

## Seasonal variations in serum vitamin D according to age and sex

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### Abstract

**Background:** Exposure to sunlight is the main source of vitamin D production. This study was performed to assess the status of serum vitamin D across the different seasons in geographic region of Babol, with latitude of 36 in northern Iran.

**Methods:** The study – female participants were 15 years old and above selected prospectively according to the inclusion criteria who attended an Outpatient clinic. The serum 25-hydroxyvitamin D 25-OHD was measured with enzyme-linked immunosorbent assay (ELISA). Serum OHD <20 ng/ml was considered as vitamin D deficiency. Serum 25-OHD levels were compared across various seasons according to sex and age. Proportions of serum 25-OHD deficiency were also compared between the various seasons according to sex and age.

**Results:** A total of 576 females and 120 males with respective mean age of 44.8±14.1 and 47.8±29 years entered into the study. The mean serum 25-OHD was 20.8±27 ng/ml, the prevalence of serum 25-OHD deficiency was 70.1%. In women compared with men, the mean serum 25-OHD was significantly lower but the proportion of deficiency was not significant (20.6±24.9 ng/ml vs 23.2±31.4 ng/l. p=0.021 and 70.8% vs 67.5% p=0.60 respectively). The mean 25-OHD and proportion of deficiency did not vary across the different seasons with regard to age. However, in the summer and in the autumn, the women had significantly lower serum 25-OHD concentrations than the men (p= 0.021 and 0.016 respectively).

**Conclusion:** The findings of this study indicated no significant seasonal variations of vitamin D in geographic regions of Babol. However, during the autumn and the winter months, the women are at high risk of vitamin D deficiency which corresponds to nadir of serum 25-OHD levels.

**Keywords:** Vitamin D, Seasonal change, Sex, Age, Deficiency.

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Vitamin D is an important factor for regulation of bone metabolism. However, its actions are not limited to the skeletal system but extend to several non-skeletal organs such as the brain, heart, prostate, colon and immune cells (1-4). Several studies have shown a link between vitamin D deficiency and the development of many clinical conditions such as diabetes, hypertension, coronary heart diseases, as well as a number of inflammatory and non-inflammatory skeletal diseases (1-3, 5-8).

The primary source of vitamin D is exposure to solar UV-B radiation with wave length 290-315nm (1, 4, 9-12). Several factors including the season, strength of the UV rays, age, place of residence, duration of UV exposure, intake of vitamin, physical activity and the amount of pigment in the skin contribute to the production of vitamin D<sub>3</sub> in the skin (9, 11, 13-16). The production of vitamin D does not occur persistently so a significant proportion of general population are predisposed to vitamin D deficiency due to intermittent and irregular production of vitamin D as well as irregular intake of vitamin D (1, 17).

These observations provide a rationale for predicting the status of serum vitamin D in high risk individual. The impact of seasonal changes over serum vitamin D has been addressed in several previous studies (9, 12-29). Lower serum vitamin D in winter months compared with summer has been shown (9, 19, 26-28, 30)

The results of publications are not similar but vary according to population or geographic region indicating a contributive role for other confounders including, clothing, dietary deficiency, and decreased cutaneous synthesis of vitamin D by ageing, latitude, and atmospheric components (16, 31, 32). For these reasons, the current study was designed to determine the levels of serum vitamin D according to season in patients presenting to an outpatient clinic located in Babol, a geographic region with temperate climate at latitude of 36 in northern Iran. In addition, the assessed serum vitamin D variations in respect to age and sex is over a two-year of the study period.

## Methods

**Population study:** The participants of this study were selected prospectively according to inclusion criteria among the females attended in an Outpatient clinic in Babol, a geographic area with temperate climate at latitude of 36°, North of Iran. The sample was recruited between September 2010 to September 2012. All patients aged 15 years and above were included. The patients with metabolic, gastrointestinal, and, renal disorders interfering vitamin D metabolism and those with skeletal, cardiac and pulmonary diseases resulted in the limitation of physical activities, patients on anticonvulsant and vitamin D containing drugs were excluded from the study. The data were collected in regard to age, previous illness, and medications by interview and filling up a questionnaire. All the participants agreed to be investigated for vitamin D status. The proposal of this research was approved by the Ethics Committee of Babol University of Medical Sciences, Babol, Iran.

**Vitamin D measurement:** Serum 25-hydroxyvitamin D (25-OHD) was measured a day after the interview and the data were collected at the time of clinical examination. Blood samples were provided by a professional laboratory technician. Serum 25-OHD was measured with enzyme-linked immunosorbent assay (ELISA) method according to the manufacturer's instruction using lyophilized competitive protein binding assay kit (DRG, instruments G mbH,

Germany). Serum 25-OHD levels less than 20 ng/ml were considered as vitamin D deficiency (4).

Sample size was calculated based on detection of a significant difference in mean serum 25-OHD levels between the two seasons. With presumptive SD value of 20ng /ml (7) a sample size of 120 subjects for each season was needed to detect 6 ng/ml difference between the two seasons with 95% confidence level ( $\alpha=0.05$ ) and 80% statistical power ( $\beta=0.20$ ).

The primary aim of this study was to determine the impact of the different seasons on serum 25-OHD concentrations by comparison of serum 25-OHD levels across various seasons. The secondary aim was to assess the relationship between the seasonal changes and sex as well as age. Mann-Whitney U test, Kruskal-Wallis and chi-square tests were applied for comparing means and proportions. SPSS software version 18 was used for the statistical analysis.

## Results

A total of 696 subjects (576 females, 120 males) with the mean age of  $45.2\pm 17.6$  years entered into the study. The mean age of women and men was  $44.8\pm 14.1$  and  $47.8\pm 29$  years, respectively. The mean serum 25-OHD in the study population was  $20.8\pm 27$  ng/ml, and the prevalence of serum 25-OHD deficiency was 70.1%. The mean serum 25-OHD level in females was significantly lower than in males ( $20.6\pm 24.9$  ng/ml vs  $23.2\pm 31.4$  ng/ml,  $p=0.021$ ). The proportion of serum 25-OHD deficiency in women and men was 70.8% and 67.5%, respectively ( $p=0.60$ ). The mean serum 25-OHD levels varied significantly across the various seasons from the lowest level at  $18.5\pm 19.4$  ng/ml in the autumn to the highest level at  $27.5\pm 44.6$  ng/ml in the spring ( $p=0.012$ ). However, despite the wide variations in mean serum 25-OHD values across seasons, the differences did not reach to a statistically significant level. Similarly, the proportion of serum 25-OHD deficiency was higher in the autumn as compared with the other seasons but the differences did not reach to a statistically significant level (table 1).

**Serum 25-OHD according to sex:** Serum 25-OHD levels in each season varied across sexes. In the spring and in the winter, serum 25-OHD concentrations did not differ between sexes but in the summer and in the autumn, the women had significantly lower serum 25-OHD

concentrations than the men ( $p=0.021$  and  $0.016$  respectively). Serum 25-OHD levels varied significantly across the different seasons in the men but not in the women (table 2). But there were no significant differences in proportion of serum-25-OHD deficiency across the different seasons in each sex

**Table 1. Serum 25-hydroxyvitamin D (25-OHD) values and proportion of 25-OHD deficiency in the study population according to seasons**

	No	Serum 25-OHD Mean $\pm$ SD	Age Mean $\pm$ SD	Serum 25 OHD deficiency No (%)
Spring	133	26.2 $\pm$ 41.5	47 $\pm$ 14.7	93 (69.9)
Summer	121	21 $\pm$ 21.2	43.3 $\pm$ 13.9	78 (64.5)
Autumn	213	18.7 $\pm$ 19.6	45.9 $\pm$ 14.4	152 (71.4)
Winter	216	19 $\pm$ 21.1	46.3 $\pm$ 22.1	155 (71.8)
Total	683	20.6 $\pm$ 26.1	45.8 $\pm$ 17.2	478 (70)
P		0.40	0.33	0.58

**Serum vitamin D and age:** Serum 25-OHD levels were positively increased by ageing. The subjects aged higher

than 60 years had the highest serum 25-OHD levels whereas, the subjects aged less than 30 years had the lowest values and the differences between the age groups of 60 years and below was significant ( $p=0.001$ ). There were wide variations in serum 25-OHD across the various seasons in all decades of age. However, the differences did not reach to a statistically significant level (table 3).

**Table 2. Serum 25-hydroxyvitamin D (25-OHD) values and proportion of 25-OHD deficiency in the study population across various seasons according sex**

	Serum 25-OHD mean $\pm$ SD			
	Women		Men	
	Mean $\pm$ SD ng/ml	Deficiency No (%)	Mean $\pm$ SD ng/ml	Deficiency No (%)
Spring	25.1 $\pm$ 39.6	76 (66)	33.8 $\pm$ 54.5	12 (75)
Summer	20.6 $\pm$ 22.4	81 (69.2)	23.6 $\pm$ 11.4	8 (47.1)
Autumn	17.2 $\pm$ 15.3	70 (67.3)	26.5 $\pm$ 33.1	21 (60)
Winter	19.1 $\pm$ 20.6	131 (73.6)	18.3 $\pm$ 23.2	36 (76.1)
Total	20 $\pm$ 24.9	120 (70.6)	23.8 $\pm$ 31.4	76 (66.7)
P	0.68	0.70	0.022	0.11

**Table 3. Variations in serum 25-hydroxyvitamin D (25-OHD) by mean $\pm$ SD in different decades of age across various seasons in women**

	<30 Mean $\pm$ SD	30-39 Mean $\pm$ SD	40-49 Mean $\pm$ SD	50-59 Mean $\pm$ SD	60+ Mean $\pm$ SD
Spring	10.7 $\pm$ 7.4	16.8 $\pm$ 19.5	21.5 $\pm$ 46.7	31.5 $\pm$ 46	37.4 $\pm$ 46
Summer	13.7 $\pm$ 11.4	17.1 $\pm$ 14	18.8 $\pm$ 19.6	27.6 $\pm$ 28.9	31.1 $\pm$ 35.1
Autumn	11.4 $\pm$ 7.1	13.5 $\pm$ 8.4	14.3 $\pm$ 11.5	18.3 $\pm$ 14	29.4 $\pm$ 26.1
Winter	16.3 $\pm$ 19.8	14.8 $\pm$ 19.9	14.7 $\pm$ 11.8	26.3 $\pm$ 25	24.7 $\pm$ 22.8
Total	13 $\pm$ 12.3	15.2 $\pm$ 16	16.5 $\pm$ 22.7	24.8 $\pm$ 29.4	30.5 $\pm$ 32.9
P	0.36	0.25	0.84	0.51	0.92

## Discussion

The findings of this study indicated variations in mean serum 25-OHD levels across the various seasons regardless of age and sex. The serum 25-OHD level in the winter months particularly in young women was at the lowest level versus the summer and the spring. Although, the differences did not reach to a significant level despite the wide fluctuations in serum vitamin D levels. The results of this study are in agreement with several published studies that addressed the relation between the seasonal changes and the

status of vitamin D (9, 26-28, 33). However, some studies have shown lower levels of serum 25-OHD in winter whereas, in a number of studies, the prevalence of vitamin D deficiency did not differ by seasonal changes and remained stable even in sunny climate (9, 26-28, 30). These observations indicate that seasonal changes should not consider the exclusive cause of vitamin D variations but many other factors are also contributed to the changes in serum vitamin D over the different seasons (13, 34-36).

In this study, lower age was related to low serum vitamin D in winter months and so should be considered as a risk factor of vitamin D deficiency in the winter particularly in women. Despite the low ability of skin in synthesis of vitamin D in elderly population, serum 24-OHD in older group of this study was close to normal indicating low synthesis of 1, 24 dihydroxycholecalciferol by ageing and resultant higher 25-OHD levels (6, 11, 37). Skin pigmentation is another limitation of vitamin D synthesis which is associated with lower synthesis of vitamin D by black skins during the summer months (9, 12-16, 21, 34). The duration of sunlight exposure is positively correlated with changes in serum 25-OHD levels (14, 20). The daily intake of vitamin D is another important factor in maintaining serum vitamin D at sufficient levels and protection against vitamin D deficiency (26, 29). Inadequate daily intake can lead to vitamin D deficiency in the summer and in the autumn despite sufficient sunlight exposure (12, 29, 38).

Geographic region and latitude affects the quantity and quality of solar radiation especially the intensity of UVB radiation reaching the earth's surface. In regions with maximum latitude, UVB has no sufficient intensity to synthesize adequate vitamin D in the autumn or in the winter (39). In addition in the winter wearing more clothes and less duration of outdoor sunlight exposure may affect serum 25-OHD levels (31). Seasonal changes in geographic regions at higher latitudes result in greater vitamin D deficiency even with higher daily intake of vitamin D (39).

Seasonal changes have been linked to a number of conditions. Bone turnover markers in postmenopausal women were lower in the summer compared with winter. These changes were in concordance with seasonal variations of serum 25-OHD (13, 24, 35, 27).

Several conditions such as diabetes or tuberculosis which seem to be associated with vitamin D deficiency may be exacerbated by seasonal changes (2, 3, 5). In one cross-sectional study, the mean number of TB notifications per quarter was lowest in the spring and highest in the autumn months consistent with higher TB at the time of low vitamin D levels (5). These findings indicate that in vitamin D deficient areas seasonal change itself has a little contributive role in the development of vitamin D deficiency but lead to further vitamin deficiency in populations who are at higher risk of vitamin D deficiency. These populations are young women, subjects living in geographic regions with high

latitudes with serum vitamin D at insufficient levels, and those who have less exposure body surface due to clothing. The results of this study have limitation in regard to the serial measurement of serum 25-OHD across various seasons. However, the results of serial measurement will be also affected by other variables including the intake of vitamin D, duration of exposure, physical activity. Although responsible variables of vitamin D changes as reported in this study may also involve general population but these findings can not be generalized but can be applied only to subjects attending medical clinics.

In conclusion, this study indicates that seasonal changes lead to no significant serum vitamin D variations with the lowest values in the winter and in the autumn and the highest values in the summer and in the spring. Although, seasonal change in itself does not cause significant reduction of serum vitamin D in geographic region of this study, but may lead to serum vitamin D reduction in subjects who are at risk of vitamin D deficiency.

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**Conflict of Interest:** None declared.

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