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Special Article - Vitamin D Deficiency: Clinical Cases & Short Reports

Vitamin D Levels and Seasonal Changes in Elderly Cretans, Men and Women

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Abstract

Background: Low serum 25-hydroxyvitamin D [s25(OH)D] levels have been reported in a high proportion of institutionalized or home bound subjects and also in ambulatory elderly people with limited exposure to sunlight due to geographical location.

Aim of this study is to investigate the s25(OH)D status as well as its seasonal variation in ambulatory elderly people permanent inhabitants of Crete, the southernmost island of Europe.

Subjects and Methods: 101 ambulatory subjects, selected after applying strict exclusion criteria, from the Centres of Open Care for the Elderly, of Heraklion-Crete, 70 women and 31 men, (70,00±5,00 years and 73,00±5,49 respectively) Serum 25(OH)D, serum parathormone (sPTH), Ca, P, Cre, BMI and grade of mobility were assessed. In a subgroup of 25 subjects, s25(OH)D and sPTH were evaluated twice (winter and summer).

Results: Mean s25(OH)D was 51,46±27,32 nmol/L in women and 71,7±28,65 nmol/L in men. Levels ≤ 30nmol/L were found to 10% of men and 30% of women whereas levels ≤ 50nmol/L were found to 29% of men and 53,6% of women.

Mean sPTH was 59,77±28,92 pg/ml in women and 63,91±24,82 in men

Subjects with mobility A had higher levels of s25(OH)D than subjects with mobility B ($t_{(99)}$=3,612 p=0,000) and summer levels of s25(OH)D were higher than the winter ones (p<0,001) whereas summer levels of sPTH were lower (p=0,007).

Conclusion: Despite of the geographic location of Crete, and the Mediterranean diet followed, there is a high prevalence of vitamin D deficiency among ambulatory community dwelling elderly, being much higher in women, which can be attributed to the inadequate exposure to sunlight and to the lack of foods fortified with vitamin D and/or the supplementation of Vitamin D.

Keywords: Vitamin D; Seasonal changes; Geographical location

Introduction

The importance of vitamin D in calcium and phosphate homeostasis and bone metabolism and also the harmful effects of its deficiency in skeletal health in infancy (rickets) as well as in adult life (osteomalacia- osteoporosis) is well known [1].

Less known is the role of vitamin D in the development and function of the muscles [2-4].

Vitamin D deficiency has been found to be associated with muscle weakness, thus implicated as a risk factor for falling and hip fractures in the elderly [5,6].

Epidemiologic studies have shown that vitamin D deficiency is common among community dwelling people in European countries regardless of geographic location [7].

Serum 25(OH)D concentration <50 nmol/L are classed as mild vitamin D deficiency or insufficiency [8], whereas levels < 25 nmol/L denote moderate vitamin D deficiency and levels < 12.5 nmol/L denote severe vitamin D deficiency [9].

Many authors however claim that the cut-off value below which vitamin D insufficiency can be present is somewhere between 20 and 40 ng/ml (50-100 nmol/L) and have tendency to target values <30 ng/ml (75 nmol/L) [10-12].

Currenty the most commonly agreed cut-off for vitamin D insufficiency is a serum 25(OH)D level < 75 nmol/L. This cut off value was derived from studies using immunoassays or protein-binding assays [13].

Vitamin D,

1) is produced endogenically by the action of solar ultra violet (UVB) rays on the skin from 7-dehydrocholesterol.

2) is taken by diet mainly from oily fish, meat, eggs and milk products.

Both sunlight and diet contribute to the store of the human body in vitamin D.

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As long as the subject can be sufficienty exposed to sunlight in regular base there is no need for dietary intake for vitamin D. The dietary intake is also important because the prolonged exposure to sunlight may be harmful to the skin and also because the geographical location, the dressing habits, the quality of the skin and the urban mode of life reduce the possibility of the people to be exposed to the sunlight. The greatest proportion of circulating 25(OH)D and of 1, 25(OH)2D is binded with DBP (80-90%) and with alboumin (10-20%), while only a very small proportion of them is free.

Thus, measurement of the free metabolites of vitamin D is not reliable index for clinical use. The half time of life of the free circulating 1, 25 (OH)2D is only 4 hours whereas that of 25(OH)D is 3 weeks.

Therefore the measurement of serum of 25(OH)D is considered to be the more reliable index to determine the vitamin D status of the subject.

Aim of the current study is to investigate the serum concentrations of 25(OH)D in community dwelling >65 years Cretans men and women.

Serum levels of parathormone (PTH), Cre, Ca and P are also investigated.

Subjects and Methods

One hundred and one community dwelling elderly subjects >/ 65 years, 70 women and 31 men were randomly enrolled from the centers of open care for the elderly in the city of Heraklion Crete. All 101 participants were informed for the purpose of the study and consent was obtained for participation and the study was approved by the local medical Committee. All 101 participants had the following characteristics:

1. 65 years of age or older
2. Community free living
3. Able to walk outdoors without or occasionally with the aid of a stick
4. No prior history of being bedridden (non ambulatory), no chronic gastrointestinal illness, renal failure, and no history of using 25(OH)D and of calcium supplementation and of drugs affecting the bone metabolism or calcium homeostasis.

More specifically the mean age of the 70 women was 70.00 ± 5.00 (65-81) and that of the 31 men was 73.00± 5.49 (65-82 years).

Clinical data

Age, body mass index (BMI) mobility, falls during preceding year, exposure to sunlight, type of diet, clothing habits, calcium intake were recorded.

The time of direct exposure to sunlight was estimated by questioning the patient about the time of direct exposure to sunlight and about the type of clothes used.

The 101 study participants followed (type A) Mediterranean diet of Crete in which the mean daily calcium intake was found to be 826mg [14]. Mobility was graded as (A) or (B) according to the ability of the participant to walk outdoors a distance of ≥ 500m and to perform her or his activities without or with the occasional aid of a stick, respectively.

Biochemical data

Fasting blood samples were obtained between 9 and 10 am in the University Hospital of Heraklion Crete, from January to April, and were immediately transferred to the laboratories of Biochemistry and Nuclear Medicine of the hospital, where the following assays were done:

-Serum 25(OH)D concentrations. IDS OCTEIA 25-OH vitamin D kit. Enzyme immunoassay for quantification of 25(OH)D in human serum. Ref values 48-144nmol/L.

-Serum Parathormone (PTH).ELSA PTH. A solid phase two-site immunoradiometric assay. Model 13-CIS biointernational SA. Ref values: 15-65 pg/ml.

-Serum calcium, phosphate and creatinine were also measured using conventional methods, in all 101 study participants.

Statistical analysis

Data is expressed as mean ± SD, range (minimum-maximum), or medians (in case of violation of normality) for continuous variables and as percentages for categorical data. The Kolmogorov–Smirnov test was utilized for normality analysis of the parameters. . The comparison of variables between different groups was performed using the independent samples t-test and the Mann–Whitney U- test were used in case of a violation of normality.

The correlation between variables was estimated using Pearson or Spearman correlation coefficients.

All tests were two-sided and a p-value < 0,05 was considered to be statistically significant.

All analyses were carried out using the statistical package SPSS vers.

13.00 (SPSS Inc., Chicago, IL, USA) for Windows.

Results

Clinical evaluation

Mobility, Falls, BMI, exposure to sunlight, diet: Able to walk a distance of ≥500 meters without the aid of a stick (mobility A), were 82% of the men vs 68%of the women, whereas 18% of the men vs 32% of the women used occasionally a stick (mobility B).

All 101 study participants performed everyday indoor and outdoors physical activity. Men spent more time in outdoors moderate to heavy physical activity including brisk walking, gardening and heavy lifting.

During the preceding year, women fell more often than men (24/70 vs 4/31 respectively) and 15 of these 24 women had mobility B.

Moreover, within the sample of 101 subjects, it was found that subjects with mobility A (63 subjects) had higher levels of 25(OH)D than subjects with mobility B (38 subjects), i.e. 63,89 ± 30.87 nmol/L vs 43.50 ± 20.59 nmol/L respectively ($t_{(99)}$ = 3,612 p = 0,000).

Thirteen of the 101 study subjects (5 males and 8 females) had a BMI<25.

Table 1: Clinical results from the 101 elderly participants.

	Men (N=31)	Women (N=70)
Mobility A	82%	68%
Mobility B	18%	32%
Falls last year	12,9% (4)	34,28% (24)
Mean BMI (kg/m²)	28,10 ± 3,99	30,60 ± 4,68
BMI>30	22,5% (7)	52,8% (37)
Diet	Mediterranean -Cretan type A (>800mg Ca/day)	

Forty four (18 males and 26 females) had a BMI between 25,1 and 30 kg/m² (overweight) and 44 (7 males and 37 females) had a BMI >30 kg/m² (obese). Thus, 84% of the subjects, were overweight and obese.

All 101 study participants wore clothing covering their arms and legs (ie long sleeves and trousers or stockings) during the study period (ie January to April), which is traditional apparel in Crete, for the period from October to the end of May. None of the study participants used sun lamps.

All study participants followed the Mediterranean type A diet of Crete (Kafatos, 2000). More specifically the majority of study subjects (n=85), consumed three portions per day and 16 consumed two portions per day of locally produced milk or dairy products. All participants consumed olive oil and wholemeal bread or rusks often home made. Meat and fish consumed twice and once a week respectively whereas locally produced vegetables and fruits were consumed daily and fried legumes were consumed once a week by most of the participants. The type of diet followed by each of the study subjects, provided a dietary calcium intake of > 800mg/day. No one consumed foods fortified with vitamin D (Table 1).

Laboratory evaluation

The mean serum 25(OH)D concentration was found to be 56,90 ± 29,49 nmol/L in the 101 study participants, being 71,70 ± 28,65 nmol/L in men and 51,46 ± 27,32nmol/L in women. The difference between men and women was statistically significant (p=0,011).

Serum concentration of 25(OH)D < 50nmol/L was found in the 35,4% of the men and to the 53,6% of the women whereas 10% of the men and 30% of the women had 25(OH)D concentrations ≤ 30 nmol/L (Figure 1).

According to the latest studies, a serum 25(OH)D concentration < 75 nmol/L, is considered as vitamin D insufficiency. However, in the present study 50 nmol/L was used as a cut off for vitamin D insufficiency to comply with previous studies. [9,13].

The mean serum PTH concentration was found to be 63,91 ± 24,82 pg/ml in men and 59,77 ± 28,92 pg/ml in women (Table 2).

Mean serum Creatinine, Phosphorus and Calcium, levels of the 101 participants, were within normal limits (0,92±0,26mg/dl 3,29±0,37 mg/dl and 9,43±0,34 mg/dl respectively).

Forty seven of the 101 study participants (11 men and 36 women) had 25(OH)D concentration <50 nmol/L. The mean 25(OH)D serum concentration in this group was 32,29±10,15 nmol/L during the period between January and April in which they were examined. In the summer of the same year (August), 25 out of the 47 subjects of this group willingly accepted to come at the University Hospital for re-evaluation of their serum 25(OH)D and parathormone concentrations.

The mean serum concentration of 25(OH)D of this group of 25 re-examined subjects in summer was 53,68± 21,23 nmol/L which is significantly higher than their mean winter concentration that was 30,32± 10,87 nmol/L (p< 0,001) whereas their serum PTH concentrations were 64,41± 29,29 pg/ml in winter and significantly lower in summer (57,02± 32,43 pg/ml (p=0,007) (Table 3).

Discussion

The present study demonstrated that in Crete, the southernmost sunny island of Greece (Latitude 35N), vitamin D insufficiency and deficiency are very common among community dwelling aged subjects men and women.

Thus, it was found that the mean serum 25(OH)D concentration was 71,7 ± 28,65 nmol/L in men and 51,46 ± 27,32 in women, the difference between men and women being statistically significant (p=0,011).

Serum 25(OH)D concentration < 50 nmol/L was found to the

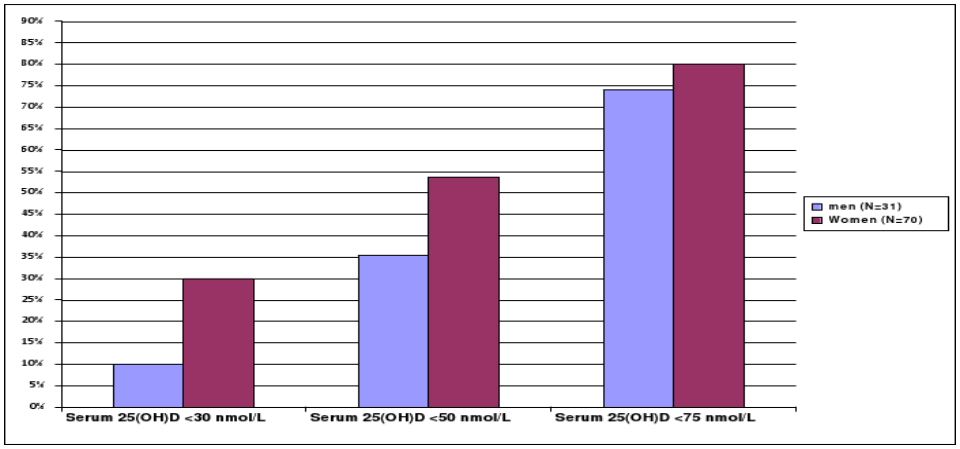

Figure 1: Percentage of men and women in the different subgroups of serum 25(OH)D concentrations.

Table 2: Serum 25(OH)D values with distribution to main groups and serum PTH.

	men	women
Mean serum 25(OH)D (nmol/L)	71,70± 28,65	51,46 ± 27,32(#)
Serum 25(OH)D <30 nmol/L	10%	30%
Serum 25(OH)D <50 nmol/L	35,4%	53,6%
Serum 25(OH)D <75 nmol/L	74%	80%
Mean serum PTH (pg/ml)	63,91±24,82	59,77± 28,92

(#): p= 0,011

Table 3: Seasonal variation of serum 25(OH)D and PTH levels. (N=25).

	Winter	Summer	p
25(OH)D nmol/L	30,32 ± 10,87	53,68 ± 21,23	< 0,001
PTH pg/ml	64,41 ± 29,29	57,02 ± 32,43	P=0,007

35,4% of the men and to the 53,6% of the women whereas 10% of the men and 30% of the women had serum 25(OH)D concentration ≤ 30nmol/L.

Serum concentration of 25(OH)D <75 nmol/L(30 ng/ml) which is the most commonly agreed cut-off for vitamin D insufficiency was found to the 74% of the men and 80% of the women. Therefore the vast majority of our study subjects could be considered to be sufferers from vitamin D insufficiency.

This findings are consistent with previous research (van der Wiellen 1995) whereas higher percentages of vitamin D deficiency have been reported in hospitalized as well as in community free elderly subjects [9,15-17].

We found that women were less mobile than men and fell more often than men during the preceding year.

Women with mobility B i.e those using occasionally the aid of a stick had significantly lower serum vitamin D concentration compared to those with mobility A (ie those who had never used a stick). (p=0,017).

It has been reported that vitamin D deficiency mainly affects the strength of the weight bearing antigravity muscles that are responsible for postural balance and walking [3,5,18-20].

Vitamin D metabolites may directly influence skeletal muscle maturation and functioning through vitamin D receptors encoded by the VDR gene [3,21]. It has been also reported that older age was significantly associated with decreased VDR gene expression [4].

Vitamin D may also affect directly skeletal muscle by increasing the relative number of type IIa fibres and improving muscle strength in vitamin D treated subjects [2,6].

The majority of the subjects in the present study (n=88, 88%)were found to be overweight and obese. Obesity was much more common in the women than in the men in this study. This is in concur with findings of a study that measured the prevalence of overweight and obese subjects among farmers living also in Heraklion, Crete [22].

A negative correlation has been described between BMI and quadriceps muscle strength [19,20,23]. This is possibly due to the fact that subjects with increased BMI are less physically active and have more comorbidities compared to those with a lower BMI [24,25].

The negative correlation between BMI and quadriceps muscle strength was reported to be greater in women than in men [20,25,26].

In conclusion the present study, demonstrated that in the sunny island of Crete, the southernmost part of Europe, vitamin D deficiency was common among ambulatory community free, aged individuals.

This could be attributed to the limited exposure of the subjects to the sunlight due to local clothing habits, to the fact that they did not consume foods fortified with vitamin D and to the possible action of factors inactivating 25(OH)D , namely cytochromes p-450, cyp23, cyp 3A4 and vitamin D binding protein (group specific component GC) (McGrath 2010, Bu 2010, Mallah 2011, Tissandié, 2006). [17,27-29].

Therefore more outdoor physical activity, adequate exposure to sunlight and dietary fortification or supplementation with 800-1000IU mainly, during winter months is recommended.

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