

## Does Aging Increase Vitamin D Serum Level in Healthy Postmenopausal Women?

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**Abstract-** Vitamin D deficiency is the most under-diagnosed medical condition in postmenopausal women. There are few epidemiologic studies on vitamin D status of postmenopausal women in Iran. This study aimed to investigate the 25-hydroxyvitamin D levels in postmenopausal women living in Tehran, capital of Iran. In this cross sectional study, 110 women were selected via convenience sampling method from menopause clinic of Tehran Women General Hospital between 2011 and 2012. For each woman, a questionnaire was completed, and 25-hydroxyvitamin D levels were determined by chemiluminescence's immunoassay. Vitamin D deficiency has been considered as a 25(OH)D of less than 20ng/ml. Vitamin D insufficiency has been defined as a 25(OH)D of 21–29ng/ml, and sufficiency as a 25(OH)D of 30–100ng/ml. The data was analyzed by using Pearson correlation test in SPSS version 16. The mean age of women was 52.67±5 years. The mean age at natural menopause onset was 47.66±4.44 years, and the median menopause age was 49.00. The median 25(OH)D level was 19.28 (Inter Quartile Range=26.08). We found vitamin D deficiency and vitamin D insufficiency 52.7% and 17.3% respectively. Serum 25(OH) D concentrations were significantly correlated with age ( $r=0.21$ ,  $P=0.024$ ). These findings indicate that 25(OH)D level in postmenopausal women from Tehran is low. There is a statistically significant positive correlation between vitamin D concentration and age in late postmenopausal period.

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**Keywords:** Aging; Postmenopausal women; Vitamin D

### Introduction

Vitamin D deficiency is the most under-diagnosed medical condition in postmenopausal women. This is largely because patients do not typically present with overt clinical signs and symptoms until the deficiency is severe and prolonged. Vitamin D deficiency in postmenopausal women can cause osteopenia, osteoporosis, osteomalacia and muscle weakness, and increase the risk of falls and fracture. In addition to the skeletal effects, it is now recognized that vitamin D

deficiency increases the risk of many chronic diseases, including cancer, autoimmune diseases, type 2 diabetes, heart disease and hypertension, infectious diseases (including upper respiratory tract infections and tuberculosis), and osteoarthritis, as well as depression and schizophrenia (1). Vitamin D deficiency is also very common in different populations across the world. Studies suggest that approximately 30-50% of the adult have vitamin D deficiency (2). Ability to synthesize vitamin D decreases with age, therefore, older adult population is more susceptible to vitamin D deficiency

because aging is related with lower 7-dehydrocholesterol levels, which is a precursor of vitamin D in the skin (3). Due to the fact that vitamin D deficiency is very common among postmenopausal women, vitamin D deficiency as an important issue in their health care is considered in the world wide.

**Materials and Methods**

In the present cross-sectional study 110, women via convenience sampling method were selected from menopause clinic of Tehran Women General Hospital in Tehran; Iran between 2011 and 2012. The women attended the clinic for routine care, which included history taking, physical and pelvic examination, laboratory study, and mammography, Pap smear, bone mineral densitometry if necessary.

For each woman, a questionnaire was completed by a general physician. Exclusion criteria were history of diseases known to alter serum levels of vitamin D metabolites such as use of vitamin D supplements, hepatic dysfunction, renal disease, metabolic bone disorders. All tests were performed in the hospital clinical laboratory using kits provided by the same manufacturer.

Serum 25-hydroxyvitamin D concentrations were measured by the DiaSorin "25-OH Vitamin D" competitive chemiluminescence's immunoassay on the automated LIAISON analyzer (USA, DIASORIN, INC). This method has 100% specificity for both 25(OH) D. Limit of detection this assay is 4ng/ml, with intra-assay coefficient of variation (CV) of 5%, and an inter-assay CV of 7%. Samples were analyzed in one continuous batch with quality control samples inserted at periodic intervals.

Vitamin D deficiency has been defined as a 25(OH)D of less than 20 ng/ml. Vitamin D insufficiency has been defined as a 25(OH)D of 21–29ng/ml, and sufficiency/adequate as a 25(OH)D of 30–100ng/ml(4). Overall by definition postmenopausal period is divided into two periods: early and late postmenopausal period,

that early postmenopausal period is defined as the first five years of menopause and after this duration is called late postmenopausal period. In our study, the mean menopausal age was 47.66. So, the early postmenopausal period is determined 52 and after that is considered late postmenopausal period.

**Statistical analysis**

The data were analysis in SPSS software by using T-test, one-way ANOVA, correlation coefficient and linear regression. The normal distribution of a continuous variable was accessed by using kolmogrov-smirnov test and due to lack of normality for vitamin D in linear regression logarithm transformation for vitamin D was used.

**Results**

The mean age of referred women was 52.67±5 years. The mean age at natural menopause onset was 47.66±4.44 years, the median menopause age was 49.00(Inter Quartile Range=5). The mean 25(OH)D was 29.90±33.02 and the median 25(OH)D was 19.28 (Inter Quartile Range=26.08).

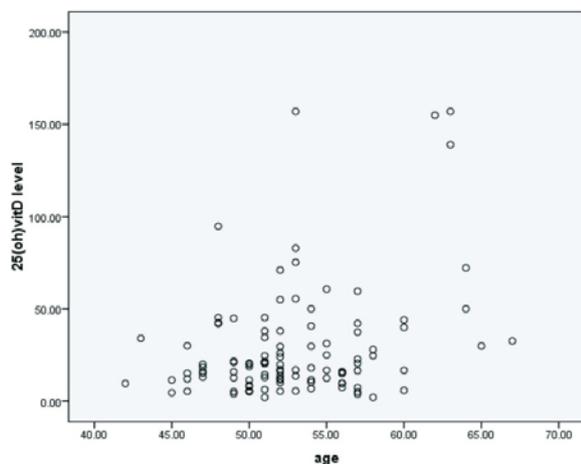
Vitamin D deficiency was seen in 58(52.72%) of the women in our study; 19(17.27%) subjects had vitamin D insufficiency; vitamin D sufficiency was seen in 33(30%) participants of this study. Overall, vitamin D inadequacy including vitamin D deficiency and insufficiency was found in 77(70%) of women in our study.

The mean age for each vitamin D levels is shown in table 1 and scatter plots of serum vitamin D levels versus age is shown in figure 1.

Results showed that the mean age in deficient and sufficient vitamin D levels was statistically significant ( $P=0.019$ ). Moreover, the difference between age inadequacy and inadequacy vitamin D levels was statistically significant ( $P=0.027$ ). Also correlation between age and serum 25(OH) D concentration was statistically significant( $r=0.21$ ,  $P=0.024$ ).

**Table 1.** Distribution of age values by serum 25(OH) Vitamin D.

	<b>Subgroup</b>	<b>Number (%)</b>	<b>Mean ± SD (Age)</b>	<b>P-value</b>
Vitamin D level	Sufficient	33(30%)	54.74±5.80	0.019
	Insufficient	19(17.27%)	53.10±4.37	
	Deficient	58(52.72%)	51.79±4	
Vitamin D adequacy	Adequate	33(30%)	54.74±5.80	0.027
	Inadequate	77(70%)	52.11±4.10	



**Figure 1.** Correlation between age and 25(OH) vitamin D level.

Univariate linear regression shows a statistically significant increase in vitamin D concentration ( $B=0.022\text{ng/ml}$ ,  $P=0.024$ ) per one year of age. When we stratified by age, we found that there are no correlation between the vitamin D concentration and age in early postmenopausal period ( $\leq 52$ ) ( $B=0$ ,  $P=0.98$ ), on the other hand this association in late postmenopausal period ( $>52$ ) ( $B=0.025$ ,  $P=0.066$ ) was seen.

## Discussion

25(OH) vitamin D levels up to 30-40ng/ml have inversely related to parathyroid hormone (1).

In addition, studies showed in healthy postmenopausal women when average blood level of 25(OH)D of 20ng/ml to 32ng/ml reached, the intestinal calcium absorption was increased by 45–65%(5). Thus, based on these and other studies, it has been suggested that vitamin D deficiency be defined as a 25(OH)D below 20ng/ml, insufficiency as a 25(OH)D of 21–29ng/ml, and sufficiency as a 25(OH)D of 30–100ng/ml (4). According to this definition we found a high prevalence of vitamin D deficiency among postmenopausal women in our menopause clinic. In our study, the prevalence of Vitamin D deficiency and insufficiency was 52.72% and 17.27%, respectively, and vitamin D inadequacy including deficiency and insufficiency was approximately 70%. This is similar to findings in other Middle East countries, such as Lebanese, Saudi Arabia, Emirati, Kuwait, Jordan and Israel (6). In the similar international study conducted in women with osteoporosis, the highest proportion of vitamin D deficiency was noted in the Middle East (7).

There was 35% for a vitamin D level lower than 25nmol/L in a study of elderly subjects from a geriatric hospital in Israel (8), and between 60% and 65% in Lebanon, Jordan (9,10).

In a study in 1210 subjects, between 20 and 69 years old, from the Tehran population, Vitamin D deficiency was diagnosed in 79.6% of the subjects (11). Therefore, our findings confirm the high prevalence of vitamin D deficiency among Iranian women. In our study, the mean 25(OH)D was  $29.90\pm 33.02$  and the median 25(OH)D was 19.28(Inter Quartile Range= $26.08$ ).

In Guilan, one of Iran's province, serum 25(OH) D was measured in 646 women (427 in urban areas and 219 women in rural areas), it was  $18.5\pm 13.5\text{ng/ml}$  and  $22.9\pm 13.8\text{ng/ml}$ , respectively. Furthermore in these urban and rural areas, 84.7% and 79.5% of the women had serum 25(OH) D levels less than 30ng/ml, respectively (12). In another study serum 25(OH) D levels were determined, 36% of early postmenopausal women referred to the Bone Densitometry Center had vitamin D levels below 12ng/ml (13). In a cross-sectional population-based study on 245 healthy menopausal women (mean age =  $57.7\pm 7.7$  and duration of menopause =  $9.4\pm 6.8$  years) living in Tehran, 5.3% had 25(OH)D < 25nmol/l and 37.6% had 25(OH)D level between 25 and 50nmol/l, overall 42.9% of subjects had vitamin D levels below 20ng/ml (14). These findings suggest that vitamin D deficiency is a prevalent problem in postmenopausal women. Moreover, vitamin D inadequacy including deficiency and insufficiency are common and may affect up to 70% of postmenopausal women. Unlike the multiple studies that showed higher prevalence of vitamin D deficiency in the elderly (15,16), in our study higher serum level of vitamin D was observed with increasing age. We found in ages less than 52, there was no correlation between the vitamin D concentration and age. However, in ages more than 52 there was a statistically significant positive correlation between vitamin D concentration and age. Our findings were similar to another study in Iran that elderly women showed statistically significant higher serum levels of vitamin D compared with young and middle aged women (17).

However, our study also has limitations. The sample sizes were relatively small. Furthermore, it was conducted in healthy postmenopausal women, and the findings may not be generalized to other groups. Also in the present study women with history use of vitamin D supplements were excluded but intramuscular injection of vitamin D in the preceding months due to musculoskeletal pain is common by elderly that could

explain the high prevalence of a high level of vitamin D at older ages.

However due to the high prevalence of vitamin D inadequacy, measurement vitamin D concentration is necessary in healthy postmenopausal women. Women with low serum 25(OH)D levels should use doses ranging from 4000 to 10,000 IU/day to achieve adequate levels. In others, adequate serum concentrations should be achieved through sun exposure (15 min per day, 3-4 times a week) or vitamin D supplementation with 800–1000 IU/day (18).

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