen C, Schulze Zur Wiesch J, Friese MA (2020) Frequent neurocognitive deficits after recovery from mild COVID-19. Brain Commun 2: fcaa205. doi: 10.1093/braincomms/fcaa205.
50. Marshall M (2020) The lasting misery of coronavirus long-haulers. Nature 585: 339-41. doi: 10.1038/d41586-020-02598-6.
51. Buonsenso D, Munblit D, De Rose C, Sinatti D, Ricchiuto A, Carfi A, Valentini P (2021) Preliminary evidence on long COVID in children. Acta Paediatr 110: 2208-11. doi: 10.1111/apa.15870.
52. Lamontagne SJ, Winters MF, Pizzagalli DA, Olmstead MC (2021) Post-acute sequelae of COVID-19: evidence of mood & cognitive impairment. Brain Behav Immun Health 17: 100347. doi: 10.1016/j.bbih.2021.100347.
53. Galluzzo V, Ciciarello F, Tosato M, Zazzara MB, Pais C, Savera G, Calvani R, Picca A, Marzetti E, Landi F (2022) Association between vitamin D status and physical performance in COVID-19 survivors: results from the Gemelli against COVID-19 post-acute care project. Mech Ageing Dev 205: 111684. doi: 10.1016/j.mad.2022.111684.
54. Haftador AM, Shirazi F, Mohebbi Z (2021) Online class or flipped-jigsaw learning? Which one promotes academic motivation during the COVID-19 pandemic? BMC Med Educ 21: 1-8. doi: 10.1186/s12909-021-02929-9.
55. Camacho A, Correia N, Zaccoletti S, Daniel JR (2021) Anxiety and social support as predictors of student academic motivation during the COVID-19. Front Psychol 12: 644338. doi: 10.3389/fpsyg.2021.644338.
56. Martin AJ, Ginns P, Collie RJ (2023) University students in COVID-19 lockdown: the role of adaptability and fluid reasoning in supporting their academic motivation and engagement. Learn Instr 83: 101712. doi: 10.1016/j.learninstruc.2022.101712.
57. Kulikowski K, Przytuła S, Sułkowski Ł (2021) The motivation of academics in remote teaching during the COVID-19 pandemic in Polish universities—opening the debate on a new equilibrium in e-learning. Sustainability 13: 2752. doi: 10.3390/su13052752.
58. Young AL, Bass IS (1995) The dietary supplement health and education act. Food & Drug LJ 50: 285.
59. Republic of Turkey Ministry of Agriculture and Forestry (2013) Turkish Food Codex Communiqué on Food Supplements, Official Gazette dated August 16, 2013 and numbered 28737.
60. Republic of Turkey Ministry of Agriculture and Forestry (2013) Regulation on Import, Production, Processing and Placing on the Market of Dietary Supplements, Official Gazette dated May 02, 2013 and numbered 28635.

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