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ORIGINAL ARTICLE

Prevalence and predictors of vitamin D deficiency in Lebanon: 2016–2022, before and during the COVID-19 outbreak

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Abstract

Background Vitamin D deficiency is very common worldwide, particularly in Middle-Eastern countries. Recent Lebanese studies demonstrated an improvement in vitamin D status over time. However, the comparison between the years before and during the COVID-19 outbreak has never been analyzed in the Middle-East area. This study aimed to determine the prevalence and the predictors of 25-hydroxyvitamin D (25(OH)D) levels during the last 7 years.

Methods Serum 25(OH)D levels from a large laboratory database were retrospectively collected from Hôtel-Dieu de France Hospital between January 2016 and June 2022 ($N = 66{,}127$). Data related to age, gender, season and year of sampling were also retrieved.

Results Mean age of the population was 50.6 ± 19 years, 62.7% were women, 5.3% were children and adolescents, 67.6% adults and 27% elderly. Mean serum 25(OH)D level was 25.7 ± 11.9 ng/mL. The overall population with vitamin D sufficiency (>30 ng/mL) was 31.9%. The increase in mean serum 25(OH)D observed between 2016 and 2022 was 6.36 ng/mL ($p < 0.0001$). The prevalence of 25(OH)D deficiency (<30 ng/mL) decreased from 76.2% in 2016 to 56.5% in 2022 ($p < 0.0001$) with a significant difference between the period before and during the COVID-19 outbreak (72.3% vs.42.5%, $p < 0.0001$). In a multivariate logistic regression, older age, female sex, summer season, years of the COVID-19 outbreak and outpatient samples were protective factors against the risk of hypovitaminosis D ($p < 0.0001$ for all variables).

Conclusion Our study showed a continuous positive change in vitamin D status time, most notably after the COVID-19 outbreak. Further studies are needed to assess the clinical impact of the pandemic on vitamin D status in our population.

Keywords Vitamin D · Prevalence · Predictors · Lebanon · COVID-19

Introduction

The classical role of vitamin D is to regulate calcium homeostasis and bone metabolism [1, 2]. The finding that the vitamin D receptor (VDR) is expressed in almost all cells of the organism, such as immune, vascular and myocardial cells, suggests that vitamin D plays a role outside the musculoskeletal tissues [1]. Vitamin D deficiency has been associated with an increased risk of skeletal disorders [1–3] but also of several chronic non-skeletal conditions such as cardiovascular, infectious, autoimmune diseases and cancer [1, 2, 4]. Old age, female gender, high body mass index (BMI), low physical activity, poor sun exposure, high latitude, dark skin pigmentation and winter season are known risk factors for hypovitaminosis D. Other factors such as multiparity, clothing style, absence of governmental directive for vitamin D food fortification, summer season, socio-economic status and urban living are more particular to the Middle East and North Africa (MENA) region [5].

Serum 25-hydroxyvitamin D (25(OH)D) concentration is the best indicator of the human body's vitamin D and is the recommended biomarker for evaluating vitamin D status [6]. The cutoff value used to define Vitamin D deficiency is still a matter of debate [7]. While the United States (US) Institute of Medicine (IOM) suggests that 25(OH)D levels higher than 50 nmol/L (20 ng/mL) are sufficient, the Endocrine Society states that levels higher than 75 nmol/L (30 ng/mL) should be used to define sufficiency while levels between 50 and 75 nmol/L are

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still insufficient and levels below 50 nmol/L are considered as deficient [8, 9].

The prevalence of hypovitaminosis D (cutoff <50 nmol/L) is about 24% in the US, 37% in Canada and 40% in Europe [7]. This deficiency is far more common in the Middle East where 30–90% of the population is affected. Despite plentiful sunshine, 25(OH)D levels in almost all Middle-Eastern studies ranged from 25 to 50 nmol/L, with lower values in women (particularly the veiled ones) than in men [10]. In Saudi Arabia, 31.5% of the population have severe vitamin D deficiency (defined as levels below 25 nmol/L) [11]. In Lebanon, several studies have shown a high prevalence of hypovitaminosis D in both pediatric and adult populations [12–16].

Worldwide, vitamin D status has improved over time in several countries as a result of increased consumption of dairy products and vitamin D supplements, while, on the opposite, other countries have experienced a worsening of their vitamin D status due to a shift to a western-style diet [17]. In the US, a clear increase in serum 25(OH)D levels was noted after 2007 and was concomitant with an increase in vitamin D supplementation [18]. In the Lebanese population, an increase in serum 25(OH)D levels of 2–5 ng/mL was observed between the years 2000–2004 and 2007–2008 [16]. A more recent Lebanese report, showed that from 2009 and 2016, serum 25(OH)D levels continued to increase by 2.2 nmol/L/year in children, 3 nmol/L/year in adults and 6.5 nmol/L/year in the elderly [15].

Because vitamin D has an immunomodulatory role in humans [1, 4], the relationship between coronavirus disease (COVID-19) and vitamin D was the focus of intense research [19]. An association between vitamin D deficiency and COVID-19 incidence and potential severity of the disease was reported in several studies and meta-analysis [19–24] even in the pediatric population [25]. This finding led to a worldwide increase in vitamin D supplementation during the pandemic [26–29]. On the other hand, social distancing measures and home quarantine may increase the risk of vitamin D deficiency [30].

To date, few worldwide studies have examined the impact of the COVID-19 pandemic on vitamin D levels [30, 31], and to our knowledge, no previous reports in the Lebanese population has been described.

The aim of the present study is to assess vitamin D status among community-dwelling and hospitalized individuals recruited from a tertiary university hospital in the greater Beirut area during the last seven years (2016–2022) to analyze the relationship between hypovitaminosis D and several variables such as age, gender, season and healthcare services; and finally, to compare between the years before and during the COVID-19 outbreak.

Materials and methods

Study population

Anonymous demographic and laboratory data of subjects, from all age groups, who underwent serum 25(OH)D measurements at Hôtel-Dieu de France Hospital between January 1, 2016, and June 18, 2022, were retrieved. Both inpatients and outpatients' samples were included in the study. Data related to age, gender, season and year of sampling were also collected. All 25(OH)D measurements were included in the analysis with no exclusion criteria. Age was categorized into three age groups: children and adolescents (≤19 years), adults (20–64 years) and elderly (≥65 years). Season was categorized as follows: winter from December 21 to March 20, spring form March 21 to June 20, summer form June 21 to September 22 and fall from September 23 to December 20. The outbreak onset time point was considered on February 20, 2020, date where the first COVID-19 case was reported in Lebanon [32].

25(OH)D measurements

Serum 25(OH)D measurements were performed using the chemiluminescent Diasorin LIAISON immunoassay (CLIA). The lowest reported value was 4 ng/mL and the interassay coefficient of variation was <10%. Hypovitaminosis D was defined according to the Endocrine Society as a 25(OH)D level below 30 ng/mL. 25(OH)D levels were categorized into four categories: levels ≥30 ng/mL were considered as sufficient, levels between 20 and 29 ng/mL mild insufficiency, levels between 10 and 19 ng/mL moderate insufficiency and levels less than 10 ng/mL severe deficiency.

Ethical considerations

The project was approved by the Ethics committee of the Hôtel-Dieu de France hospital (reference CEHDF 1992). No informed consent was requested by our institutional review board since the data collection was anonymous.

Statistical analysis

The distribution of quantitative variables was investigated using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Categorical and normally distributed continuous variables were expressed as frequencies or percentages and mean ± standard deviation (SD), respectively.

χ^2 test and Student's test were used to compare percentages and normally distributed variables, respectively. Pearson correlation was used to assess the association between quantitative normally distributed variables. Finally,

Table 1 Mean serum 25(OH)D levels in the total population, by sex, age categories, healthcare services, year of sampling, COVID-19 and season

Characteristics	Number (*N*)	Frequency (%)	25(OH)D (ng/mL)	*p* value
Total population	66,127	100	25.71 ± 11.89	
Sex				
Men (or boys)	24,678	37.3	24.07 ± 11.54	<0.0001[a]
Women (or girls)	41,449	62.7	26.7 ± 12.00	
Age category				
≤19 years	3527	5.3	22.46 ± 10.69	<0.0001[b]
20–64 years	44,727	67.6	24.84 ± 11.48	
≥65 years	17,873	27	28.54 ± 12.63	
Healthcare services				
Inpatient	904	1.4	20.02 ± 13.09	<0.0001[a]
outpatient	65,223	98.6	25.80 ± 11.86	
Year of sampling				
2016	11,464	17.3	23.14 ± 10.81	<0.0001[b]
2017	12,102	18.3	24.06 ± 10.97	
2018	11,463	17.3	25.12 ± 11.04	
2019	10,794	16.3	25.40 ± 11.37	
2020	8576	13	26.39 ± 12.13	
2021	7821	11.8	30.73 ± 13.7	
2022	3907	5.9	29.50 ± 13.06	
COVID-19 status				
Pre-COVID-19	47,410	71.7	24.38 ± 11.09	<0.0001[a]
During COVID-19	18,717	28.3	29.10 ± 13.13	
Season				
Winter	18,077	27.3	23.97 ± 12.10	<0.0001[b]
Spring	17,826	27	25.71 ± 12.43	
Summer	15,463	23.4	27.43 ± 11.30	
Fall	14,761	22.3	26.07 ± 11.30	

25(OH)D levels are expressed as mean ± standard deviation (SD)

[a] Independent *t*-test

[b] One-way ANOVA

a univariate and a multivariate binary logistic regression analysis were performed to assess possible predictors of vitamin D deficiency defined with the three following cut-offs, as 25(OH)D <10, <20 and <30 ng/mL. Significance level was set at 5% (*p* value <0.05). Data were analyzed using the SPSS software (IBM corp. IBM SPSS Statistics for Windows, version 26.1. Armonk, NY). GraphPad Prism 8.00 (GraphPad Prism Software, Inc. La Jolla, USA) was used for plotting of results.

Results

Population

The characteristics of the study population are shown in Table 1. The number of serum 25(OH)D samples assessed during the study period was 66,127. A total of 62.7% of the population were women and 37.3% men. The mean age of the overall population was 50.6 ± 19 years with a minimum of 6 months and a maximum of 100 years. Men were significantly older than women (respectively 52.02 ± 19.4 vs.49.8 ± 18.7 years, $p < 0.0001$). Of the total population, 5.3% were children and adolescents, 67.6% adults and 27% elderly. In all, 98.6% of the serum 25(OH)D samples were carried out in an outpatient setting, 27.3% during the winter season, 27% during spring, 23.4% during summer and 22.3% during fall.

Serum 25(OH)D levels

25(OH)D values in the overall population and according to age and gender

The mean 25(OH)D level in the entire study population was 25.7 ± 11.9 ng/mL with lower values in men than in women (24.1 ± 11.5 vs 26.7 ± 12 ng/mL, $p < 0.0001$) (Table 1).

There was a significant correlation between 25(OH)D levels and age ($r = 0.23$, $p < 0.0001$). The respective mean 25(OH)D levels among children and adolescents, adults and elderly were respectively 22.46 ± 10.69, 24.84 ± 11.48, and 28.54 ± 12.6 ng/mL ($p < 0.0001$) (Table 1).

Among children and adolescents, the mean 25(OH)D levels among boys were significantly higher compared to girls (respectively 23.27.15 ± 10.49 vs 21.91 ± 10.79, $p < 0.0001$) (Table 2). Conversely, adults and elderly

Table 2 Mean serum 25(OH)D levels by age group according to sex, healthcare services, season and COVID-19 status

	≤19 years	20–64 years	≥65 years	p value[b]
Sex				
Men (or boys)	23.27 ± 10.49	23.03 ± 10.94	26.39 ± 12.57	<0.0001
Women (or girls)	21.91 ± 10.79	25.82 ± 11.64	30.10 ± 12.44	<0.0001
p value[a]	<0.0001	<0.0001	<0.0001	
Healthcare services				
Inpatient	26.88 ± 20.25	18.06 ± 11.46	20.41 ± 12.82	0.019
Outpatient	22.39 ± 10.47	24.88 ± 11.46	28.80 ± 12.53	<0.0001
p value[a]	0.003	<0.0001	<0.0001	
Season				
Winter	19.67 ± 10.30	22.90 ± 11.65	27.39 ± 12.72	<0.0001
Spring	21.38 ± 10.88	24.65 ± 11.87	28.97 ± 13.28	<0.0001
Summer	25.92 ± 10.78	26.96 ± 11.03	29.18 ± 11.97	<0.0001
Fall	22.52 ± 9.39	25.17 ± 10.81	28.84 ± 12.18	<0.0001
p value[b]	<0.0001	<0.0001	<0.0001	
COVID-19 status				
Pre-COVID-19	21.69 ± 10.22	23.58 ± 10.70	26.92 ± 11.77	<0.0001
During COVID-19	24.46 ± 11.59	28.04 ± 12.69	32.59 ± 13.73	<0.0001
p value[a]	<0.0001	<0.0001	<0.0001	
Year of sampling				
2016	21.30 ± 10.93	22.40 ± 10.44	25.44 ± 11.37	<0.0001
2017	21.62 ± 10.29	23.43 ± 10.71	26.21 ± 11.45	<0.0001
2018	22.36 ± 10.42	24.25 ± 10.53	27.88 ± 11.94	<0.0001
2019	21.86 ± 9.26	24.54 ± 10.95	28.07 ± 12.19	<0.0001
2020	22.49 ± 10.36	25.45 ± 11.74	29.40 ± 12.78	<0.0001
2021	26.11 ± 12.26	29.64 ± 13.37	34.44 ± 14.09	<0.0001
2022	23.27 ± 11.42	28.11 ± 12.53	33.67 ± 13.39	<0.0001
p value[b]	0.26	<0.0001	<0.0001	

Data presented as mean ± SD, $p < 0.05$ considered significant

25(OH)D levels are expressed as mean ± standard deviation (SD)

[a] Independent t-test

[b] One-way ANOVA

women had significantly higher mean 25(OH)D levels compared to men (25.82 ± 11.64 and 30.10 ± 12.44 ng/mL vs 23.03 ± 10.94 and 26.39 ± 12.57 ng/mL, respectively, $p < 0.0001$ for both comparisons) (Table 2).

25(OH)D values according to season and COVID-19 pandemic

The respective mean values of 25(OH)D during winter, spring, summer and fall were 23.97 ± 12.10, 25.71 ± 12.43, 27.43 ± 11.30 and 26.07 ± 11.30 ng/mL, with a significant difference between seasons ($p < 0.0001$), with the highest values in summer and the lowest ones in winter (Table 1 and Fig. 1A). The mean 25(OH)D was significantly higher during the COVID-19 pandemic compared to the pre-COVID-19 period (respectively 24.38 ± 11.09 and 29.10 ± 13.13 ng/mL, $p < 0.0001$) (Table 1 and Fig. 1B).

25(OH)D values according to healthcare services

Serum 25(OH)D levels measured in an outpatient setting were significantly higher than those measured in an inpatient setting (25.79 ± 11.86 vs 20.02 ± 13.09 ng/mL, $p < 0.0001$) (Table 1). Further stratification by age groups indicated that mean 25(OH)D levels, in adults and elderly, were significantly lower in the inpatient subgroup compared to the outpatient one (respectively for adults 18.06 ± 11.46 vs. 24.88 ± 11.46 and for elderly 20.41 ± 12.82 vs. 28.80 ± 12.53 ng/mL, $p < 0.0001$ for both comparisons) (Table 2).

25(OH)D according to year of sampling

The mean 25(OH)D levels were the lowest in 2016 and subsequently showed a consistent trend of increase during the next 7 years (Table 1 and Fig. 1A). The increase in mean serum 25(OH)D levels was 6.36 ng/mL between the years 2016 and 2022 ($p < 0.0001$) (Table 1 and Fig. 1A).

Hypovitaminosis D prevalence

The prevalences of severe vitamin D deficiency, moderate and mild vitamin D insufficiency, and vitamin D sufficiency are shown in Table 3. Of the total population, 21,096

Table 3 Prevalence of hypovitaminosis according to gender, age categories, season and year of sampling

	Vitamin D status				p value
	Severe deficiency	Moderate insufficiency	Mild insufficiency	Sufficient	
Total	5156 (7.8%)	16,652 (25.2%)	23,223 (35.1%)	21,096 (31.9%)	
Sex					
Women (or girls)	2874 (55.7%)	9194 (55.2%)	14,808 (63.8%)	14,573 (69.1%)	<0.0001
Men (or boys)	2282 (44.3%)	7458 (44.8%)	8415 (36.2%)	6523 (30.9%)	
Age category					
≤19 years	338 (6.5%)	1231 (7.4%)	1261 (5.4%)	697 (3.3%)	<0.0001
20–64 years	3624 (70.3%)	12,276 (73.7%)	16,098 (69.3%)	12,729 (60.3%)	
≥65 years	1194 (23.2%)	3145 (18.9%)	5864 (25.2%)	7670 (36.4%)	
Healthcare services					
Inpatient	238 (4.6%)	274 (1.6%)	206 (0.9%)	186 (0.9%)	<0.0001
Outpatient	4918 (95.4%)	16,378 (98.4%)	23,017 (99.1%)	20,910 (99.1%)	
Season					
Winter	2140 (41.5%)	5172 (31%)	5693 (24.5%)	5072 (24%)	<0.0001
Spring	1545 (30%)	4554 (27.3%)	5950 (25.6%)	5777 (27.4%)	
Summer	615 (12%)	3235 (19.4%)	6107 (26.3%)	5506 (26.1%)	
Fall	856 (16.5%)	3691 (22.2%)	5473 (23.6%)	4741 (22.5%)	
COVID-19 status					
Pre-COVID-19	4198 (81.4%)	13,066 (78.5%)	16,999 (73.2%)	13,147 (62.3%)	<0.0001
During COVID-19	958 (18.6%)	3586 (21.5%)	6224 (26.8%)	7949 (37.7%)	
Year of sampling					
2016	1230 (23.8%)	3415 (20.5%)	4088 (17.6%)	2731 (12.9%)	<0.0001
2017	1120 (21.7%)	3391 (20.4%)	4389 (18.9%)	3202 (15.2%)	
2018	854 (16.5%)	2976 (17.9%)	4233 (18.2%)	3400 (16.1%)	
2019	805 (15.6%)	2825 (16.9%)	3773 (16.2%)	3391 (16.1%)	
2020	629 (12.2%)	2026 (12.2%)	2982 (12.8%)	2939 (13.9%)	
2021	347 (6.7%)	1259 (7.6%)	2481 (10.7%)	3734 (17.7%)	
2022	171 (3.5%)	760 (4.5%)	1277 (5.5%)	1699 (8%)	

Data are expressed as number and percentages

The χ^2 test was used

subjects (31.9%) had sufficient 25(OH)D levels (>30 ng/mL), 39,875 subjects (60.3%) had mild to moderate vitamin D insufficiency (between 10 and 30 ng/mL), and 5156 subjects (7.8%) were severely deficient (<10 ng/mL). The prevalence of hypovitaminosis D (25(OH)D <30 ng/mL) was higher in men compared to women (73.5% vs 64.8% respectively, $p < 0.0001$). This prevalence was the highest during winter and the lowest during summer (71.9% vs 64.4%, $p < 0.0001$). It was also the highest among children and adolescents (80.2%) compared to 71.5% in adults and 57.1% in elderly ($p < 0.0001$).

Finally, there was a significant decrease in the prevalence of hypovitaminosis D between 2016 and 2022 (76.2% vs 56.5%, $p < 0.0001$) and a significant difference between the pre-COVID-19 period and the COVID-19 pandemic (72.3% vs.42.5%, $p < 0.0001$) (Fig. 2).

Predictors of vitamin D deficiency

The ORs for having serum 25OHD levels below 10, 20 and 30 ng/mL, before and after adjustment for variables that are significant at the bivariate level are presented in Table 4. The variables introduced in the model include age, sex, season, hospital status and COVID-19 period. Using multivariate regression analysis, all the introduced variables were significant independent predictors for serum 25(OH)D level <10, 20 and 30 ng/mL. The likelihood of having a serum 25OHD level <20 ng/mL decreases by 2.1% for every 1-year increase in age. Women had a 41% lower risk of serum 25(OH)D concentrations below the same level compared to men. Outpatient and COVID-19 period groups had a significantly lower risk (respectively 64% and 48%) of having a 25(OH)D serum level <20 ng/mL. The lowest prevalence of hypovitaminosis D is in the summer season, followed by fall and spring, in all age groups (Table 4). A similar pattern is seen using the 10 and 30 mg/mL cutoffs (Table 4).

Discussion

In the present study, we analyzed vitamin D status during the last 6 years in a large laboratory database collected from a tertiary referral academic center, and we compared serum 25(OH)D levels before and during the COVID-19 pandemic. Our results showed that the mean 25(OH)D level

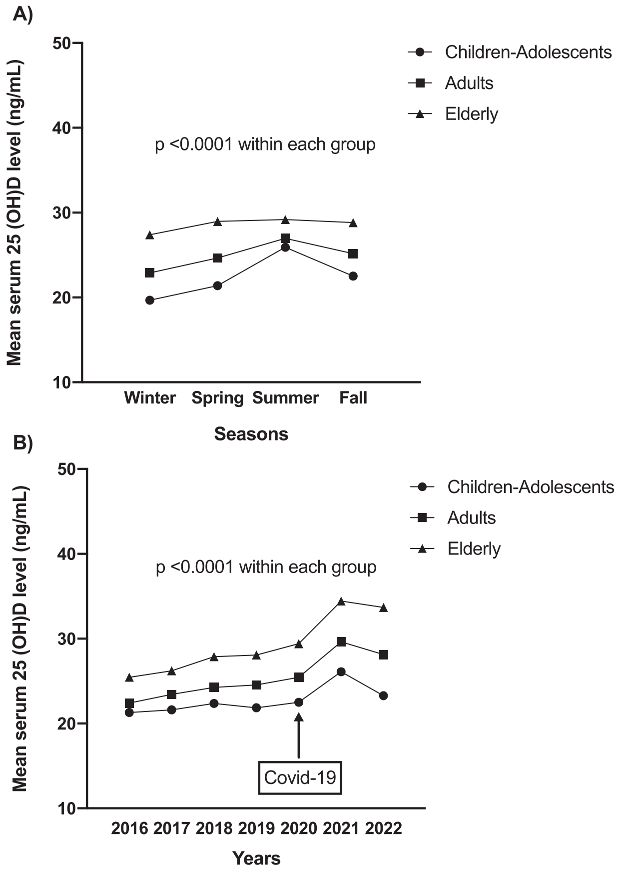

Fig. 1 Mean serum 25(OHD) levels, in children/adolescents, adults and elderly groups per season (**A**) and per year, from 2016 to 2022 (**B**). Seasonal and time variation is statistically significant within each group ($p < 0.0001$, one-way ANOVA)

was 25.71 ng/mL with a significant increase of 6.36 ng/mL level during the study period and a significant decrease in the prevalence of hypovitaminosis vitamin D from 76.2% in 2016 to 56.5% in 2022. Previous studies showed large variations in vitamin D status in the Lebanese population with the first reports showing very low 25(OH)D levels [12, 14] and later ones showing an improvement in 25(OH) D levels [5, 13, 15, 16].

Our findings are consistent with two previous Lebanese reports. In the first one, Hoteit et al. [16] using a database of 9147 subjects mostly outpatients described a rise in 25(OH) D levels of 2–5 ng/mL in both pediatric and adult groups between 2000–2004 and 2007–2008. In the second one, Saad et al. [15] analyzed the trend in 25(OH)D levels from 2009 and 2016 from a large laboratory database (151,705 subjects) and reported a similar positive time trend in vitamin D status across all age groups with a yearly increase of 0.9 ng/mL/year in pediatrics, 1.2 ng/mL/year in adults and 2.7 ng/mL/year in the elderly. Moreover, in this same study, there was a significant increase in the proportion of subjects with 25(OH)D levels ≥45 ng/mL, from 2.8% in 2009 to 19.8% in 2014 and 19.7% in 2016. The improvement of vitamin D status that we observed during the last 7 years in our study is also consistent with the report of the US NHANES study [18] and its extended study by Herrick et al. [33]. This finding was mainly attributed to vitamin D supplement use in the US population, which increased from 40.8% to 67.1% between the two study periods (1998–2000) and (2009–2011) [34]. A similar positive trend over 11 years was also seen in Finland after mandatory fortification of milk and dairy products in 2003 leading to a decrease in vitamin D deficiency from 58.5% to 13.7% [35]. In contrast, Andersen et al. [36] demonstrated a worsening of vitamin D status over 20 years in the Inuit population of Canada due to a change from a traditional fish diet (Paleo diet) to a Western diet. In the MENA region, similarly, a trend to a decrease in vitamin D deficiency was seen in several countries. In a longitudinal study in Iran, performed between 2001 and 2013, the prevalence of vitamin D deficiency (serum 25(OH)D <25 nmol/L) decreased from 30% to 24% [37]. Another report from South Arabia [38] also showed a decrease in vitamin D deficiency from 2008 to 2017. This trend in most MENA regions could be explained by the recent increase in vitamin D awareness, leading to an increase in both 25(OH)D testing and vitamin D supplementation [17]. In addition, the reasonable price of vitamin D, its good safety and tolerability make vitamin D a good preventive measure and adjuvant therapy for skeletal and extraskeletal diseases at different stages of life, including childhood, pregnancy, postmenopause and old age [1, 2, 4, 7]. The need for good vitamin D supplementation was also endorsed by the updated Lebanese guidelines for osteoporosis [39].

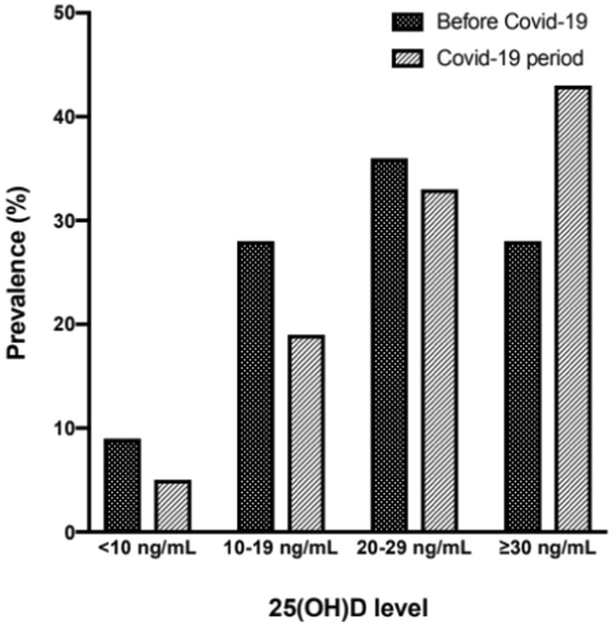

Fig. 2 Prevalence of vitamin D deficiency before and during the years of the COVID-19 outbreak according to 25(OH)D categories

Table 4 Univariate and multivariable logistic regression models of predictors of vitamin deficiency D according to different cutoffs of 25(OH)D

	Unadjusted OR (95% CI)	*p* value	Adjusted OR (95% CI)	*p* value
Predictors of 25(OH)D <10 ng/mL				
Age (years)	0.99 (0.990–0.993)	<0.001	0.989 (0.987–0.990)	<0.001
Women (vs men)	0.73 (0.69–0.774)	<0.001	0.72 (0.68–0.77)	<0.001
Outpatient (vs inpatient)	0.228 (196–0.265)	<0.001	0.25 (0.22–0.30)	<0.001
Season (vs winter)				
Spring	0.71 (0.66–0.76)	<0.001	0.74 (0.69–0.79)	<0.001
Summer	0.31 (0.28–0.34)	<0.001	0.30 (0.27–0.33)	<0.001
Fall	0.46 (0.42–0.50)	<0.001	0.46 (0.43–0.50)	<0.001
COVID-19 (vs pre-COVID-19)	0.56 (0.52–0.60)	<0.001	0.56 (0.52–0.60)	<0.001
Predictors of 25(OH)D <20 ng/mL				
Age (years)	0.982 (0.981–0.983)	<0.001	0.979 (0.978–0.980)	<0.001
Women (vs men)	0.63 (0.61–0.65)	<0.001	0.59 (0.57–0.61)	<0.001
Outpatient (vs inpatient)	0.37 (0.32–0.42)	<0.001	0.36 (0.31–0.41)	<0.001
Season (vs winter)				
Spring	0.77 (0.73–0.80)	<0.001	0.81 (0.77–0.84)	<0.001
Summer	0.49 (0.47–0.51)	<0.001	0.45 (0.42–0.47)	<0.001
Fall	0.65 (0.63–0.66)	<0.001	0.65 (0.62–0.68)	<0.001
COVID-19 (vs pre-COVID-19)	0.56 (0.54–0.58)	<0.001	0.54 (0.52–0.57)	<0.001
Predictors of 25(OH)D <30 ng/mL				
Age (years)	0.978 (0.977–0.979)	<0.001	0.976 (0.975–0.977)	<0.001
Women (vs men)	0.66 (0.64–0.69)	<0.001	0.61 (0.59–0.63)	<0.001
Outpatient (vs inpatient)	0.55 (0.47–0.65)	<0.001	0.53 (0.44–0.62)	<0.001
Season (vs winter)				
Spring	0.81 (0.78–0.85)	<0.001	0.87 (0.83–0.91)	<0.001
Summer	0.70 (0.67–0.74)	<0.001	0.65 (0.62–0.68)	<0.001
Fall	0.82 (0.79–0.86)	<0.001	0.83 (0.79–0.87)	<0.001
COVID-19 (vs pre-COVID-19)	0.52 (0.50–0.54)	<0.001	0.51 (0.49–0.53)	<0.001

OR odds ratio, *CI* confidence interval

Few studies looked at the impact of the pandemic on vitamin D status. An interrupted time series before and after the pandemic [30] described a post-outbreak monthly decline in 25(OH)D levels among infants and toddlers at a rate of 6.32 nmol/L. Similarly, another cross-sectional Chinese study [31] found lower 25(OH)D levels after confinement among children aged 3–6 years. In both studies, home confinement with social distancing measures and consequently low sunlight exposure were found to have a negative impact on vitamin D status among children. On the opposite, our study showed an improvement in 25(OH)D levels during the pandemic, possibly due to an increase in vitamin D consumption [26–28, 40, 41]. The open access to vitamin D supplements, the frequent commercial promotions on social media, as well as to the newly published data on the relationship between vitamin D status and COVID-19 infection and /or severity are probably the main contributors to this increase [19–24, 42]. This finding was also documented in the Lebanese population, where a recent study [29] demonstrated an increase in vitamin D intake from 35.5% to 41% during the pandemic in comparison to the pre-pandemic period.

We then looked at the gender difference in vitamin D status. We found that hypovitaminosis D was surprisingly more common in men than in women (73.5% vs 64.8%, respectively). Several studies from Middle-Eastern countries including Lebanon showed divergent results with some showing lower levels in women [11, 12, 14] and others showing no gender differences [13] or higher levels in women [15]. Similarly to our results, Saad et al. [15] showed that the male sex in adults and elderly is a negative predictor of 25(OH)D levels. This may be explained in part by the fact that postmenopausal women are more commonly supplemented in vitamin D since vitamin D intake is considered one of the major measures in osteoporosis prevention and treatment [39, 43]. It has also been reported that females during the pandemic were the major consumers of vitamin D supplements (59%) [44]. Moreover, females with positive COVID-19 status were more likely to use vitamin D supplements compared to men (26.9% vs. 10.5%) [45].

Paradoxically, our study also showed that mean 25(OH)D levels were higher among male children and adolescents compared to their female counterparts; this is in line with other reports [15, 16] showing that adolescent girls are the most at risk of hypovitaminosis D [46].

Aging was found to decrease the efficient production of vitamin D by the skin and to reduce the cutaneous expression of VDRs [47] therefore increasing the risk of hypovitaminosis D. Surprisingly, our study and in concordance with recently published data [11, 15] showed that older subjects have better 25(OH)D status compared to younger people since 43% of our elderly individuals had sufficient 25(OH)D levels. This was seen in both men and women (26.39 and 30.10 ng/mL, respectively) and could be due to the impact of public health awareness campaigns on osteoporosis as well as to the increase in vitamin D supplementation among this high-risk population [34, 39, 43].

We found a seasonal effect on the prevalence of hypovitaminosis D with the highest levels during winter and the lowest during summer (71.9% vs 64.4%). Sun exposure has a known protective effect on vitamin D status since the ultraviolet B provided by the sun increases cutaneous vitamin D synthesis. Several studies in the MENA region described the same seasonal variations [12–16, 38]; this can be explained by the lower sunlight exposure and cutaneous vitamin D synthesis during winter. Nevertheless, this seasonal variation was not seen in postmenopausal Lebanese women [48]. Finally, a study from the Arabian Peninsula [49] revealed that vitamin D insufficiency was significantly associated with hot months of the year and this was explained by the limited time spent outdoors during summer due to extreme heat and humidity [3].

Vitamin D status is worse in our hospitalized population compared to the outpatients' one (20.02 vs 25.79 ng/mL). This difference is more accentuated in elderly individuals. Similarly, Saad et al. [15] reported that hospitalization is a significant predictor of low 25(OH)D in all age groups especially in the elderly. The lower vitamin D binding protein in hospitalized patients can explain this finding and makes 25(OH)D measurement an unreliable biomarker of vitamin D status in this setting [50].

Our study has a few limitations. Its cross-sectional nature precludes any causality assessment. In addition, data were collected from the laboratory database; therefore, information related to several clinical variables was unavailable. This includes demographic variables such as BMI, coexistent medical conditions, vitamin D supplements use or lifestyle habits such as veiling or sunscreen use. Other biological variables such as calcium, parathormone or creatinine levels were also not available. Finally, despite the fact that our study is monocentric, our hospital is a tertiary university medical center that receives patients from all regions of Lebanon; hence, the data are representative of the overall Lebanese population.

On the other hand, our study has several strengths. It is a very large database study, over 90% are an outpatient population, all age groups were studied across all seasons, and over a duration of 7 years including the pandemic period. In addition, 25(OH)D measurements through the study period were done using the same vitamin D assay and in the same laboratory minimizing variation secondary to the assay.

In conclusion, our study showed that women, elderly, outpatient subjects have better 25(OH)D status compared to men, younger subjects and inpatient setting. In addition, 25(OH)D levels were the lowest during the winter season. Furthermore, a positive change in vitamin D status was observed over the last 7 years most notably after the COVID-19 outbreak. Further studies are needed to assess if this positive effect on vitamin D status will improve both skeletal and extraskeletal outcomes in our population.

Data availability

Data are available upon request from the corresponding author.

Author contributions D.H.: conceptualization, data curation, writing—original draft preparation. N.G.: software, formal analysis, writing—reviewing and editing. M.-H.G.-Y.: conceptualization, supervision, formal analysis, methodology, software, writing—original draft, reviewing and editing.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

References

1. A. Zendehdel, M. Arefi, Molecular evidence of role of vitamin D deficiency in various extraskeletal diseases. J. Cell Biochem. **120**(6), 8829–8840 (2019). https://doi.org/10.1002/jcb.28185
2. R. Bouillon, C. Marcocci, G. Carmeliet, D. Bikle, J.H. White, B. Dawson-Hughes et al. Skeletal and extraskeletal actions of vitamin D: current evidence and outstanding questions. Endocr. Rev. **40**(4), 1109–1151 (2019). https://doi.org/10.1210/er.2018-00126
3. H. Glerup, K. Mikkelsen, L. Poulsen, E. Hass, S. Overbeck, J. Thomsen et al. Commonly recommended daily intake of vitamin D is not sufficient if sunlight exposure is limited. J. Intern. Med. **247**(2), 260–268 (2000). https://doi.org/10.1046/j.1365-2796.2000.00595.x
4. J. Bartley, Vitamin D: emerging roles in infection and immunity. Expert Rev. Anti Infect. Ther. **8**(12), 1359–1369 (2010). https://doi.org/10.1586/eri.10.102
5. D. Bassil, M. Rahme, M. Hoteit, G.E.H. Fuleihan, Hypovitaminosis D in the Middle East and North Africa: prevalence, risk factors and impact on outcomes. Dermatoendocrinol **5**(2), 274–298 (2013). https://doi.org/10.4161/derm.25111

6. A.A. Yates, S.A. Schlicker, C.W. Suitor, Dietary Reference Intakes: the new basis for recommendations for calcium and related nutrients, B vitamins, and choline. J. Am. Diet. Assoc. **98**(6), 699–706 (1998). https://doi.org/10.1016/S0002-8223(98)00160-6
7. K. Amrein, M. Scherkl, M. Hoffmann, S. Neuwersch-Sommeregger, M. Köstenberger, A. Tmava Berisha et al. Vitamin D deficiency 2.0: an update on the current status worldwide. Eur. J. Clin. Nutr. **74**(11), 1498–1513 (2020). https://doi.org/10.1038/s41430-020-0558-y
8. A.C. Ross, J.E. Manson, S.A. Abrams, J.F. Aloia, P.M. Brannon, S.K. Clinton et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J. Clin. Endocrinol. Metab. **96**(1), 53–58 (2011). https://doi.org/10.1210/jc.2010-2704
9. H.A. Bischoff-Ferrari, E. Giovannucci, W.C. Willett, T. Dietrich, B. Dawson-Hughes, Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am. J. Clin. Nutr. **84**(1), 18–28 (2006). https://doi.org/10.1093/ajcn/84.1.18
10. P. Lips, K.D. Cashman, C. Lamberg-Allardt, H.A. Bischoff-Ferrari, B. Obermayer-Pietsch, M.L. Bianchi et al. Current vitamin D status in European and Middle East countries and strategies to prevent vitamin D deficiency: a position statement of the European Calcified Tissue Society. Eur. J. Endocrinol. **180**(4), P23–P54 (2019). https://doi.org/10.1530/EJE-18-0736
11. A.N. Hussain, A.H. Alkhenizan, M. El Shaker, H. Raef, A. Gabr, Increasing trends and significance of hypovitaminosis D: a population-based study in the Kingdom of Saudi Arabia. Arch. Osteoporos. **9**, 190 (2014). https://doi.org/10.1007/s11657-014-0190-3
12. M.H. Gannagé-Yared, R. Chemali, N. Yaacoub, G. Halaby, Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. J. Bone Min. Res. **15**(9), 1856–1862 (2000). https://doi.org/10.1359/jbmr.2000.15.9.1856
13. M.H. Gannagé-Yared, E. Helou, V. Zaraket, S. Abi Akl, L. Antonios, M.L. Moussalli et al. Serum 25 hydroxyvitamin D in employees of a Middle Eastern university hospital. J. Endocrinol. Invest. **37**(6), 541–546 (2014). https://doi.org/10.1007/s40618-014-0061-1
14. A. Arabi, R. El Rassi, G. El-Hajj Fuleihan, Hypovitaminosis D in developing countries-prevalence, risk factors and outcomes. Nat. Rev. Endocrinol. **6**(10), 550–561 (2010). https://doi.org/10.1038/nrendo.2010.146
15. R.K. Saad, V.C. Akiki, M. Rahme, S. Ajjour, M. Assaad, G.A. El-Hajj Fuleihan, Time trends and predictors of hypovitaminosis D across the life course: 2009-2016. Metabolism **105**, 154138 (2020). https://doi.org/10.1016/j.metabol.2020.154138
16. M. Hoteit, L. Al-Shaar, C. Yazbeck, M. Bou Sleiman, T. Ghalayini, G.E.H. Fuleihan, Hypovitaminosis D in a sunny country: time trends, predictors, and implications for practice guidelines. Metabolism **63**(7), 968–978 (2014). https://doi.org/10.1016/j.metabol.2014.04.009
17. P. Lips, R.T. de Jongh, N.M. van Schoor, Trends in vitamin D status around the world. JBMR Plus **5**(12), e10585 (2021). https://doi.org/10.1002/jbm4.10585
18. R.L. Schleicher, M.R. Sternberg, D.A. Lacher, C.T. Sempos, A.C. Looker, R.A. Durazo-Arvizu et al. The vitamin D status of the US population from 1988 to 2010 using standardized serum concentrations of 25-hydroxyvitamin D shows recent modest increases. Am. J. Clin. Nutr. **104**(2), 454–461 (2016). https://doi.org/10.3945/ajcn.115.127985
19. M. Pereira, A. Dantas Damascena, L.M. Galvão Azevedo, T. de Almeida Oliveira, J. da Mota Santana, Vitamin D deficiency aggravates COVID-19: systematic review and meta-analysis. Crit. Rev. Food Sci. Nutr. **62**(5), 1308–1316 (2022). https://doi.org/10.1080/10408398.2020.1841090
20. J.M. Rhodes, S. Subramanian, E. Laird, G. Griffin, R.A. Kenny, Perspective: vitamin D deficiency and COVID-19 severity – plausibly linked by latitude, ethnicity, impacts on cytokines, ACE2 and thrombosis. J. Intern. Med. **289**(1), 97–115 (2021). https://doi.org/10.1111/joim.13149
21. E. Cereda, L. Bogliolo, C. Klersy, F. Lobascio, S. Masi, S. Crotti et al. Vitamin D 25OH deficiency in COVID-19 patients admitted to a tertiary referral hospital. Clin. Nutr. Edinb. Scotl. **40**(4), 2469–2472 (2021). https://doi.org/10.1016/j.clnu.2020.10.055
22. G.E. Carpagnano, V. Di Lecce, V.N. Quaranta, A. Zito, E. Buonamico, E. Capozza et al. Vitamin D deficiency as a predictor of poor prognosis in patients with acute respiratory failure due to COVID-19. J. Endocrinol. Invest. **44**(4), 765–771 (2021). https://doi.org/10.1007/s40618-020-01370-x
23. A. Radujkovic, T. Hippchen, S. Tiwari-Heckler, S. Dreher, M. Boxberger, U. Merle, Vitamin D deficiency and outcome of COVID-19 patients. Nutrients **12**(9), E2757 (2020). https://doi.org/10.3390/nu12092757
24. S. Sabico, M.A. Enani, E. Sheshah, N.J. Aljohani, D.A. Aldisi, N.H. Alotaibi et al. Effects of a 2-week 5000 IU versus 1000 IU vitamin D3 supplementation on recovery of symptoms in patients with mild to moderate COVID-19: a randomized clinical trial. Nutrients **13**(7), 2170 (2021). https://doi.org/10.3390/nu13072170
25. M. Miraglia Del Giudice, C. Indolfi, G. Dinardo, F. Decimo, A. Decimo, A. Klain, Vitamin D status can affect COVID-19 outcomes also in pediatric population. PharmaNutrition **22**, 100319 (2022). https://doi.org/10.1016/j.phanu.2022.100319
26. A. Puścion-Jakubik, J. Bielecka, M. Grabia, A. Mielech, R. Markiewicz-Żukowska, K. Mielcarek et al. Consumption of food supplements during the three COVID-19 waves in Poland-focus on zinc and vitamin D. Nutrients **13**(10), 3361 (2021). https://doi.org/10.3390/nu13103361
27. S. Çimke, D. Yıldırım Gürkan, Determination of interest in vitamin use during COVID-19 pandemic using Google Trends data: infodemiology study. Nutrition **85**, 111138 (2021). https://doi.org/10.1016/j.nut.2020.111138
28. M. Mikulic, Change in usage of dietary supplements due to COVID-19 among U.S. adults as of August 2020, by gender. https://www.statista.com/statistics/1180357/dietary-supplement-usage-change-due-to-covid-us-adults-by-gender/
29. H. Mohsen, N. Yazbeck, A. Al-Jawaldeh, N. Bou Chahine, H. Hamieh, Y. Mourad et al. Knowledge, attitudes, and practices related to dietary supplementation, before and during the COVID-19 pandemic: findings from a cross-sectional survey in the Lebanese population. Int. J. Environ. Res. Public Health **18**(16), 8856 (2021). https://doi.org/10.3390/ijerph18168856
30. R.S. Wong, K.T.S. Tung, H.K. So, W.H.S. Wong, S.Y. Wong, H.W. Tsang et al. Impact of COVID-19 pandemic on serum vitamin D level among infants and toddlers: an interrupted time series analysis and before-and-after comparison. Nutrients **13**(4), 1270 (2021). https://doi.org/10.3390/nu13041270
31. L. Yu, H.J. Ke, D. Che, S.L. Luo, Y. Guo, J.L. Wu, Effect of pandemic-related confinement on vitamin D status among children aged 0-6 years in Guangzhou, China: a cross-sectional study. Risk Manag. Healthc. Policy **13**, 2669–2675 (2020). https://doi.org/10.2147/RMHP.S282495
32. A.R. Bizri, H.H. Khachfe, M.Y. Fares, U. Musharrafieh, COVID-19 pandemic: an insult over injury for Lebanon. J. Community Health **46**(3), 487–493 (2021). https://doi.org/10.1007/s10900-020-00884-y
33. K.A. Herrick, R.J. Storandt, J. Afful, C.M. Pfeiffer, R.L. Schleicher, J.J. Gahche et al. Vitamin D status in the United States, 2011-2014. Am. J. Clin. Nutr. **110**(1), 150–157 (2019). https://doi.org/10.1093/ajcn/nqz037
34. D.M. Mitchell, K. Ruppert, N. Udupa, F. Bassir, K. Darakananda, D.H. Solomon et al. Temporal increases in 25-hydroxyvitamin D

in midlife women: longitudinal results from the Study of Women's Health Across the Nation. Clin. Endocrinol. (Oxf.) **91**(1), 48–57 (2019). https://doi.org/10.1111/cen.13986

35. T. Jääskeläinen, S.T. Itkonen, A. Lundqvist, M. Erkkola, T. Koskela, K. Lakkala et al. The positive impact of general vitamin D food fortification policy on vitamin D status in a representative adult Finnish population: evidence from an 11-y follow-up based on standardized 25-hydroxyvitamin D data. Am. J. Clin. Nutr. **105**(6), 1512–1520 (2017). https://doi.org/10.3945/ajcn.116.151415
36. S. Andersen, P. Laurberg, B. Hvingel, K. Kleinschmidt, L. Heickendorff, L. Mosekilde, Vitamin D status in Greenland is influenced by diet and ethnicity: a population-based survey in an Arctic society in transition. Br. J. Nutr. **109**(5), 928–935 (2013). https://doi.org/10.1017/S0007114512002097
37. H. Khosravi-Boroujeni, N. Sarrafzadegan, M. Sadeghi, H. Roohafza, S.K. Ng, A. Pourmogaddas et al. Prevalence and trends of vitamin D deficiency among Iranian adults: a longitudinal study from 2001–2013. J. Nutr. Sci. Vitaminol. (Tokyo) **63**(5), 284–290 (2017). https://doi.org/10.3177/jnsv.63.284
38. N.M. Al-Daghri, S.D. Hussain, M.G.A. Ansari, M.N.K. Khattak, N. Aljohani, Y. Al-Saleh, et al. Decreasing prevalence of vitamin D deficiency in the central region of Saudi Arabia (2008-2017). J. Steroid Biochem. Mol. Biol. **212**, 105920 (2021). https://doi.org/10.1016/j.jsbmb.2021.105920
39. M. Chakhtoura, W.D. Leslie, M. McClung, A.M. Cheung, G.E.H. Fuleihan, The FRAX-based Lebanese osteoporosis treatment guidelines: rationale for a hybrid model. Osteoporos. Int. **28**(1), 127–137 (2017). https://doi.org/10.1007/s00198-016-3766-5
40. R. Lordan, Dietary supplements and nutraceuticals market growth during the coronavirus pandemic – implications for consumers and regulatory oversight. PharmaNutrition **18**, 100282 (2021). https://doi.org/10.1016/j.phanu.2021.100282
41. J. Hamulka, M. Jeruszka-Bielak, M. Górnicka, M.E. Drywień, M.A. Zielinska-Pukos, Dietary supplements during COVID-19 outbreak. Results of Google Trends analysis supported by PLifeCOVID-19 online studies. Nutrients **13**(1), E54 (2020). https://doi.org/10.3390/nu13010054
42. W.B. Grant, H. Lahore, S.L. McDonnell, C.A. Baggerly, C.B. French, J.L. Aliano et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. Nutrients **12**(4), E988 (2020). https://doi.org/10.3390/nu12040988
43. G. El-Hajj Fuleihan, R. Baddoura, H. Awada, A. Arabi, J. Okais, First update of the Lebanese guidelines for osteoporosis assessment and treatment. J. Clin. Densitom. **11**(3), 383–396 (2008). https://doi.org/10.1016/j.jocd.2008.02.006
44. H.A. Algaeed, M.I. AlJaber, A.I. Alwehaibi, L.I. AlJaber, A.M. Arafah, M.A. Aloyayri et al. General public knowledge and use of dietary supplements in Riyadh, Saudi Arabia. J. Fam. Med Prim. Care **8**(10), 3147–3154 (2019). https://doi.org/10.4103/jfmpc.jfmpc_511_19
45. S. Hussain, M. Elnajeh, Prevalence and risk factors for hypovitaminosis D among healthy adolescents in Kota Bharu, Kelantan. J. ASEAN Fed. Endocr. Soc. **35**(2), 176–180 (2020). https://doi.org/10.15605/jafes.035.02.05
46. H.A. Alfawaz, N. Khan, G.A. Aljumah, S.D. Hussain, N.M. Al-Daghri, Dietary intake and supplement use among Saudi residents during COVID-19 lockdown. Int J. Environ. Res. Public Health **18**(12), 6435 (2021). https://doi.org/10.3390/ijerph18126435
47. P. D'Amelio, L. Quacquarelli, Hypovitaminosis D and aging: is there a role in muscle and brain health? Nutrients **12**(3), E628 (2020). https://doi.org/10.3390/nu12030628
48. M.H. Gannagé-Yared, G. Maalouf, S. Khalife, S. Challita, Y. Yaghi, N. Ziade et al. Prevalence and predictors of vitamin D inadequacy amongst Lebanese osteoporotic women. Br. J. Nutr. **101**(4), 487–491 (2009). https://doi.org/10.1017/S0007114508023404
49. N.M. Al-Daghri, O.S. Al-Attas, M.S. Alokail, K.M. Alkharfy, E. El-Kholie, M. Yousef et al. Increased vitamin D supplementation recommended during summer season in the gulf region: a counterintuitive seasonal effect in vitamin D levels in adult, overweight and obese Middle Eastern residents. Clin. Endocrinol. (Oxf.) **76**(3), 346–350 (2012). https://doi.org/10.1111/j.1365-2265.2011.04219.x
50. S.A. Quraishi, C.A. Camargo, Vitamin D in acute stress and critical illness. Curr. Opin. Clin. Nutr. Metab. Care **15**(6), 625–634 (2012). https://doi.org/10.1097/MCO.0b013e328358fc2b