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The Effect of COVID-19 Pandemic on Dietary Food Supplement Usage Habits

COVID-19 Salgınının Besin Takviyesi Kullanım Alışkanlıklarına Etkisi

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Abstract

With COVID-19 pandemic, it is seen that people are in demand for dietary food supplements in order to protect themselves from this virus-related disease. In this study, we aimed to evaluate what extent the COVID-19 pandemic affects people's food supplement usage habits by controlling blood levels of vitamin D, vitamin B12 and zinc. In this retrospective study design, we examined patients test results collected from laboratory information system over a two-year period including one year before and after the date of first COVID-19 infection in Türkiye. There were 197,669 eligible test results for statistical evaluation. Mean vitamin D levels for preCOVID group spring, summer, autumn and winter were 22.3, 25.2, 25.4, and 21.9 ng/mL, respectively. As for the postCOVID group, identical values were 21.3, 22.7, 23.8, and 24.4 ng/mL. For vitamin D levels, there were statistically differences between subgroups (seasons) but no difference between main groups ($p>0.05$). Mean vitamin B12 levels were 262.6 pg/mL and 264.1 pg/mL ($p>0.05$), and mean zinc levels were 84.0 µg/dL and 91.1 µg/dL ($p<0.001$) for preCOVID and postCOVID groups, respectively. In recent years, as integrative medicine has become popular all over the world, interest in dietary food supplements has started to climb. The belief on such food supplements increase protection against viral diseases suggested that the increased usage of these products in the pandemic period. In this study, except zinc there was no statistically difference between pre and postCOVID periods in terms of serum levels. The results showed us the change of supplement usage behavior due to COVID-19 is suspicious.

Keywords: COVID-19, Dietary food supplement, Vitamin D, Vitamin B12, Zinc.

Özet

COVID-19 salgınıyla birlikte insanların bu viral hastalıktan korunmak için diyet gıda takviyelerine talep gösterdiği görülmektedir. Bu çalışmada, D vitamini, B12 vitamini ve çinko kan seviyelerini kontrol ederek, COVID-19 salgınının insanların gıda takviyesi kullanım alışkanlıklarını ne ölçüde etkilediğini değerlendirmeyi amaçladık. Bu retrospektif çalışma tasarımında, Türkiye'de ilk COVID-19 enfeksiyonunun görüldüğü tarihten bir yıl öncesini ve sonrasını kapsayan iki yıllık bir süre boyunca hastaların laboratuvar bilgi sisteminden toplanan test sonuçlarını inceledik. İstatistiksel değerlendirme için 197.669 uygun test sonucu vardı. COVID öncesi grup için ortalama D vitamini düzeyleri ilkbahar, yaz, sonbahar ve kış sırasıyla 22.3, 25.2, 25.4 ve 21.9 ng/mL idi. COVID sonrası grupta ise aynı değerler 21.3, 22.7, 23.8 ve 24.4 ng/mL idi. D vitamini düzeyleri için alt gruplar (mevsimler) arasında istatistiksel olarak fark vardı, ancak ana gruplar arasında fark yoktu ($p>0.05$). Ortalama B12 vitamini seviyeleri, COVID öncesi ve COVID sonrası gruplar için sırasıyla 262.6 pg/mL ve 264.1 pg/mL ($p>0.05$) ve ortalama çinko seviyeleri ise 84.0 µg/dL ve 91.1 µg/dL idi ($p<0.001$). Son yıllarda bütünleştirici tıbbın tüm dünyada popüler hale gelmesiyle birlikte diyet gıda takviyelerine olan ilgi de artmaya başladı. Bu tür gıda takviyelerinin viral hastalıklara karşı korumayı arttırdığına dair inanç, bu ürünlerin pandemi döneminde kullanımının arttığını düşündürmektedir. Bu çalışmada çinko dışında serum düzeyleri açısından COVID öncesi ve sonrası dönemler arasında istatistiksel olarak bir fark bulunmadı. Sonuçlar bize, COVID-19 nedeniyle besin takviyesi kullanım davranışındaki değişikliğin şüpheli olduğunu gösterdi.

Anahtar Kelimeler: COVID-19, Besin takviyesi, D vitamini, B12 vitamini, Çinko.

Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has affected millions of people worldwide and caused **co**rona**v**irus disease 20**19** (COVID-19) pandemic [1]. The ongoing studies provide promising results but still a definitive treatment could not be discovered for an infected person. Several drugs such as remdesivir, hydroxychloroquine, chloroquine, ribavirin, ritonavir, lopinavir, favipiravir, interferons, tocilizumab, azithromycin, etc. are either have been tried and given up or still being in treatment protocol [2]. The best offer for protection from virus seems "not to be infected", in this respect, people rely upon newly developed vaccines. Adding to vaccines, dietary food supplements also take place in terms of boosting or strengthening immune defense with the aim of not to be infected [3]. For that purpose, almost all dietary food supplements gain popularity, lots of them have been incorporated into scientific study designs. The main ones are vitamin D, zinc, vitamin C, omega-3 fatty acids, curcumin, cinnamaldehyde, probiotics, selenium, quercetin, vitamin B12, lactoferrin, vitamin B-complex, etc. [4,5].

Vitamin D is considered to be an important factor in immune homeostasis [6]. Vitamin D strengthens cellular immunity, reduces cytokine storm and improves antioxidants production [7]. Also, vitamin D has modulatory effects on angiotensin-converting enzyme 2 (ACE-2) receptors which takes place in SARS-CoV-2 infection pathogenesis, and potential protective functions toward acute lung injuries, including severe COVID-19 [6]. Lots of studies were designed to present the linkage between vitamin D and COVID-19.

Zinc is one of the most significant essential trace elements affecting immunological resistance [5,8]. From the viewpoint of COVID-19's pathophysiological mechanism; zinc inhibits T-cell activation and macrophage infiltration, thereby attenuating production of pro-inflammatory cytokine, lung inflammation and ultimately, cytokine storm, oxidative stress and organ damage [9]. Beside zinc, vitamin B types (B1, B2, B3, B5, B6, B9 and B12) have been thought to take place in COVID-19 infection pathogenesis and clinical presentations in terms of adaptive immunity, viral replication, cytokine storm and hypercoagulability [4,10].

Dietary food supplement popularity has been increased all over the world since outbreak of pandemic [11]. Supplementation with several micronutrients was proposed because of its potentially beneficial effects for COVID-19 infected individuals [12]. In this study, we aimed to investigate whether COVID-19 pandemic affected dietary food supplement intake habits of a restricted area in Türkiye.

Material and Method

Ethical approval was obtained from local ethics committee (Date: 02.03.2022. Decision number: 2022/24).

Study setting and participants

In this retrospective data analysis, we examined the data collected from the laboratory information system (LIS). The date of 11 March 2020 was the first COVID-19 case in Türkiye. Therefore, this date was selected as the center point and the collected data comprised one year before and after this point. Naturally, we had two groups; the first group consists of the period before COVID infection (named as preCOVID group; Group 1) and the second group consists of the period after COVID infection (named as postCOVID group; Group 2). Vitamin D, zinc, and vitamin B12 results were drawn from LIS.

Patient results originated from oncology, hematology and nephrology clinics were excluded from the study. Also, results from other clinics of patients with all vitamin deficiencies, pregnancy, rachitism and hyperparathyroidism were also eliminated. Lastly, we excluded under 18 and over 90 years old participants.

Sample collection and laboratory instruments

Venous blood was drawn into 10 mL red cap blood collection tubes with clot activator (BD Vacutainer, Becton Dickinson and Co., Franklin Lakes, NJ, USA) for analysis vitamin D and vitamin B12. For zinc analysis, same brand 6 mL royal blue cap blood collection tubes with clot activator were used. All collection tubes were then centrifuged at 4000×g for 10 minutes in a refrigerated centrifuge in 1 hour after collection time. Later, supernatant sections were separated and then measurements were performed within 1 hour.

Measurement of serum 25-OH vitamin D3 levels were performed with a high-performance liquid chromatography (HPLC) device (Shimadzu HPLC system, Kyoto, Japan), using an ion exchange chromatography column. Serum vitamin B12 levels were determined using an immunoassay autoanalyzer (Beckman Coulter DxI 800 Unicel, Beckman Coulter, USA). Serum zinc assessments were accomplished with flame atomic absorption spectrometry (iCE 3000 Series-Thermo, Thermo-Scientific, Hemel Hempstead, Hertfordshire, UK). All the devices have been involved an external quality control program (Bio-Rad's EQAS) beside of daily internal quality assessments. All values were within acceptable range according to external quality control program during study period.

Statistical analysis

All statistical analyses were performed using SPSS 22.0 (SPSS Inc., Chicago, IL, USA) statistical package program. Distributions were evaluated using the one-sample Kolmogorov–Smirnov test. Mean, standard deviation (SD), median, minimum (min) and maximum (max) values were used for the described data. Student's t-test was used to compare serum vitamin D, vitamin B12 and zinc levels. In statistical analysis values of $p<0.05$ were considered as statistically significant.

Results

There were 245,390 test results in total. After applying exclusion criteria 197,669 test results were included in the study. Group 1 consisted of 130,683 test results (33,363 for vitamin D; 95,285 for vitamin B12; 2,035 for zinc) and it was 66,986 for Group 2 (13,724 for vitamin D; 51,720 for vitamin B12; 1,542 for zinc). As the number suggests, people have tended not to go to hospital after pandemic burst out.

Basic characteristics of groups were shown in Table 1. Although there were statistically differences between groups in terms of total test results, population characteristics like sex ratio and age were similar between groups. The laboratory results show us big majority of outpatients were female in both periods and they were in great harmony.

Table 1. Main characteristic features of groups.

Variable	N (f/m %)		Age (±SD)		Mean (±SD)	
	pre-COVID	*post-COVID*	*pre-COVID*	*post-COVID*	*pre-COVID*	*post-COVID*
Vitamin D total	33,363* (72.6-27.4)	13,724 (73.2-26.8)	49.7 (±17.2)	49.2 (±16.9)	23.6 (±12.7)	23.4 (±12.9)
Vitamin D spring	10,446* (71.7-28.3)	1,744 (71.8-28.2)	50.7 (±17.4)	50.5 (±16.5)	22.3* (±12.8)	21.3 (±13.3)
Vitamin D summer	6,914* (75.1-24.9)	3,443 (75.5-24.5)	48.8 (±17.4)	49.2 (±18.3)	25.2* (±12.6)	22.7 (±11.6)
Vitamin D autumn	8,139* (71.9-28.1)	3,770 (72.2-27.8)	48.9 (±17.2)	48.4 (±16.5)	25.4* (±12.6)	23.8 (±12.3)
Vitamin D winter	7,864* (72.5-27.5)	4,767 (72.9-27.1)	49.9 (±17.1)	49.5 (±16.2)	21.9 (±12.5)	24.4* (±13.8)
Vitamin B12	95,285* (70.9-29.1)	51,720 (71.2-28.8)	49.7 (±17.9)	48.0 (±17.8)	262.6 (±202)	264.1 (±207)
Zinc	2,035* (74.5-25.5)	1,542 (70.6-29.4)	38.4 (±14.9)	41.5 (±16.3)	84.0 (±19.4)	91.1* (±18.9)

*p<0.05.

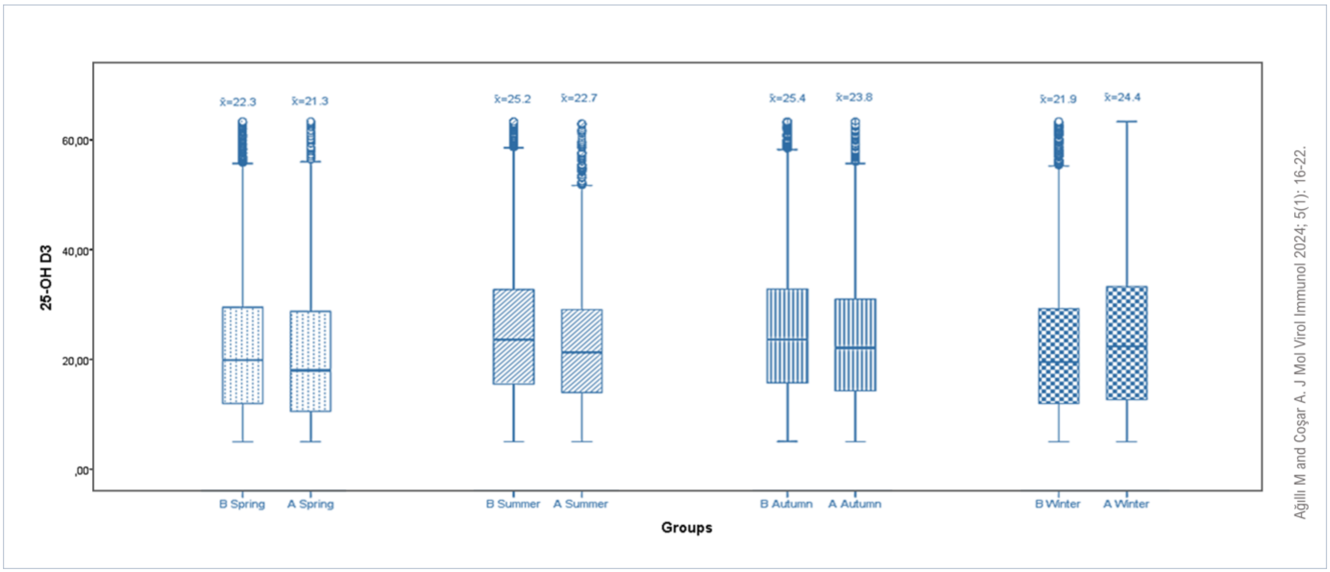

Figure 1. 25-OH vitamin D mean levels (ng/mL) of preCOVID (shown as B) and postCOVID (shown as A) periods on seasonal basis. Vitamin D levels were higher in preCOVID periods of spring, summer, and autumn ($p<0.001$), and postCOVID period of winter ($p<0.001$).

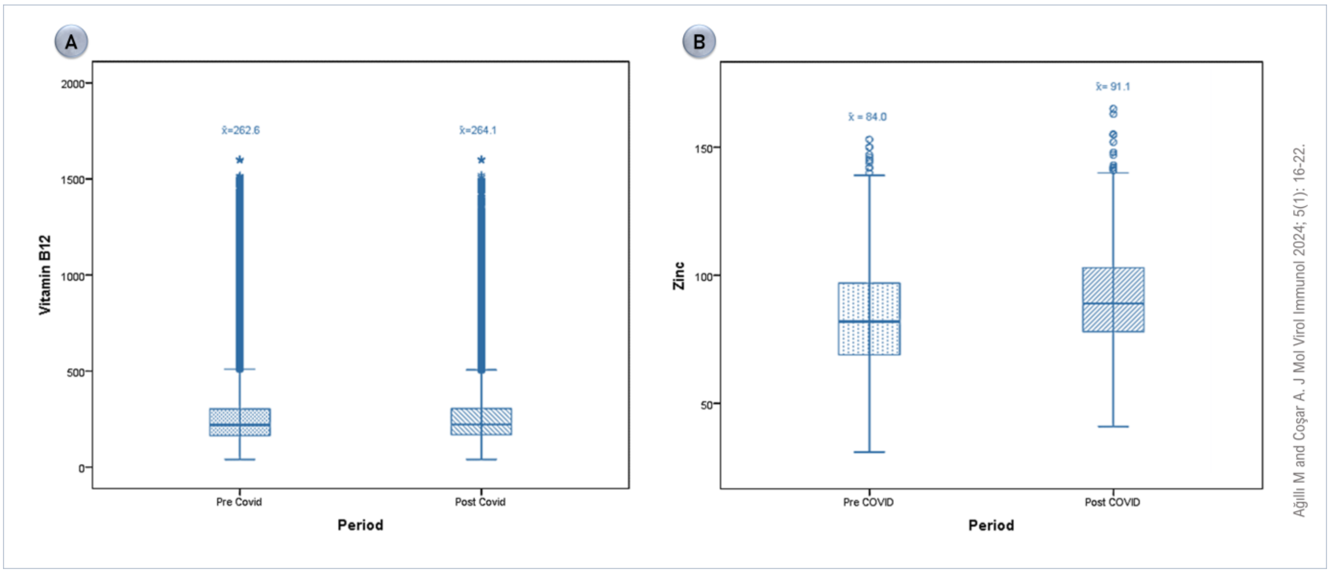

Figure 2. (**A**) Vitamin B12 levels (pg/mL) were almost the same in two groups. Mean values were 262.6 and 264.1 ng/mL for preCOVID and postCOVID groups respectively ($p>0.05$). (**B**) Serum zinc levels (ug/dL) were significantly higher in the postCOVID group ($p<0.001$). Mean values were 84.0 and 91.1 for preCOVID and postCOVID groups, respectively.

To compare vitamin D levels between groups, we divided groups to seasonal subgroups to view seasonal variations. Mean vitamin D levels for Group 1 spring, summer, autumn and winter were 22.3, 25.2, 25.4, and 21.9 ng/mL, respectively. As for Group 2, mean vitamin D levels for spring, summer, autumn and winter were 21.3, 22.7, 23.8, and 24.4 ng/mL, respectively. There were statistically differences between subgroups; higher in preCOVID periods of spring, summer, and autumn ($p<0.001$), and postCOVID period of winter ($p<0.001$), but no difference between main groups (Figure 1). Mean vitamin B12 levels were 262.6 pg/mL and 264.1 pg/mL for Group 1 and Group 2, respectively. There was no statistically difference between groups (Figure 2A). When we handle zinc levels, there has been seen statistically difference between two groups (Figure 2B). Mean zinc levels were 84.0 ug/dL and 91.1 ug/dL for Group 1 and Group 2, respectively.

Discussion

In this study, we have indirectly tested whether dietary food supplement usage was increased after COVID-19 pandemic had burst. Heightened serum mean zinc levels in postCOVID period provide insight about the rise of zinc containing dietary food supplement usage. However, there was no change in the levels of vitamin D and vitamin B12 which we have thought consumption of these two vitamins containing dietary food supplements have not changed.

In recent years, as alternative therapies and integrative medicine have become popular all over the world, interest in dietary food supplements has started to climb [11]. The belief of their effectiveness in the prevention and treatment of various diseases, we experience today, COVID-19 pandemic, has caused this interest to rise even more [13].

In a comprehensive meta-analysis, Shah et al. concluded that vitamin D supplementation reduced severity of the disease [14]. Chalmers et al. showed that bronchitis patients with low serum vitamin D levels were more prone to have increased respiratory tract inflammation with bacterial colonization [15]. Mamani et al. found that vitamin D deficiency was associated with higher incidence of community-acquired pneumonia and the disease severity [16]. In a meta-analysis, the authors declared that vitamin D deficiency was associated with an increased risk of COVID-19 [17]. In parallel to these scientific findings and growing popularity of vitamin D in the area of TV, social media, and other news sources during the pandemic period, we naturally have expected higher vitamin D levels in the postCOVID period than previous period. But the results were not as our thoughts. In this point, some possible causes come to our minds; (i) The people who thought to protect themselves against COVID-19 by using dietary food supplements did not apply to the hospital unless needed, in other saying dietary food supplement users might have played safer than nonusers, so they have not gone to hospital where the contamination risk is very high. (ii) Vitamin D supplements have not been used in sufficient doses and duration. (iii) Bioavailability of widely used vitamin D preparations were not good enough. (iv) Vitamin D usage was not increased as it was thought to be.

Vitamin B12 deficiency, coupled with its resultant defects in one-carbon metabolism which is crucial for DNA synthesis, cellular regulation and repair mechanism [18], was shown to be a major modifiable risk factor in COVID-19 morbidity and mortality [19]. In a comprehensive review, it was concluded that vitamin B12 deficiency associates in multiple areas very similar to where COVID-19 exhibits its damaging effects: immunologically (innate/adaptive immunity, cellular/humoral responses, inflammation), hematologically (coagulation), microbiologically (gut microbiome), and endothelial cell signaling (more inflammation) [19]. Notwithstanding the fact that vitamin B12 is not first dietary food supplement come to mind for COVID-19, we again expected higher vitamin B12 levels in postCOVID period. However, there was no statistically differences between groups like as vitamin D. We think the underlying causes of this result are similar to ones of vitamin D.

During pandemic, one of the most popular dietary food supplements has become zinc. Zinc is considered as a potential assistive treatment in COVID-19 infection due to its immune modulatory and direct antiviral effect [20,21]. te Velthuis and colleagues showed that Zn^{2+} cations especially in combination with zinc ionophore pyrithione inhibited SARS-coronavirus RNA polymerase activity by decreasing its replication [22]. Also, previous meta-analyses demonstrated that zinc supplementation reduces the duration of acute respiratory tract infection substantially [23]. In our study, serum zinc levels were higher in postCOVID period than preCOVID period opposed to vitamin D. Apparently, the public have attached more importance to zinc rather than vitamin D and B12 according to our results as we expected. Also, zinc containing dietary food supplements might take place more than vitamin D containing ones in the market.

As mentioned before, we have searched supplement consumption with an indirect method via using laboratory tests. The study could be designed as a simple questionnaire that asks participants whether they use supplements or not, but it would be almost impossible to reach as extensive data as this study. Consequently, the best way to evaluate dietary food supplement usage, we thought to handle robust and objective data. Nonetheless, a retrospective study design has its own deficits; we could not control any confounders or ask any questions to the participants.

Conclusion

In conclusion, the present report describes vitamin D, vitamin B12 and zinc containing dietary food supplement usage behavioral change due to COVID-19 pandemic in a local region of Türkiye. Future studies on large populations may be necessary to fully understand the COVID-19 dependent change in supplement usage.

Conflict of interest: The authors declare that there is no conflict of interest. The authors alone are responsible for the content and writing of the paper. **Financial disclosure:** There is no financial support to this study.

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