Vičič V, Pandel Mikuš R. Vitamin D supplementation during COVID-19 lockdown and after 20 months: Follow-up study on Slovenian women aged between 44 and 66. Zdr Varst. 2023;62(4):182-189. doi: 10.2478/Sjph-2023-0026.

VITAMIN D SUPPLEMENTATION DURING COVID-19 LOCKDOWN AND AFTER 20 MONTHS: FOLLOW-UP STUDY ON SLOVENIAN WOMEN AGED BETWEEN 44 AND 66

DODAJANJE VITAMINA D PRI SLOVENSKIH ŽENSKAH, STARIH MED 44 IN 66 LET, MED COVID-19 ZAPRTJEM IN SPREMLJANJE PO 20 MESECIH

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Received: Sep 06, 2023
Accepted: Sep 11, 2023

Original scientific article

ABSTRACT

Introduction: The main objective was to assess the impact of the COVID-19 pandemic on vitamin D supplementation habits and their changes in the follow-up, 20 months after the study in Slovenian premenopausal and postmenopausal women.

Methods: A cross-sectional study was conducted between March and May 2021. 176 healthy women aged 44 to 65 from the Central Slovenian region were included in the final analysis. Vitamin D status was determined by measuring 25(OH)D concentration. After 20 months an online follow-up questionnaire was sent out, to which 123 participants responded with complete data.

Results: Between March and May 2021, 61% of the participants were supplementing vitamin D. 55% of the supplementers and 88% of the non-supplementers had insufficient levels (total 25(OH)D <75 nmol/L). After 20 months in the follow-up, it was found that 62% of participants were taking vitamin D supplements, but only 70% of those who had initially reported taking supplements were still doing so. In the follow-up 61% of participants stated that they started or increased vitamin D intake due to COVID-19.

Conclusions: Vitamin D supplementation increased 7-fold compared to pre-pandemic levels and remained at a high level after 20 months. However, a significant number of participants discontinued supplementation, and only one-fifth were taking vitamin D throughout the entire year. Supplementation is effective for vitamin D deficiency prevention only at the individual level, however due to low compliance it should not be the only strategy for preventing vitamin D deficiency in the population.

Keywords:
Vitamin D
Postmenopausal women
Premenopausal women
COVID-19
Follow-up
Supplementation

IZVLEČEK

Uvod: *Cilj je bil oceniti vpliv pandemije covida-19 na navade dodajanja vitamina D med pandemijo in po 20 mesecih pri slovenskih premenopavznih in pomenopavznih ženskah.*

Metode: *Med marcem in majem 2021 smo izvedli presečno epidemiološko študijo, ki je zajela 319 žensk, starih med 44 in 65 let. V končno analizo smo ob upoštevanju izključitvenih dejavnikov vključili 176 preiskovank. Status vitamina D smo določili z meritvijo koncentracije 25(OH) vitamina D. Po 20 mesecih je bil udeleženkam poslan spletni vprašalnik za nadaljnje spremljanje. 123 udeleženk je odgovorilo s popolnimi podatki.*

Rezultati: *Med marcem in majem 2021 je 61 % preiskovank dodajalo vitamin D. Nezadostnost vitamina D (skupni 25(OH)D < 75 nmol/L) je bila ugotovljena pri 55 % žensk, ki so dodajale vitamin D, in 88 % žensk, ki niso dodajale vitamina D. Po 20 mesecih jih je vitamin D dodajalo 62 %, vendar je vitamin D dodajalo le 70 % od tistih, ki so prvotno dodajale vitamin D. V spremljanju je 61 % preiskovank povedalo, da so začele ali povečale dodajanje vitamina D zaradi covida-19.*

Zaključki: *Dodajanje vitamina D se je v primerjavi z obdobjem pred pandemijo povečalo za 7-krat in po 20 mesecih ostalo na visoki ravni. Precejšnje število udeleženk je prenehalo z dodajanjem in le petina jih je dodajala vitamin D celo leto. Dodajanje vitamina je učinkovita strategija za preprečevanje pomanjkanja vitamina D samo na ravni posameznika, vendar ni učinkovito pri preprečevanju pomanjkanja v populaciji.*

Ključne besede:
vitamin D
pomenopavza
predmenopavza
covid-19
dodajanje vitamina D

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1 INTRODUCTION

In recent years, the status of vitamin D has gained a lot of attention in connection with respiratory infections, especially with COVID-19. A recent systematic review and meta-analysis of randomized control trials has found that vitamin D supplementation reduces the risk of acute respiratory infections compared with a placebo (1). Meta-analyses have found an association between vitamin D status, the risk of COVID-19 transmission and clinical outcomes in COVID-19 patients. Vitamin D status was also identified as a risk factor for severe COVID-19 illness (2-4). Similarly, in a systematic review and meta-analysis by Chiodini et al. (5), the results showed a connection between vitamin D status and COVID-19 severity (defined as "Acute Respiratory Distress Syndrome requiring admission to intensive care unit") and mortality. Patients with low vitamin D levels on hospital admission had a higher risk of respiratory distress and death (5). In severely deficient patients in the late phases of COVID-19 pneumonia the role of vitamin D supplementation is still unclear (6).

However, the COVID-19 pandemic has also affected daily life, including dietary habits and lifestyle factors. The effects of the pandemic on these factors varied, depending on the type and severity of responses and actions taken by different countries. In a large cross-sectional survey conducted in Spain between April and June 2020, 35% of participants reported an increase in food intake, while 41% reported a decrease in snacking compared to before the lockdown. The majority of participants said their time spent cooking had increased (7). In an online survey conducted in the Netherlands between July and November 2020, the majority of responders (66%) reported no change in eating habits compared to the pre-lockdown period, 22% reported eating healthier and 12% less healthy than before (8).

An online survey report on the effects of the COVID-19 pandemic on different lifestyle factors in a sample of the Slovenian population (n=1026) found that about 14% of the participants reported a negative change in dietary habits, and 14% reported having better dietary habits; others reported no change. 32% of participants reported using food supplements during the COVID-19 pandemic (38% by women and 26% by men), and almost half of the participants (49%) who reported better dietary habits during the pandemic also reported taking food supplements (9). Another study done in Poland, which examined the use of food supplements, specifically the use of zinc and vitamin D, found that both were more often chosen by people with higher education (59%) and with medical and related education (55%). Food supplements containing only vitamin D were used by 23% of participants in the first wave, 38% in the second wave and 33% in the third wave of COVID-19 (10).

In a study by Vičič et al. (11) (March-May 2021), vitamin D status in Slovenian premenopausal and postmenopausal women was assessed. One of the main findings was that premenopausal women had 11.8% lower total 25(OH)D and 32.2% lower bioavailable 25(OH)D. Additionally, significant predictors of vitamin D status were identified, of which supplemental vitamin D intake was most important (r (175)=0.56, p<0.001), followed by time spent outside (r (175)=0.23, p [0.003]). Food vitamin D intake, physical activity and BMI were not significant. The odds of having vitamin D insufficiency (<75 nmol/L total 25(OH)D) between the vitamin D non-supplementers and supplementers (>5 µg of vitamin D/day) were: OR = 6.23(p<0.001; 95% CI [2.72, 14.274]) (11).

Compared with the results of Hribar et al. (NUTRIHEALTH study, February-April 2019) (12), Vičič et al. (11) found that the prevalence of vitamin D deficiency (<50 nmol/L) in the adult population was much lower: 24.4% compared with 81.6%. Similarly, the prevalence of insufficient 25(OH)D levels (<75 nmol/L) was much lower: 67.6% compared with 98.0% This can be explained by supplement use, which was much higher than in the NUTRIHEALTH study (61.4% compared with 8.8%, respectively) (11,12).

This is a substantial change that was influenced by expert recommendations (13) and media coverage of vitamin D supplementation effects on COVID-19 disease severity and infection risk (14). Žmitek et al. (14) investigated the effect of educational intervention - a press release to the mass media. They compared the results from the pre-intervention survey (April 2020, first COVID-19 lockdown) and post-intervention survey (December 2020, second COVID-19 lockdown). The supplementation rate increased from 33% in April to 56% in December 2020.

To further investigate, Vičič et al. (11) suggested that follow up studies should be performed to determine if COVID-19-inspired vitamin D supplementation would persist after the pandemic.

Therefore, the main objective was to assess the impact of the COVID-19 pandemic on vitamin D supplementation habits and their changes in the follow-up, 20 months after the study in Slovenian premenopausal and postmenopausal women.

2 MATERIALS AND METHODS

2.1 Study's design and participants

Between March and May 2021, a cross-sectional HIS (Health Interview Survey) and HES (Clinical Health Examination Survey) (15) study was conducted. Three hundred and nineteen (319) healthy women aged 44 to 65 from the Central Slovenian region were recruited for the study, of whom 176 participants met all the inclusion criteria. The flowchart of the study is presented in Figure 1.

2.2 Data collection

Participants were initially recruited by healthcare workers at two health centres during preventive health visits. A telephone survey was performed by trained registered nurses (RN) and nutritionists (MNutr). The questionnaire was based on a shortened food frequency questionnaire (FFQ), and questions on self-reported body weight and height, health status, use of food supplements with vitamin D, food intake, menstrual status, sun exposure status, skin type, socio-economic and socio-demographic status were added (supplementary material is available on request from the corresponding author). The participants named the specific products and dosage. Supplemental intake (μg/d) was calculated from the product label.

During the phone interview, a visit to the laboratory was arranged. Due to the challenges presented by the third COVID-19 lockdown, we employed snowball sampling as a method of recruitment (16). We provided all participants with values of 25(OH)D, including those who did not meet the inclusion criteria, with enclosed explanation. They were given a link to an online contact form where new participants could apply. This has proven an effective tool for recruiting new participants and assured truthful answers (supplementary material is available on request from the corresponding author).

The collection of blood samples was carried out during regular working hours in the selected healthcare centres and University Medical Centre Ljubljana between 1 March 2021 and 31 May 2021. All samples were transported to a central laboratory at the University Medical Centre in Ljubljana, where laboratory analysis was carried out.

Detailed description of the study' s design, inclusion and exclusion criteria, the content validity of the questionnaire, data collection process, laboratory analysis and the calculation of bioavailable 25(OH)D are presented in a previous article (11).

2.3 Follow-up design and participants

On October 17, 2022, we sent an online follow-up questionnaire about vitamin D supplementation. The short questionnaire was made using the web-based platform 1ka.si (17). It was optimized for maximum response rate and composed of 4 to 9 questions, opening depending on the participant's answers. We repeated the same questions concerning vitamin D supplementation from the study questionnaire and attached additional questions on months of supplementation, COVID-19 impact on time spent outside and effect of participation in the study on vitamin D supplementation. The mean time required for completion was 2:04 minutes. In contrast to the study, this questionnaire was filled in by participants themselves (supplementary material is available on request from the corresponding author).

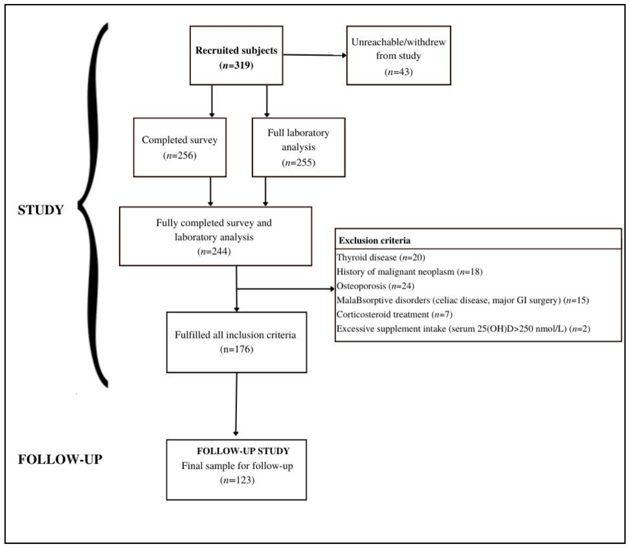

Figure 1. Flowchart of the study that included healthy women aged 44 to 65 from the Central Slovenian region. The study was carried out between March and May 2021, and the follow-up study between October and November 2022.

The last response was received on November 22, 2022. Out of 176 participants who met the criteria, 123 participants responded with complete data.

2.4 Statistical analysis

Endocrine Society cut-off values were used for assessment of total 25(OH)D levels in serum: target concentration for optimal vitamin D effects: 75–125 nmol/L, insufficiency: 50–75 nmol/L and deficiency: <50 nmol/L (18,19).

Supplementers were defined as participants with supplemental intake from foods, food supplements, or vitamin D medicines >5 μg per day. This corresponds to 25% of the Recommended Dietary Allowance (RDA) for adults, as set by DGE (the German Nutrition Society) (20).

Participants' reported highest level of completed education was classified into categories as defined by the International Standard Classification of Education (ISCED) (21).

Values are presented as a mean±SD or as a percentage (%). The data were distributed normally. A two independent samples t-test was used to examine differences between groups. For proportions the differences between groups were examined with a Z-test (22).

The statistical analysis was conducted using SPSS (IBM, version 27) and MS Excel 2019.

3 RESULTS

Population characteristics, supplementation rates and vitamin D intake via food in the participants of the study are presented in Table 1.

3.1 Study between March and May 2021

A total of 61.4% of the participants were supplementing vitamin D with prescription vitamin D or food supplements. Vitamin D supplementers had 33.3% higher 25(OH)D (76.2±27.1 nmol/L) than non-supplementers (50.8±19.6 nmol/L; t(174)=[6.718], p<0.000) and 35.8% higher bioavailable 25(OH)D (6.7±4.9 nmol/L) than non-supplementers (4.3±3.1 nmol/L; t(174)=[3.61], p<0.001). Mean vitamin D intake from food and supplementation (food supplements, vitamin D medicine) was 2.5±3.3 µg/d in non-supplementers and 37.6±25.2 µg/d in supplementers (Table 1, Figure 2). 10.2% of the supplementers and 47.1% of non-supplementers were found vitamin D deficient (total 25(OH)D <50 nmol/L), and 54.6% of the supplementers and 88.2% of non-supplementers were found with insufficient levels (total 25(OH)D <75 nmol/L) (Table 1). 88% of supplementers supplemented with dosages of 20 µg/d or more. Only 3% of non-supplementers reached food vitamin D intake >5 µg/d (Figure 2).

Table 1. Population characteristics, vitamin D status, supplementation and food intake of healthy women aged 44 to 65, from the Central Slovenian region. The study was carried out between March and May 2021 (n=176).

Variables	Category/ Unit	Total n=176	Supplementers n=108	Non-supplementers n=68	p-value
Age	year	53.8±5.0	54.3±4.8	53.1±5.2	0.120 ^{t}
Menstrual status	Premenopause	39.2%	34.3%	47.1%	0.091 ^{z}
	Postmenopause	60.8%	65.7%	52.9%	0.091 ^{z}
BMI (self-reported)	kg/m^2	25.7±4.4	25.5±4.2	26.1±4.6	0.375 ^{t}
Smoking	Current smoker	13.1%	13.0%	22.1%	0.114 ^{z}
Education (ISCED)	Primary (L1)	3.4%	1.9%	5.9%	
	Secondary (L2-3)	29.0%	27.8%	30.9%	
	Short-cycle tertiary (L5)	14.2%	14.8%	13.2%	
	Bachelor's or eq. (L6)	13.6%	13.0%	14.7%	
	Master's or eq. (L7)	29.0%	31.5%	25.0%	
	Doctoral or eq. (L8)	10.8%	11.1%	10.3%	
Time spent outside	min	53.3±17.7	54.3±16.4	51.8±19.6	0.363 ^{t}
Moderate physical activity	h/week	3.2±4.2	3.0±3.3	3.5±5.4	0.447 ^{t}
Sunscreen use		90.9%	92.6%	88.2%	0.322 ^{z}
Suntanning habits	High exposure	6.8%	4.6%	10.3%	0.1443 ^{z}
	Medium exposure	64.2%	58.3%	73.5%	**0.040** ^{z}
	Low exposure	29.0%	37.0%	16.2%	**0.003** ^{z}
Laboratory analysis					
25(OH)D	nmol/L	66.4±27.4	76.2±27.1	50.8±19.6	**<0.001** ^{t}
	<30	8.5%	3.7%	16.2%	**0.004** ^{z}
	30-50	15.9%	6.5%	30.9%	**<0.001** ^{z}
	50-75	43.2%	44.4%	41.2%	0.675 ^{z}
	>75	32.4%	45.4%	11.8%	**<0.001** ^{z}
DBP	mg/L	576±436	608±485	526±342	0.226 ^{t}
Albumin	g/L	47.1±2.2	47.5±2.2	46.5±2.1	**0.003** ^{t}
Bioavailable 25(OH)D	nmol/L	5.7±4.5	6.7±4.9	4.3±3.1	**<0.001** ^{t}
Vitamin D intake and supplementation					
Food intake (µg/d)		2.2±1.3	2.2±1.4	2.1±1.2	0.627 ^{t}
Supplement use (≥5 µg vitamin D/d)		61.4%	100,0%	0.0%	
Supplemental intake (µg/d)		21.7±26.2	35.4±25.3	0±0.08	**<0.001** ^{t}
Intake all sources (µg/d)		24.1±26.2	37.6±25.2	2.5±3.3	**<0.001** ^{t}

BMI=body mass index, DBP=vitamin D binding protein. All values are presented as a mean±SD or %. The p - value was determined using a two independent samples t-test (^{t}) or two sample Z-test for proportions (^{z}). p<0.05 was considered statistically significant (p-values of significant variables are in bold print).

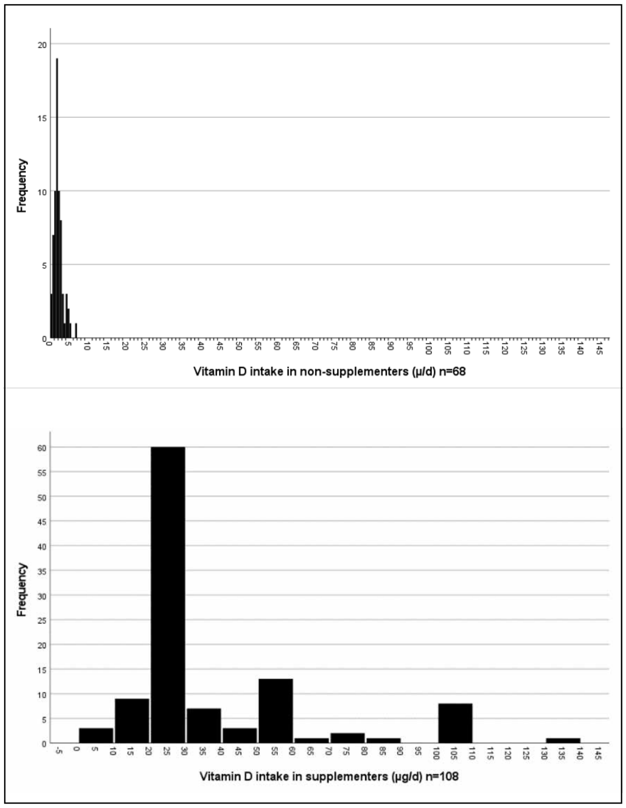

Figure 2. Total vitamin D intake of non-supplementers (top) and supplementers (bottom) (>5 µg/d). Both histograms are at the same scale (0-145 µg/d).

3.2 Follow-up between October and November 2022

As shown in Table 2, vitamin D supplementation after 20 months remained at similar levels.

Compared to the study in March and May 2021, the percentage of participants who reported starting or increasing vitamin D supplementation in the follow-up increased (Figure 3).

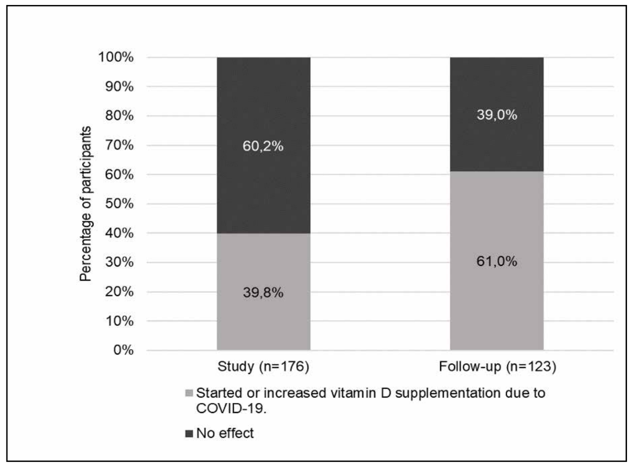

Figure 3. Percentage of participants who have reported to have started or increased vitamin D supplementation due to COVID-19, in study and follow-up.

Table 2. Results from the online follow-up questionnaire of 123 healthy women aged 44 to 65 from the Central Slovenian region, included in the follow-up study carried out between October and November 2022 (n=123).

Variables	Category/ Unit	Total n=123	Supplementers n=76	Non-supplementers n=47	p-value
Vitamin D supplementation					
Supplement use (≥5 µg vitamin D/d)		61.8%	100,0%	0.0%	
Supplemental intake	µg/d	21.6±25.9	34.9±24.9	0.12±0.7	<0.001 [t]
COVID-19 related changes in lifestyle and vitamin D supplementation					
Started/increased vitamin D supplementation		61.0%	63.2%	57.4%	0.522 [z]
COVID-19 impact on time spent outside	No impact	51.2%	51.3%	51.1%	0.984 [z]
	Increased	37.4%	38.2%	36.2%	0.826 [z]
	Decreased	11.4%	10.5%	12.8%	0.697 [z]
Effect of participation in study on vitamin D supplementation	No effect	51.8%	42.0%	62.8%	0.026 [z]
	Positive effect	48.2%	57.8%	37.2%	0.026 [z]

All values are presented as a mean±SD or %. The p - value was determined using a two independent samples t-test (t) and two samples Z-test for proportions (Z). $p<0.05$ was considered statistically significant (p-values of significant variables are in bold print).

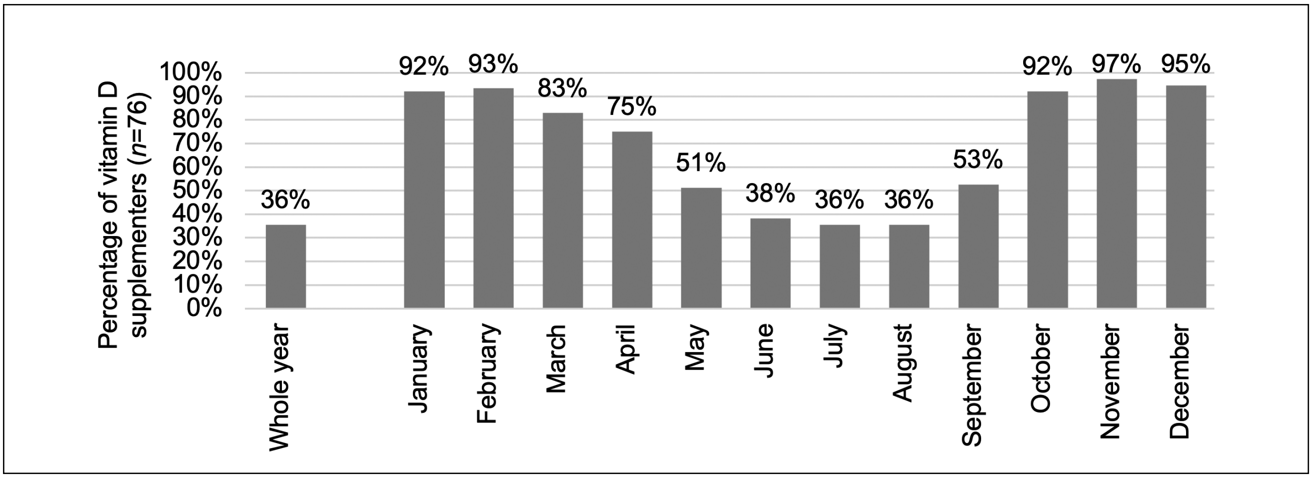

Figure 4. Seasonal rate of supplementation with vitamin D during the year in premenopausal and postmenopausal women vitamin D supplementers aged 44-65 from the Central Slovenian region (n=76). Participants marked each month individually or chose the whole year.

The results of the follow-up also show changes in supplementation habits. While the overall percentage of supplement use between study and follow-up did not change (61.4% vs. 61.8%, respectively), certain changes can be noted when comparing supplementers and non-supplementers. After 20 months, only 69.7% of the original supplementers were still supplementing vitamin D, 48.9% of non-supplementers started supplementing and 51.1% maintained non-supplementation.

When asked about months of supplementation, 36% of the supplementers supplemented vitamin D throughout the year, and more than 50% supplemented vitamin D from October till March (Figure 4).

4 DISCUSSION

The results from our study clearly indicate a major positive influence of the COVID-19 pandemic on supplement intake and serum 25(OH)D levels of the Slovenian population, when compared to previous Slovenian studies (23). Other studies also found a major increase in the vitamin D supplementation rate (10, 14) and increased supplementation with food supplements containing vitamin D, vitamin C, selenium or zinc with the intention of improving immune system function (9). However, there was a lack of data on actual vitamin D supplementation dosages.

Interestingly, other studies found a major negative impact of the COVID-19 pandemic on 25(OH)D levels in the paediatric population. This negative effect was attributed to a decrease in sun exposure due to lockdowns (24–26). In premenopausal and postmenopausal women, we report the opposite. In our follow-up 37% of participants reported an increase and 11% reported a decrease in time spent outdoors.

High supplement use and lower prevalence of deficiency or insufficiency in our study could be attributed to Slovenian leading experts rapidly recommending vitamin D supplementation in the general population. The emphasis was on supplementation in vitamin D deficient, vulnerable, high-risk individuals and COVID-19 patients (27). Supplementation with 20 to 50 μg (800 – 2000 IU) of vitamin D was recommended from October to May as a preventive measure in healthy individuals who get enough sun exposure during the summer months (13).

In a meta-analysis of clinical studies on vitamin D supplementation in postmenopausal women, 10 studies reported a compliance rate with vitamin D supplementation over 80% (28). Despite the COVID-19 pandemic, the overall rate of vitamin D supplementation did not decrease in our study. However, there was a shift in the supplementers, as 30% stopped taking supplemental vitamin D, and almost half of non-supplementers started supplementation.

The high supplementation rate in the follow-up could be due to the effect of our study, as participation in our study had a significant impact on vitamin D supplementation (Table 2), with nearly half of the participants reporting that they initiated or increased their intake after the study. Participants were informed about their 25(OH)D level, its significance and about recommended supplementation (supplementary material is available on request from the corresponding author).

The COVID-19 pandemic also caused a lot of misinformation concerning vitamin D, especially on the internet (29), which can result in cases of supplement induced vitamin D toxicity (30,31). In our study, two cases (in a sample of 244 cases) were detected with 25(OH)D >250 nmol/L. They were not included in the analysis. We talked with the participants and in both cases, they were using high-dosage vitamin

D bought online. In the first case the subject was taking 1750 µg/day in the form of 7 capsules, each containing 250 µg of cholecalciferol. The product was imported from the USA. In the second case the subject bought legal product in the form of highly concentrated drops (25 µg/drop). She was taking the product in unmeasured sips, directly from the bottle with the intention “to prevent COVID-19”. The actual dosage was unknown.

Supplementation is an effective strategy for vitamin D deficiency prevention only at the individual level. Use of food supplements is usually associated with healthier lifestyle (32), higher education, light skin colour and overall health (33). Our results also show that only 45% of supplementers reached 25(OH)D levels of >75 nmol/L, despite mean supplemental intake of 35.4±25.3 µg/d. This may mean that for most of our population higher levels of supplementation is needed to reach optimal levels.

Food fortification could be a viable solution for improvement of vitamin D status in the population. In our previous publication we provided a fortification model and an economic evaluation of biofortification of hen eggs, with or without milk (including yoghurt) fortification (34).

4.1 Strengths and limitations of the study

This follow-up study’s unique strength is that it examines vitamin D supplementation habits during the COVID-19 pandemic and 20 months after. We collected qualitative data and actual vitamin D dosages. Therefore, it shows long-term compliance with vitamin D supplementation.

Due to COVID-19 restrictions, BMI was calculated from self-reported weight and height. Several studies have evaluated the relation between self-reported and actual BMI. BMI computed from self-reported weight and height can differ from actual BMI, especially in people with higher BMI (35,36).

Another limitation of our study was the focus of questions on current supplementation and not supplementation in past months, which also contributed to 25(OH)D levels.

5 CONCLUSIONS

The results from our study indicate a major positive influence of the COVID-19 pandemic on serum 25(OH)D levels and an almost sevenfold increase in the prevalence of vitamin D supplementation compared to the Slovenian population before the pandemic. However, a significant number of the participants discontinued supplementation, and only one-fifth were taking vitamin D throughout the year. Supplementers had considerably better 25(OH) D levels, however less than half reached >75 nmol/L. Supplementation is an effective strategy for vitamin D deficiency prevention at the individual level, however due to low compliance it is not a reliable long-term strategy to prevent deficiency in the population.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

FUNDING

The study was financed by: Department of Public Health, Faculty of Medicine, University of Ljubljana research programme ARRS grant No. P3-0360, Slovenian research programme for comprehensive cancer control SLORApro and University Medical Centre Ljubljana, The Division of Gynaecology and Obstetrics, research programme ARRS grant No. P3-0124, Metabolic and hereditary factors of reproductive health, delivery II.

ETHICAL APPROVAL

The study protocol was approved by the Slovenian National Medical Ethics Committee (Ministry of Health, Republic of Slovenia), identification number KME 0120-68/2019/9 (approval letter ID 0120-68/2019/9, date of approval: 22 March 2019).

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on request from the corresponding author.

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