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Original Article

Serum Vitamin D Status in Older Adults: A Cohort Study

Simin Mouodi, MD, MPH, PhD; Sajedeh Delbari, MD; Seyed Reza Hosseini, MD; Reza Ghadimi, MD, PhD; Ali Bijani, MD, PhD

Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

Correspondence:
Ali Bijani, MD, PhD;
Social Determinants of Health Research Center, Health Research Institute,
Babol University of Medical Sciences,
Ganj-afrooz Ave.,
Postal code: 47176-41367,
Babol, Iran
Tel: +98 11 32194720
Fax: +98 11 32197667
Email: alibijani@yahoo.com
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Abstract

Background: Vitamin D is best known as a key regulator of bone metabolism and calcium and phosphate homeostasis. This study aimed to assess the effect of different factors on the five-year changes in serum vitamin D concentration among older adults.

Methods: This cohort study was conducted on adults aged ≥60 years living in Amirkola, in the North of Iran, from 2012 to 2017. Serum 25-hydroxyvitamin D (25-OH vitamin D) concentrations of <20, 20-29.99, and ≥30 ng/mL, respectively, were used to designate vitamin D deficiency, insufficiency, and sufficiency. Any variation between the second and baseline values of the 25-OH vitamin D concentration was reported as a five-year difference. Data were analyzed using SPSS version 17.0, and Chi square, *t* test, one-way ANOVA, and Tukey HSD *post hoc* tests were employed. P values less than 0.05 were considered statistically significant.

Results: The mean serum concentration of 25-OH vitamin D at baseline and follow-up examination in 1011 individuals was 34.68±33.18 and 23.88±14.91, respectively (P<0.001). Following a five-year follow-up, vitamin D deficiency, insufficiency, and sufficiency were found in 452 (44.7%), 334 (33.0%), and 225 (22.3%) cases, respectively. The reduction in serum 25-OH vitamin D concentration after five years was significantly influenced by the administration of vitamin D (P=0.013) and calcium (P=0.007) supplements, serum profile of parathyroid hormone (PTH) (P=0.010), calcium (P=0.021), and phosphorous (P=0.021). However, age, sex, body mass index, metabolic syndrome, and physical activity had no significant impact (P>0.05).

Conclusion: Regardless of age, sex, body mass index, metabolic syndrome, or physical activity, the mean serum concentration of vitamin D decreased over a five-year follow-up.

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Keywords ● Vitamin D ● Aging ● Vitamin deficiency

What's Known

- Vitamin D has a significant influence on different essential biological pathways in older individuals.

What's New

- After a five-year follow-up, 44.7% and 33.0% of older adults aged ≥60 had vitamin D deficiency or insufficiency, respectively.
- Administration of vitamin D and calcium supplements, as well as serum profile of PTH, calcium, and phosphorous had a significant impact on the reduction of serum vitamin D concentration after five years.

Introduction

Vitamin D, as a hormone obtained through dietary intake or skin production, is primarily known as an important modulator of bone metabolism and calcium and phosphate homeostasis. However, recent studies have demonstrated its impact on different essential biological pathways, such as neuromuscular function, cardiovascular health, immunomodulation, and infectious diseases prevention.[1] Given the antioxidant, anti-inflammatory, and neuroprotective properties of vitamin D, its deficiency may contribute to cognitive impairment in the elderly.[2-4] According to previous studies, low serum vitamin D levels were associated with many other disorders, such as insulin resistance, diabetes-related complications, migraine, cardiovascular diseases, and various malignancies.[5, 6]

It was estimated that 34-37% of adults in the United States and 51% of adults in Iran had serum 25-hydroxyvitamin D (25-OH vitamin D) concentrations lower than 50 ng/mL,[7] and older adults were predicted to have a more severe and prevalent Vitamin D deficiency.[5, 8] In a systematic review and meta-analysis in Iran, the overall prevalence of vitamin D deficiency was reported to be 56% of the general population.[9]

Although vitamin D has been identified as a critical component of healthy aging,[5] many older adults do not receive enough vitamin D. As a result, they experience symptoms of vitamin D insufficiency and deficiency, including musculoskeletal disorders and pains,[10] falls and bone fractures,[11] cognitive dysfunctions,[2, 12] and a higher risk of developing other diseases.[1] Furthermore, a number of factors, including comorbid disorders, smoking,[13] obesity,[5] metabolic syndromes,[14] serum parathyroid hormone (PTH) concentration,[15] medications, and supplements administration, might have an impact on older adults' vitamin D status.[5] The objective of this study was to investigate contributing factors among older adults and assess the five-year change in serum vitamin D concentration.

Patients and Methods

Study Design and Procedure

The present historic cohort study was a part of the Amirkola Health and Ageing Project, 2012-2017.[16, 17] The research was carried out on older adults aged ≥60 living in Amirkola, near the Caspian Sea (Iran). All the elderly in this region were invited to participate in the study, through the census. Individuals who participated in the study were all followed for five years.

All of the participants were informed about the objectives, length, and methodology of the study. Written informed consent was obtained from all the older adults who participated in the first phase of the research. The study was approved by the Ethics Committee of Babol University of Medical Sciences, Babol, Iran (code: IR.MUBABOL.REC.1399.246).

The study included individuals whose serum samples were obtained at least twice, with a five-year interval, to be tested for the 25-OH vitamin D concentration. The enzyme-linked immunoassay (ELISA) method was used to determine the serum level of 25-OH vitamin D. Serum 25-OH vitamin D concentrations of 20, 20–29.99, and ≥30 ng/mL were used to define vitamin D deficiency, insufficiency, and sufficiency, respectively.[18] Any categorical drop in the second value of 25-OH vitamin D concentration compared to the baseline value was reported as a five-year difference. When the serum vitamin D level was classified as insufficient at the baseline test, it would be reported as a categorical drop, if the second value of serum vitamin D reached the deficiency range. Elderly patients with vitamin D deficiency or insufficiency were referred to their family physician for further evaluation and any necessary intervention.

During the direct interview with the participants, personal information such as age, sex, degree of education, marital status, living condition, comorbid disorders, smoking history, and the number of consumed medicines were obtained. To measure the serum levels of 25-OH vitamin D, parathyroid hormone (PTH), calcium, and phosphorus, as well as to assess renal function (blood urea nitrogen and serum creatinine), a morning venous blood sample was taken. These laboratory tests were carried out twice, once during phase one (baseline examination) and once during phase two (after five years).

Body weight (Kg) and height (m) were measured using standard scales, based on which the body mass index (BMI, Kg/m^2) of each participant was calculated. Then, they were classified as normal (<25), overweight (25-29.9), and obese (≥30). Metabolic syndrome (MetS) was defined by the 2005 Adult Treatment Panel (ATP) III as high serum triglyceride (≥150 mg/dL), low HDL cholesterol (<40 mg/dL in males and <50 mg/dL in females), and high blood pressure (systolic blood pressure [BP]≥130 and/or diastolic BP≥85 mm Hg), as well as central obesity, previously diagnosed type 2 diabetes or fasting plasma glucose ≥100 mg/dL, and a waist circumference of ≥102 in men and ≥88 cm in women.[19]

Physical activity was measured using the physical activity scale for the elderly (PASE). This questionnaire measures a person's activity in three areas, including activity during leisure time, activity at home, and job-related activities. The participants were divided into two groups based on their total PASE score. The PASE score of the first group was less than 150, and the second group was ≥150. Higher scores represent more physical activity. The physical activity score was described using the mean±SD.[20] Previous studies approved the reliability and validity of the Persian version of this questionnaire.[21]

Statistical Analysis

All statistical analyses were performed using IBM SPSS software (IBM Corporation, Armonk, USA), version 17.0. The acquired data were analyzed using the Chi square, *t* test, one-way ANOVA, and Tukey HSD *post hoc* test. P values less than 0.05 were considered statistically significant.

Results

The present study included 1011 older adults, with a mean age of 68.1±6.7 years, including 569 (56.3%) males and 442 (43.7%) females. Among them, 611 (60.4%) were illiterate; 33 (3.3%) had an academic education, and the remaining 367 (36.3%) had less than a high school diploma.

At the baseline examination, 353 (34.9%), 333 (32.9%), and 325 (32.1%) of older adults had a serum concentration of 25-OH vitamin D <20, 20-29.99, and ≥30 ng/mL, respectively. After a five-year follow-up, 452 (44.7%), 334 (33.0%), and 225 (22.3%) individuals had vitamin D deficiency, insufficiency, and sufficiency, respectively. Furthermore, in 386 (38.2%) individuals vitamin D levels decreased, 255 (25.2%) increased, and 370 (36.6%) indicated no change in vitamin D concentration. At the baseline and follow-up examinations, the mean serum concentration of 25-OH vitamin D was 34.68±33.18 and 23.88±14.91, respectively (P<0.001). The mean difference between the two serum 25-OH vitamin D values was 10.80±35.75 ng/mL. The distribution of serum concentration of 25-OH vitamin D over two examination times, sexes, and different ages is presented in figures 1, 2, and 3.

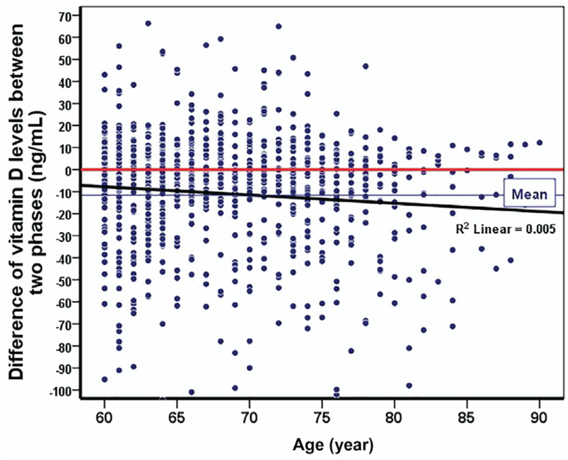

Figure 1: The changes in vitamin D after five years had no significant correlation with the age of older adults.

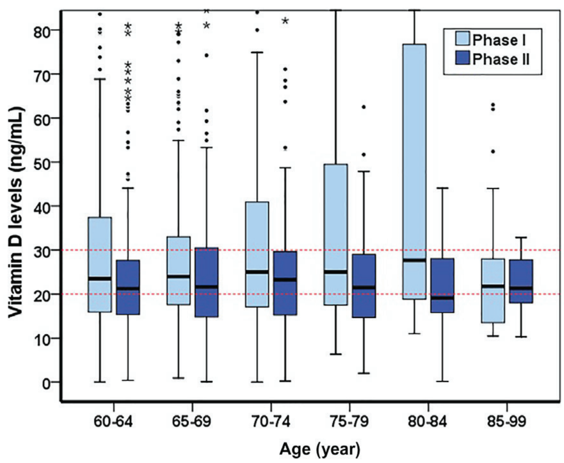

Figure 2: According to the reported median and interquartile range, a reduction was observed in vitamin D levels among all different age groups in the two phases of the research.

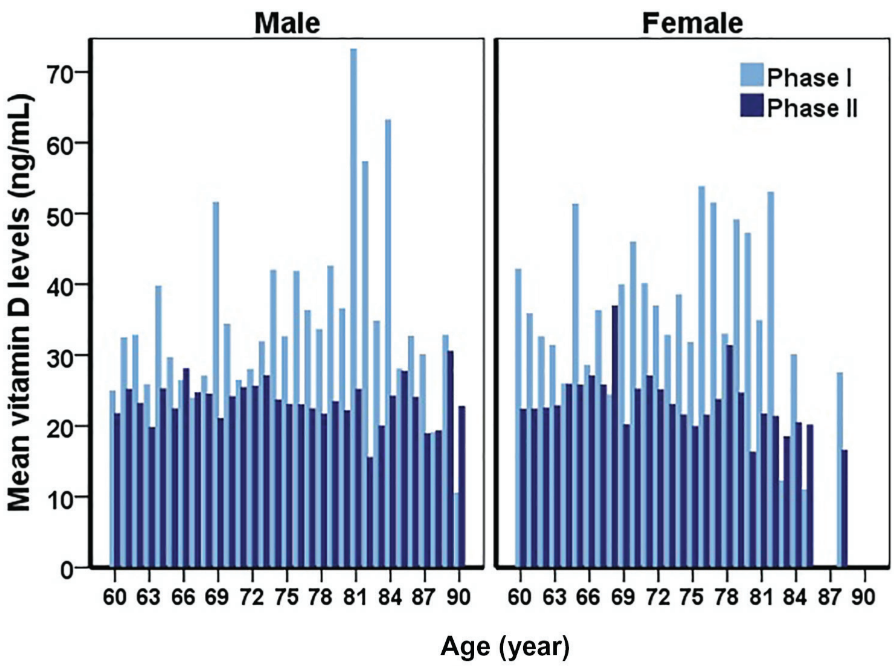

Figure 3: Mean vitamin D levels were reduced in different ages and two sexes after five years of the study.

Figure 1 showed that although the mean serum concentration of vitamin D decreased by ≥10ng/mL after five years, there was no significant correlation between this decline and the age of the participants. Actually, a decline in vitamin D serum concentration was observed in all age groups. Figures 2 and 3 demonstrated a significant reduction in vitamin D serum levels in older adults after five years.

Serum vitamin D deficiency (<20 ng/mL) at baseline examination had a significant correlation with the administration of calcitonin (P=0.033), vitamin D (P<0.001), and calcium (P<0.001) supplements. However, no significant correlation was found between serum vitamin D deficiency and the participants' age (P=0.426), sex (P=0.073), marital status (P>0.999), BMI category (P=0.457), PASE score (P=0.087), and metabolic syndrome (P=0.604).

The relationship between any change in serum 25-OH vitamin D concentration and the studied variables is summarized in tables 1 and 2. The administration of vitamin D (P=0.013) and calcium supplements (P=0.007), serum

Table 1: The association of any change in serum 25-OH vitamin D concentration with the examined characteristics of the older adults after five years

Variables		Changes in serum 25-OH vitamin D concentration after five years			P value
		No change (n=370) n (%)	Decreased (n=386) n (%)	Increased (n=255) n (%)	
Age group (year)	60-64 (n=402)	152 (37.81)	145 (36.07)	105 (26.12)	0.079
	65-69 (n=234)	75 (32.05)	89 (38.03)	70 (29.91)	
	70-74 (n=185)	66 (35.68)	70 (37.84)	49 (26.49)	
	75-79 (n=126)	55 (43.65)	50 (39.68)	21 (16.67)	
	80-84 (n=46)	16 (34.78)	25 (54.35)	5 (10.87)	
	85-99 (n=18)	6 (33.33)	7 (38.89)	5 (27.78)	
Sex	Male (n=569)	214 (37.61)	213 (37.43)	142 (24.96)	0.744
	Female (n=442)	156 (35.29)	173 (39.14)	113 (25.57)	
Marital status	Married (n=876)	329 (37.55)	331 (37.79)	216 (24.66)	0.253
	Single (n=135)	41 (30.37)	55 (40.74)	39 (28.89)	
Body Mass Index (Kg/m^2)	<25 (n=294)	97 (32.99)	111 (37.76)	86 (29.25)	0.175
	25-29.99 (n=456)	167 (36.62)	184 (40.35)	105 (23.03)	
	≥30 (n=261)	106 (40.61)	91 (34.87)	64 (24.52)	
Physical Activity (PASE score)	<150 (n=774)	284 (36.69)	304 (39.28)	186 (24.03)	0.234
	≥150 (n=237)	86 (36.29)	82 (34.60)	69 (29.11)	
Metabolic syndrome	No (n=275)	105 (38.18)	106 (38.55)	64 (23.27)	0.656
	Yes (n=736)	265 (36.01)	280 (38.04)	191 (25.95)	
Vitamin D supplement administration	No (n=821)	302 (36.78)	298 (36.30)	221 (26.92)	0.011
	Yes (n=190)	68 (35.79)	88 (46.32)	34 (17.89)	
Calcium supplement administration	No (n=809)	299 (36.96)	292 (36.09)	218 (26.95)	0.009
	Yes (n=202)	71 (35.15)	94 (46.53)	37 (18.32)	
Calcitonin intake	No (n=945)	342 (36.19)	360 (38.10)	243 (25.71)	0.355
	Yes (n=66)	28 (42.43)	26 (39.39)	12 (18.18)	

P<0.05 was considered statistically significant.

Table 2: The association of any change in serum 25-OH vitamin D concentration with the examined characteristics of the older adults after five years

Variables	Change in serum 25-OH vitamin D concentration after five years			P value
	No change (n=370) mean±SD	Decreased (n=386) mean±SD	Increased (n=255) mean±SD	
Age (year)	68.21±6.74	68.52±6.91	67.29±6.10	0.067
The number of comorbid disorders	2.61±1.94	2.82±2.06	2.60±1.79	0.254
Body mass index (Kg/m^2)	27.79±4.52	27.46±4.22	27.19±4.29	0.233
Serum PTH concentration (pg/mL)	58.06±35.60 [ab*]	52.71±36.48 [a]	60.24±41.19 [b]	0.028
Total PASE score	110.64±59.11	109.28±58.20	119.29±68.84	0.106
The number of administered drugs	2.59±2.68	2.78±2.68	2.51±2.51	0.410
Blood Urea Nitrogen (mg/dL)	17.96±5.37	17.98±5.61	17.58±4.25	0.578
Serum creatinine (mg/dL)	0.95±0.23	0.95±0.25	0.95±0.19	0.985
Serum calcium concentration (mg/dL)	9.26±0.44 [ab]	9.29±0.44 [a]	9.19±0.44 [b]	0.009
Serum phosphorous concentration (mg/dL)	3.90±0.63 [ab]	3.96±0.59 [a]	3.82±0.60 [b]	0.020

PTH: Parathyroid hormone; PASE: Physical activity scale for the elderly; *Tukey HSD *post hoc* test; similar letters represent no significant statistical difference between groups in each row.

concentration of PTH (P=0.010), calcium (P=0.021), and phosphorous (P=0.021) had a significant impact on the reduction of serum 25-OH vitamin D concentration after five years, while other variables had no significant impact (P>0.05). Mean serum phosphorous and PTH levels were lower. However, mean serum calcium levels were higher in older adults who had a drop in serum 25-OH vitamin D concentration after five years than those who had no categorical drop in their serum vitamin D levels.

Discussion

This study found that after five years, the mean serum level of vitamin D in the study population decreased. At the baseline examination, serum concentration of vitamin D was in the range above 30 ng/mL; however, after five years it dropped to 23.88 ng/mL. Aging affects the production of the active form of vitamin D. Due to age-related declines in renal function, the production of 25-dihydroxy vitamin D in the elderly might be reduced by up to 50%. Decreased vitamin D plasma concentration can cause secondary hyperparathyroidism. Even in mild vitamin D deficiency, there is an increase in calcium absorption from the bones and a decrease in bone mass. Aging also causes a decrease in calcium absorption, which can occur even 10-15 years before a decline in 25-OH vitamin D. Vitamin D deficiency causes a further reduction in the formation of the biologically-active form of this vitamin, which exacerbates the mentioned vicious cycle.[22]

At baseline, approximately one-third of the participants in the population aged 60 and over were in each of the three categorized groups of vitamin D plasma level, and nearly 35% of the elderly had a serum concentration of less than 20 ng/mL. However, after five years, almost 45% of the elderly had vitamin D deficiency. Aspell and others assessed 6,400 persons over the age of 50 in their population-based study in the United Kingdom. Almost all of the participants in the study were Caucasian and white. There were two cut-off points of vitamin D plasma concentration: 50 nmol/L (20 ng/mL) as vitamin D deficiency and 30 nmol/L (12 ng/mL) as severe vitamin D deficiency. The findings revealed that 58.7% and 26.4% of the study group, had vitamin D plasma concentrations less than 20 and less than 12 ng/mL, respectively, which was higher than the observed prevalence of vitamin D deficiency in the present study.[23] Wei and colleagues compared the frequency of vitamin D deficiency in Chinese and American adults over 65 years. The results indicated that the serum level of vitamin D in the Chinese elderly people (mean=45.1 nmol/L) was significantly lower than that in the American elderly people (83.5 nmol/L). Moreover, vitamin D deficiency affected 70.3% of Chinese older adults, and 30.6% of them had severe deficiencies, whereas equivalent figures in the American elderly were 17.4% and 3.4%, respectively.[24] Differences in vitamin D serum level and the prevalence of vitamin D deficiency in different studies could be attributed to ethnical and regional differences, the age and sex distribution of the studied population, economic differences, and lifestyle behaviors such as sun exposure, nutrition, physical activity, and alcohol consumption, all of which might affect vitamin D plasma concentration.[25]

The current study found no significant correlation between a five-year decrease in vitamin D serum concentration and age in older adults. This finding had similarities and differences with previous studies. In a study, Wyskida and colleagues found that age was a significant determinant of plasma concentration of vitamin D. They also suggested that inadequate income and poor economic condition, low level of education, low physical activity, poor health, obesity, and low exposure to sunlight, as well as the prevalence of chronic diseases in the elderly, such as chronic liver or kidney diseases, predisposed these individuals to vitamin D deficiency.[26] A hospital-based study in Turkey showed an age-related increase in vitamin D concentrations in both men and women.[27] Kim and others conducted a study on orthopedic Korean patients aged ≥50. They reported that vitamin D concentration had no significant correlation with age and sex.[28] It is worth mentioning that all of the participants in our study were over the age of 60. If other age groups, such as middle-aged adults, were included in this study, more differences between younger and older adults might be observed.

According to the findings of the present study, there was no significant correlation between the five-year decrease in vitamin D serum concentration and sex. Previous studies highlighted the significant correlation between vitamin D serum level and sex. They reported a higher prevalence of vitamin D deficiency in women than men. In the same line, Chen and others investigated Chinese older adults aged 65-95 years and reported that men had higher levels of vitamin D than women.[29] Similar to the finding of the present study, Aspell and others reported that out of 3317 adults over the age of 50 in the United Kingdom whose vitamin D serum levels were less than 20 ng/mL, the percentage of vitamin D deficiency among men and women in the age groups of 60-69, 70-79 and ≥80 years, were (51.8 and 52.3), (50.1 and 56.4) and (58.2 and 68.4), respectively. They concluded that in the age group of 80 years and older, there was a significant difference between men and women in terms of vitamin D deficiency. However, in the age group of 60-79 years, this difference between the two sexes was not statistically significant.[23]

In the present study, no significant correlation was found between a five-year decrease in serum level of vitamin D and the BMI of the participants. Previous studies reported a significant correlation between vitamin D plasma concentration level and BMI. According to the findings of Aspell and others, a normal BMI was associated with a 20% reduction in vitamin D deficiency in adults over the age of 50.[23] Savastano and colleagues reviewed some studies that found a positive association between low vitamin D concentration and obesity.[30] In a study on Chinese older adults, Cheng and colleagues found that people with low BMI had lower levels of vitamin D.[29] It is not clear whether a low plasma level of vitamin D predisposes a person to obesity, or whether obesity causes low vitamin D concentration. Although the skin produces more than 90% of the vitamin D in the human body, other possible pathways might be involved in the association between vitamin D deficiency and changes in the BMI. For instance, altered leptin secretion, and insulin resistance are key factors that predispose adults to BMI changes. Furthermore, outdoor activities, sunlight exposure, cutaneous capacity for vitamin D production, intestinal absorption, and altered vitamin D metabolism could all affect the vitamin D plasma concentration in obese or non-obese individuals.[31]

There was no significant association between the number of comorbid diseases or medication consumed by the elderly and a decrease in vitamin D serum levels. Caravaca and colleagues examined the effect of chronic kidney disease on vitamin D plasma concentration.[32] Kupisz-Urbańska and others investigated the relationship between vitamin D serum concentration and a variety of disorders that affect the elderly.[33] It was reported that the relationship between vitamin D and concurrent chronic disorders or medication consumption was not a simple phenomenon. In some cases, a persistent illness and its related medical interventions predispose the person to develop vitamin D deficiency, and in other cases, vitamin D deficiency may promote the development of other serious diseases.[34] According to the findings of Aspell and others' study, some features such as geographical area (northern or southern regions), latitude, and season of measuring vitamin D serum level (summer and winter differences) were identified as effective factors on plasma concentration of vitamin D. Therefore, even a small change in latitude, up to one degree, can have an impact of up to 11% on the prevalence of vitamin D deficiency.[23] These factors might support the findings of this study. Furthermore, the high prevalence of vitamin D deficiency in the Iranian population might affect the relationship between vitamin D serum concentration and concurrent chronic diseases in the current research.[9]

Although physical activity was reported as an effective factor in vitamin D plasma concentration,[23] in the present study, no significant correlation was found between the level of physical activity of the elderly and vitamin D concentration. A higher level of physical activity might be associated with a higher concentration of vitamin D over time, and this association was independent of the amount of time a person spent outdoors. It was claimed that higher vitamin D concentration was not affected by increased physical activity merely owing to exposure to sunlight. Even indoor exercise could increase vitamin D levels.[35]

Our finding revealed a significant negative relationship between vitamin D concentration and supplementation with calcium or vitamin D. Amrein and others reported that sometimes no expected effect of vitamin D supplementation on serum concentrations of this vitamin. This could be due to different doses of vitamin D being administered. Besides, it's important to consider how to examine the plasma concentration of this vitamin and the bioavailability of different supplements.[36] Borel reported some factors, such as dietary fiber type and amount, as well as genetic variation in proteins involved in vitamin D intestinal absorption.[37] In recent years, more attention has been paid to regular periodic examinations of vitamin D serum levels and consumption of vitamin D supplements. However, further studies are still required to understand the factors that affect vitamin D absorption and metabolism. According to some scientific research, vitamin D supplements should be administered by different age groups, particularly the elderly, to maintain the desired concentration of this vitamin.[1, 4, 38]

In this study, the serum concentration of PTH, calcium, and phosphorous had a significant effect on the reduction in serum 25-OH vitamin D levels after five years. The response to vitamin D supplementation might be influenced by variables such as PTH plasma levels and genetic parameters.[39] The observed negative relationship between a five-year drop in vitamin

D and supplementation in the elderly could also be attributed to the influence of these factors. Individuals who were prescribed vitamin D supplements might also be prone to low vitamin D concentrations due to their physical condition and underlying disorders.

The strong points of this study were the large sample size and five-year follow-up of the elderly. Our study, however, had several limitations. The dose and method of administration of calcium or vitamin D supplements, as well as the type of other medications used by the participants, were not taken into account in the design of the study. Elderly patients who were referred to their family physicians for vitamin D deficiency or insufficiency were not followed up to collect their prescribed interventions. Besides, we did not assess the participants' sunlight exposure behaviors. Therefore, it is recommended that future studies investigate them.

Conclusion

During the five-year follow-up, the mean serum concentration of vitamin D decreased. The administration of vitamin D and calcium supplements, serum profile of PTH, calcium, and phosphorous significantly reduced serum 25-OH vitamin D concentration after five years. However, variables such as age, sex, BMI, metabolic syndrome, and physical activity had no significant effect.

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Authors' Contribution

A.B, S.M, and S.D: Research design, data collection, data analysis, interpretation, and drafting; SR.H and R.Gh: Research design, data collection, and drafting; All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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