



Research Paper

Determination of Vitamin D Serum Levels in Women Receiving Vitamin Supplementation: The PERSIAN Guilan Cohort Study



Tayebeh Ramaji¹, Sedigheh Pakseresht², Farahnaz Joukar³, Parvaneh Reza Soltani¹, Zahra Atrkar Roshan³, Fariborz Mansour-Ghanaei^{3*}

1. Department of Midwifery, School of Nursing and Midwifery, Guilan University of Medical Sciences, Rasht, Iran.

2. Department of Midwifery, Social Determinants of Health Research Center, Reproductive Health Research Center, School of Nursing and Midwifery, Guilan University of Medical Sciences, Rasht, Iran.

3. Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran.



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ABSTRACT

Background: Vitamin D is a basic nutrient and plays a very crucial role in preventing various diseases, so it is known as an indicator of health and survival.

Objectives: This study was conducted to determine the serum level of vitamin D in women receiving vitamin supplementation in Persian Guilan cohort study (PGCS).

Materials & Methods: In this analytic cross-sectional study that was conducted on PERSIAN Guilan cohort, 614 subjects from 5633 women aged 35 to 70 years old who were taking vitamin D supplements were selected through census method. Required data were collected in two sections of demographic and social characteristics and serum measurement 25-hydroxy vitamin D3 at three levels of deficient (<10), insufficient (10-20) and sufficient (>20 ng/mL). Data analysis was done using descriptive and inferential statistics. P<0.05 was considered statistically significant.

Results: The mean age of people was 50.3±8.7 years, of which 5.2 % of the subjects had vitamin D deficiency, 29.5% had insufficient serum level and 65.4% subjects with sufficient serum levels. Based on the results, there was a significant relationship between employment status, place of residence and housing area with vitamin D level (P<0.05), and non-employed persons (P=0.044), living in the city (P=0.002) and a residential house with a higher area (P=0.014) had higher levels of vitamin D. There was no significant association between serum vitamin D levels with age, body mass index, marital status, alcohol consumption, level of education and how to take vitamin D supplementation.

Conclusion: In the present study, about one third of vitamin consumers did not have a sufficient serum level despite taking the supplement, so it is expected that the country's health system, health officials, and policymakers pay attention to the education program of optimum consumption as well as appropriate prescription of vitamin D supplement.

Keywords:

Deficiency, Vitamin D, Supplement, Cohort study

* Corresponding Author:

Fariborz Mansour-Ghanaei, MD.

Address: Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran.

Tel: +98 (13) 15535116

E-mail: fmansourghanaei@gmail.com



Introduction

Vitamin D is a fat-soluble vitamin and a hormone precursor [1] and is known as a very important indicator of health [2]. This vitamin is both a nutrient and a hormone precursor and has many benefits for human health. The health benefits of vitamin D go beyond bone health, as confirmed in various studies. In addition to regulating calcium metabolism, this vitamin also regulates insulin, reduces the risk of diabetes and cancer, produces renin, and helps to eliminate infectious agents and regulate cell growth. Strengthens the immune system, this vitamin also helps to cure many important diseases [2, 3]. Recently, vitamin D has attracted a great deal of attention around the world, and it has been attributed as a drug of the last decade due to its widespread deficiency in the world [3]. Vitamin D also plays a significant role in human fertility [4], and has several effects on pregnancy, maternal and fetal health [5]. Vitamin D is available in two forms: Vitamin D₂ (ergocalciferol) and vitamin D₃ (cholecalciferol) [6]. Sources of vitamin D are nutrition, sunlight and supplements [7]. Vitamin D is measured through determination of 25 hydroxyvitamin D₃, which is present in the serum. It is biologically neutral and has a half-life of 2-3 weeks [8-10]. Vitamin D deficiency usually refers to serum levels of 25-hydroxy D₃ plasma <50 nmol per liter (20 ng/mL) [11]. The main risk factors for vitamin D deficiency include old age, dark skin pigmentation, and any barrier to the sun's ultraviolet light reaching the skin, such as full body coverage, spending more time at home, and air pollution [12]. Vitamin D deficiency is a public health concern around the world [13]. Prevention, early diagnosis and treatment of vitamin D deficiency is a key tool to reduce the effects of vitamin D deficiency on the health of the body, especially in the elderly [14]. If left untreated, it can lead to reduced quality of life and increased costs due to a lack of proper attention to this health problem [13].

Vitamin D deficiency has been reported in all over the world [15]. Its prevalence is recorded in all age groups, including toddlers, school children, adult men and women, the elderly, pregnant women, and infants in rural and urban areas [16]. Vitamin D deficiency has affected more than one billion people worldwide [11]. In a review study by Chakhtoura et al, in the Middle East and North African region, prevalence of hypovitaminosis D among children and adolescents is 12-96%, in pregnant women, 90 to 54%, and in adults between 96 and 44% with an average of 25 hydroxy D₃ between 11 and 20 ng/mL [17]. There is a high prevalence of vitamin D deficiency in Iran in different age groups [18]. In a review study by Tabarizi et al, the percentage of vitamin D deficiency

in pregnant women was 60.4% and among adult women was 61.9% [4]. Inadequate intake of vitamin D from its main source, which is sunlight, due to the type of clothing worn by women, the presence of many cloudy and rainy days in the year, latitude, lack of exposure to sunlight, and the use of sunscreen creams are possible reasons for the prevalence of deficiency of vitamin D among women in northern Iran [3, 19]. The complications of vitamin D deficiency can be prevented by effective preventive measures such as vitamin D supplementation. Therefore, a preventive policy, including distribution of vitamin D mega dose supplementation was implemented in recent years in Iran (50000 units of vitamin D supplement tablets per month), including in Guilan. But there is lack of awareness about the serum status of vitamin D in women covered by this project in Guilan. So, the aim of this study was to determine the serum levels of vitamin D in women participating supplementation program.

Materials and Methods

This study was conducted to investigate the serum status of vitamin D among women receiving vitamin supplementation participating in the PERSIAN Guilan Cohort study (PGCS). PGCS is a prospective, population-based cohort study in Guilan, the northern province of Iran, recruited between October 8, 2014, and January 20, 2017 [20], as part of the prospective epidemiological research studies in Iran (PERSIAN) [21]. Different districts of the province were chosen to include different socioeconomic status levels including urban areas and 39 villages. The sampling and data collection methods have been previously described in detail [20].

This cross-sectional analytical study was conducted on a subset of PGCS, which aimed to determine the serum level of vitamin D in women receiving vitamin D supplements (50000 IU pearl vitamin D). A total of 614 people (10.9%) out of 5633 eligible women were included. The desired information was collected through interviews from the women referring to the primary health service centers (health centers and comprehensive urban health service centers) in Some'e Sara district, Guilan Province. Demographic and social characteristics including weight, height, body mass index, age, employment status, level of education, marital status, place of residence status, housing area, alcohol consumption, and how to take vitamin D supplement tablets were collected using a data collection form. Weight was measured by a scale with minimal cloths without shoes in kilograms and height in a normal standing position using a tape measure. Body mass index (BMI) was measured as weight in kilogram divided by square of height in meter. BMI of the participants was classified in four categories of underweight (BMI <18.5), normal (BMI between 18.5 and 24.9), overweight (BMI between 25 and 29.9), and obese (BMI >30) [20].

In the second part to assess the serum status of vitamin D, 2 cc of venous blood samples were taken from 563 participants (51 non-participants in the study). Blood samples were collected from all individuals using Vacutainers (Greiner Bio-One International GmbH, Kremsmunster, Austria). Whole blood samples were collected in EDTA (K3) tubes (Becton Dickinson, France). Serum 25(OH) D_3 was determined by using a commercially available electrochemiluminescence immunoassay with Roche Elecsys 2010 and Cobas E411 auto analyzer (Roche Diagnostics GmbH, Mannheim, Germany) [22]. Serum levels of vitamin D were then classified into deficient: 25(OH) D_3 <10, insufficient: 10-20, and sufficient: >20 ng/mL [23].

Data analysis was performed using SPSS statistical software, version 22 (SPSS Inc, Chicago, IL, USA). Descriptive and inferential statistics were also used in data analysis, so that categorical variables were presented as frequency (number) and percentage and quantitative variables as Mean \pm SD. Participants due to the concentration of 25-hydroxy D_3 serum in to 3 categories of deficiency (<10), insufficient (between 10-20) and sufficient (>20 ng/mL) were divided, and the chi-square test was used to compare how to take vitamin D supplements (weekly, monthly, and annually) and individual-social specifications with serum vitamin D levels, and P <0.05 to statistically significant.

Results

Of the 5633 women participating in the cohort study, 614(10.9%) were vitamin D supplement users. The results of this study showed that Mean \pm SD age of subjects were 50.3 \pm 8.7 (ranged 36 to 70) years. Demographic and social characteristics of supplementary consumers showed that 42.8% the subjects were in the age group 40-50 years old, 48.2% were obese, 77.4% of them were unemployed, 29.8% had high school level of education,

88.1% are married, 87.5% have home as a owner, 63% have a residential house with an area of 71 to 116 square meters, 62.2% urban, 99.8% have no alcohol consumption, and 65.3% have an annual consumption Vitamin D supplementary tablets. The majority of participants (65.4%) had sufficient serum levels of vitamin D. The Mean \pm SD of serum vitamin D was 31.63 \pm 15.336 ng/mL (Table 1).

Regarding to the timing of consumption, 34 subjects were weekly (5.5%), 177 subjects were monthly (28.8%) and 401 subjects (65.3%) were annually taking the supplements. There was no significant difference between the timing of consumption and the status of Vitamin D serum level. The highest percentage of vitamin D deficiency (5.7%) was among annual consumers of vitamin D supplementary tablets (50000 IU mega doses) and the lowest percentage was among weekly consumers (3.4%) (P =0.960) (Figure 1).

Comparison of demographic characteristics of the subjects in the two groups of subjects with serum levels of vitamin D above and below 20 ng/mL showed a significant association between employment status, place of residence, and housing area with vitamin D level (P <0.05). The employed subject had higher percentage of vitamin D serum level below than 20 ng/mL (29.5%) compared to employed subjects (21.1%). Urban residence and residence in small housing area had higher percentage of low vitamin D (P <0.05) (Table 2).

Discussion

The aim of this study was to determination the serum level of vitamin D in vitamin D supplement consumers among women participating in the Persian Guilan cohort study. The results of this study showed that despite taking vitamin D supplementation in the subjects, one

Table 1. Serum vitamin D status among participants

Serum Vitamin D Status	No. (%)
Deficiency (25 (OH)D <10 ng/mL)	29(5.2)
Insufficiency (25 (OH)D 10-20 ng/mL)	166(29.5)
Sufficiency (25 (OH)D >20 ng/mL)	368(65.4)
Minimum-Maximum	3-99
Mean \pm SD	31.63 \pm 15.336
95% CI	30.42–32.90

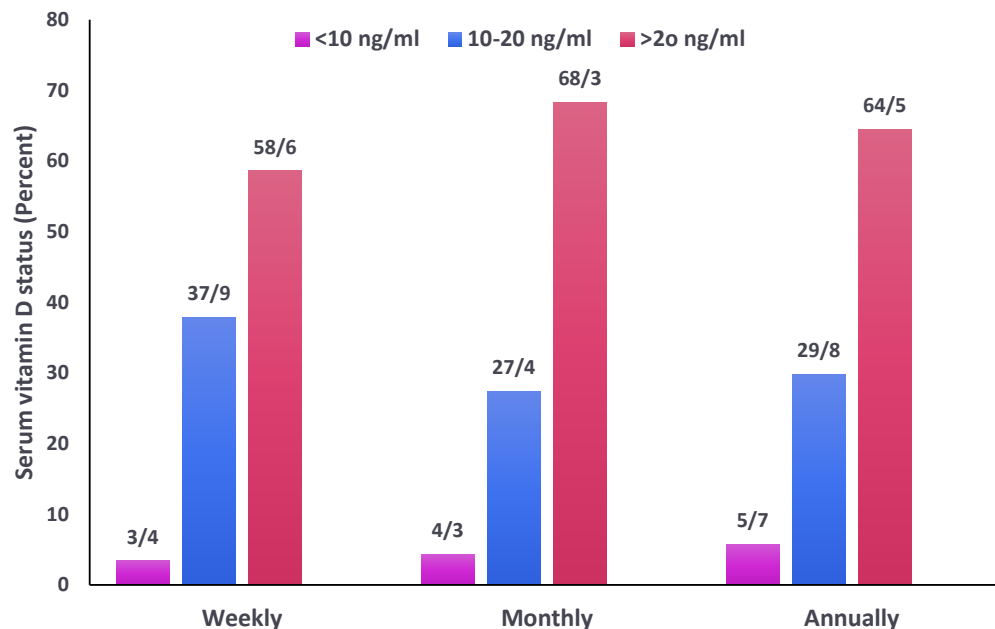


Figure 1. Serum status of vitamin D according to timing of consumption



third of them still did not have a sufficient serum level of vitamin D (serum level more than 20 ng/mL). Moderate to severe vitamin D deficiency was reported to be over 45% in different age groups among males and females in some urban areas in Iran [18, 24]. In the research of Mousavi Bahar et al., the prevalence of vitamin D deficiency was 38.73% in Hamedan City [25]. While in the study of Abbasian et al. the prevalence of vitamin D deficiency among pregnant women in Shahroudi was 1.1% [26], the study of Shahabi et al. showed the prevalence of vitamin D deficiency to be 80.96% among women working in Kerman hospital [27]. It seems that factors such as geographical location, humidity above 70% and the climate of Guilan, which has a temperate and often “cloudy and rainy” climate, as well as the clothing and style of clothing worn by women, this causes subjects to be deprived of direct sunlight skin contact, and restricting access to fortified foods or not using foods rich in vitamin D is effective in causing this deficiency in the present study.

Kaddam et al. [28] reported a vitamin D deficiency of 44% in their study, as well as 3.2% deficiency in the study of Tangoh et al. [29], 26.5% in the study of Fung et al. [30], 85.7% of deficiency in the study of Binobeat et al. [31], and 98.8% of deficiency was reported in the study of Roomi et al. [32]. Since various factors, including environmental and lifestyle factors, as well as demographic factors, determine the concentra-

tion of 25 hydroxy D₃ serum. Some studies suggest that the rate consumption of vitamin D, sex, outdoor activity, geographical location, season, age and body fat are the main determinants of serum 25-hydroxy D₃ concentrations [33, 34]. Therefore, the difference between the results of the present study and other studies can be due to differences in geographical location, age range, sex, sample size, research community, exposure to sunlight, differences in vitamin D cut off and season. According to the results of this study, out of a total of 5633 women participating in the project, only 10.9% of them included 614 subjects taking vitamin D supplements, in terms of how to take the supplement, only 28.8% of them took supplements monthly. In a study by Binobeat et al. [31], 20.6% of participants, Fung et al. [30], 75% of women and 40% of men and Darling et al. [35], 39% of women were taking vitamin D supplementation.

In the present study, the prevalence of deficiency in urban areas (30%) was higher than in rural areas. It seems that the results of this study can be due to low level of awareness and knowledge of subjects about vitamin D, less access to supplements, not taking vitamin D supplement, incorrect use of vitamin D supplements (50000 IU of tablets per month), spending most of the time of the day indoor and use any type of coverage to prevent sunlight from reaching the surface of the skin (such as hats, gloves and sun protect cream).

Table 2. Comparison of individual-social characteristics of the subjects in two groups with serum levels of vitamin D above and below 20 ng/mL

Variables	No. (%)		Total	P		
	25 (OH)D<20	25 (OH)D>20				
Age (y)	30-40	29(35.8)	52(64.2)	81	0.936	
	40-50	53(22.3)	185(77.7)			238
	50-60	35(21.9)	125(78.1)			160
	>60	13(16)	71(84)			84
Body mass index (kg/m ²)	18.5-24.9	14(20.3)	55(79.6)	69	0.851	
	25-29.9	50(22.9)	168(77.1)	218		
	>30	63(23.5)	205(76.5)	268		
Employment status	Yes	39(29.5)	93(70.5)	132	0.044	
	No	91(21.1)	340(78.9)	431		
Level of education	Illiterate	15(24.2)	47(75.8)	62	0.482	
	Primary school	27(21.3)	100(78.8)	127		
	High school	46(27.7)	120(72.3)	166		
	Diploma	28(19.3)	117(80.7)	145		
	Academic	14(22.2)	46(77.8)	63		
Marital status	Unmarried	5(23.8)	16(76.2)	21	0.521	
	Married	115(23.3)	378(76.7)	493		
	Divorced	6(15.8)	32(84.2)	38		
	Widowed	4(36.4)	7(63.6)	11		
Residence status	Private property	110(22.4)	382(77.6)	492	0.295	
	Rent	15(32.6)	31(67.4)	46		
	Organizational	0(0)	4	4		
	Kinship	5(23.8)	16(76.2)	21		
Place of residence	Rural	64(18.7)	279(81.3)	343	0.002	
	Urban	66(30)	156(70)	220		
Housing area (m ²)	25-70	35(35.4)	64(64.6)	99	0.014	
	71-116	73(20.7)	280(79.3)	353		
	117-222	22(20.2)	87(79.8)	109		
Alcohol consumption	Yes	0(0)	1	1	0.583	
	No	130(23.1)	432(76.9)	562		
How to take vitamin D supplementation	Weekly	7(24)	22(76)	29	0.570	
	Monthly	32(19.5)	132(80.5)	164		
	Annually	91(24.7)	278(75.3)	369		

There was no significant association between BMI with serum vitamin D levels in a study by Iqbal et al. [36], in a study by Safarzadeh et al. [37], Joshi & Mandul [38] and Man et al. [39] between age and BMI, Tangoh et al. [29] between marital status and level of education and Binobead et al. [31] between employment status with serum vitamin D levels no found significant association. While in studies by Altowijri et al. [40] and Rabenberg et al. [41] there was a significant relationship between BMI with serum vitamin D levels. In a study by Suryanarayana et al. [42] between level of education and BMI. Binobead et al. [31] between age and BMI with serum vitamin D levels significant relationship was reported. A study by Man et al. [39], found association between alcohol consumption and serum levels of vitamin D. No found significant association between serum vitamin D levels with place of residence and the marital status in the study Altowijri et al. [40].

In a study by Jaaskelainen et al. [43] and Naugler et al. [44], a significant relationship was reported between higher education and high income with increased serum levels of vitamin D. However, in Daly et al.'s study [45], there was no relationship between the level of education and high income with increase in serum levels of vitamin D. Rabenberg et al. [41], also found that socioeconomic status was lower with low serum levels of vitamin D. Differences in the results of the present study with the studied results could be due to differences in age range, community and sample size, geographical location, differences in nutritional, cultural, and lifestyle habits.

Conclusion

The present study revealed that the majority of participants did not follow the correct consumption pattern, one third of people still did not have enough vitamin D levels despite taking supplements, also between employment status, place of residence and housing area were significantly associated with vitamin D levels, while there was no significant association between age, BMI, marital status, alcohol consumption, level of education, and how to take vitamin D supplementation with serum vitamin D levels. Therefore, based on the results obtained, managers and health officials should improve the awareness of subjects in the community on ways to prevent vitamin D deficiency, improve lifestyle, counseling and encourage subjects to take supplements and create the necessary facilities such as sports facilities and enrichment projects of eating foods with vitamin D to improve vitamin D status, reduce the risk of developing deficiency and prevent side effects.

The limitations of this research include the impossibility of identifying women with diseases that interfere with the absorption of vitamin D, the lack of investigating the duration of exposure to sunlight during the day, the type of supplement consumed, and the cross-sectional nature of the research.

Ethical Considerations

Compliance with ethical guidelines

The present study was approved by ethics committee of [Guilan University of Medical Sciences](#) (Code: IR.GUMS.REC.1398.276).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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