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High Prevalence of Vitamin D Deficiency in Women Presenting to Rheumatology Clinic in North of Iran: An Inverse Relation with Age

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Abstract

Background: Vitamin D deficiency is linked to bone mass attainment during adolescence period and to the development or progression of several rheumatic diseases that commonly appears in young females.

There is a gap in the existing literature pertaining to vitamin D levels across the life-stages. This study was designed to investigate the status of serum vitamin D according to age in women presnting to rheumatology clinic in north of Iran.

Methods: A total of 843 women were consecutively entered to study. Serum 25-hydroxyvitamin D (25-OHD) was measured by ELISA method and concentratins <20 ng/ml was considered as deficiency. Mean 25-OHD and proportions of 25-OHD deficiency was compared according to decades of age and between premenopausal (<50) and postmenpausal (≥ 50 years) women using Mann-Whitney and chi-square tests. Spearman's test was used for correlation.

Results: The median age was 50 (range 15-91) years. Overall 52.8% had 25-OHD deficiency and 24.6% had 25-OHD<10 ng/ml. Mean 25-OHD and proportion of deficiency diferred significantly across various decades of age (P=0.0001 for both).Mean 25-OHD positively correlated to age (r=0.300 P=0.0001) and proportion of 25-OHD deficiency inversely correlated with age (P=0.0001). Mean 25-OHD was lower and proportion of 25-OHD deficiency was higher in premenopausal versus postmenopausal women (P=0.001 for both).

Conclusion: These findings indicate an inversly age- related high prevalence of vitamin D deficiency particularly in premenopausal women presenting to rheumatology clinic. Regarding a link between vitamin D deficiency and development of several rheumatic diseases as well as bone mass impairment these findings suggest early recognition of vitamin D deficiency in young women.

Keywords: Vitamin D deficiency; Age; Women; Rheumatic disease; Bone mineral density

Introduction

Vitamin D deficiency is a highly prevalent condition in approximately 30% to 50% of the general population even in tropical countries [1-3]. Sufficient level of this vitamin is important not only for maintenance of bone health and calcium metabolism but also in reducing the risk of many extra skeletal diseases [1,2]. Vitamin D deficiency is associated with excess mortality in the general population as well as in patients with cardiovascular disease [1].The impacts of vitamin D on bone mass vary according to life-stages and ranges from bone mass attainment during the adolescence period to bone mass preservation as well as fracture prevention throughout the perimenopausal and postmenopausal periods [2]. Insufficient levels of serum vitamin D impair adequate attainment of peak bone mass and reduce bone mass acquisition and maintenance [4-7].

There is a positive correlation between serum vitamin D level and Bone Mineral Density (BMD) in young subjects who are at age of peak bone mass attainment as well as in postmenopausal women [8-10].

Vitamin D has anti-inflammatory action and exerts immunomodulatory effects on immune cells [11,12]. Vitamin D deficiency is linked to the development of or progression of several rheumatic diseases which are prevalent particularly in young women [13-17].

Rheumatic diseases in women are not homogenously distributed across age decades, but most rheumatic disorders particularly autoimmune rheumatic diseases are common in young women. Concerning a possible contribution of vitamin D deficiency in the development of autoimmune rheumatic diseases, awareness to age distribution of vitamin D deficiency may provide additional informations in this context.

Despite many studies regarding vitamin D deficiency there is a gap in the existing literature pertaining to vitamin D status across the life-stages in women.

These observations along with high prevalence rate of suboptimal serum vitamin D among patients presenting to rheumatology clinics [18-20], emphasize the importance of vitamin D status in women particularly at earlier stages of life when, they are prone for development of several autoimmune diseases [13-17]. Whereas, correction of serum vitamin D to sufficient levels by vitamin D intake might reduce the incidence or severity of these diseases [18,21,22]. We have recently demonstrated a positive association between vitamin D deficiency and a number of skeletal conditions such as non-specific skeletal pain, knee osteoarthritis, and undifferentiated arthritis mostly in women [23-25].

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For these reasons the present study was designed to investigate the status of serum vitamin D across different life stages in women who presented to a rheumatology clinic in northern of Iran.

Patients and Methods

Study population

Participants of this study were selected consecutively according to inclusion criteria among women presented to an outpatient rheumatology clinic affiliated to a university teaching hospital in Babol, a geographic area with temperate climate at 36°N located in northern Iran. The study population recruited between May 2009 and June 2011. Samples were previded across all seasons. Proportions of samples taking in spring, summer, autumn, and winter were 21.4%; 17.3%; 303%; and 30.9%, respectively.

These women presented with a number of nonspecific skeletal symptoms. However, a number of patients had no symptoms at presentation but a history of these symptoms, and presented to be investigated for presence of rheumatic diseases. Details of the skeletal symptoms were described more clearly elsewhere [23]. In brief, patients presented with localized or generalized nonspecific muscloskeletal pain over lower limb bones, muscles, joints or localized bone over ribs or sternum were included. These symptoms could not be attributed to any specific conditions such as rheumatologic or metabolic bone diseases based on clinical examinations, as well as appropriate laboratory tests. These symptoms developed over 1-3 months prior to patients presenting to rheumatology clinic and diminished or disappeared in about half of the study population at the time of investigation.

Sampling

Sample size was calculated based on detection of difference in mean serum 25-OHD levels between premenopausal and postmenopausal age groups (<50 years and ≥ 50 years) with presumptive SD value of 28 (23). A sample size of 400 women for each group was needed to detect 6 ng/ml difference between the two age groups with 95% confidence level (α=0.05) and 80% statistical power (β=0.20) [26]. Since in the general population of this study, menopausal period usually begins around the age of 50 years, we therefore considered 50 years old as cut off value for differentiation of premenopausal from postmenopausal women.

Participants selection

All women aged 15 years old and older were candidate to inclusion except those with systemic illness, inflammatory rheumatic diseases, chronic gastrointestinal, respiratory, renal, and hematological disorders, limitated physical activities. Hospitalized patients and nursing home residents did not include as well.

In addition patients taking vitamin D, calcium+vitamin D, multivitamin supplements, anticonvulsant medications or drugs interfering vitamin D metabolism were also excluded.

Data collection

Data were collected in regard to age, previous illness, medication, the status of menstruation, duration of menopause, Body Mass Index (BMI) by interview and fill in questionnaire. Additional data were provided in regard to season of taking blood samples for vitamin D assessment. All data were collected at the time of clinical examination. All participants accepted to be investigated for vitamin D status. The proposal of this research was approved by the Ethics Committee of the Babol University of Medical Sciences, Babol, Iran.

Vitamin D measurement

Serum vitamin D was assessed by measurement of serum 25-hydroxyvitamin D (25-OHD) level a day after interview. Serum samples were provided by a professional laboratory technician. Serum 25-OHD was measured with enzyme-linked immunosorbent assay (ELISA) method according to manufacturer's instruction using lyophilized competitive protein binding assay kit (DRG, instruments GmbH, Germany).

Serum 25-OHD levels less than 20 ng/ml were considered as vitamin D deficiency, levels at ≥ 20-29 ng/ml as insufficiency and levels ≥ 30 as sufficient and levels less than 10 ng/ ml as severe deficiency [27,28].

Statistical analysis

The primary aim of this study was to determine the prevalence of vitamin D deficiency in women according to age decades and its relation with age. The secondary aim was to compare vitamin D status between premenopausal (< 50 years and postmenopausal (≥ 50 years) women.

The status of distribution for all variables was examined by measures of skewness and kurtosis. Normality of distribution was confirmed by using Kolmogorov-Smirnov test.

Mann-Whitney U test, Kruskal-Wallis and chi-square tests were applied for comparison of means and proportions. Correlation between serum 25-OHD and age was assessed by calculation of Spearman Correlation Coefficient. SPSS soft ware version 18 was used for statistical analysis

Results

Data were provided for 881 women but, 38 persons due to intake of medication such as calcium + vitamin D (n=12) 2, intake of anticonvulsants (n=5), limitation of physical activities (n=21) were excluded and 843 participants with median age of 50 years (range 15-91 years) were studied. Almost half of the study population (50.2%) was postmenopausal women with mean (± SD) menopausal age and menopausal duration of 51.5 ± 4.5 and 10.7 ± 15 years, respectively.

Serum vitamin D distribution was significantly skewed to the right whereas the age distribution was significantly skewed to the left.

Overall, 52.8% women had serum 25-OHD deficiency, 24.6% had severe deficiency. Proportion of women with insufficient and sufficient levels of serum 25-OHD were 18% and 29.2%, respectively (Table 1). The means (± SD) and proportions of serum 25-OHD deficiency differed significantly across various decades of age as presented in table 1 (P=0.0001 for all).The means of serum 25-OHD among younger age group were lower and proportions of serum 25-OHD deficiency were higher compared with older age groups. Proportions of serum 25-OHD deficiency in various age groups are shown in table 1.

Mean (± SD) serum 25-OHD value in premenopausal women (age <50 years) was 20.8 ± 22.3 ng/ml and in postmenopausal women (≥ 50 years) was 35.2 ± 34.3 ng/ ml (P=0.0001). Corresponding values for serum 25-OHD deficiency were 61.6% and 38.4 % respectively (P=0.0001). Only 17.6% of premenopausal women and 35.8% of postmenopausal participants had sufficient 25-OHD levels (P=0.001).

Mean serum 25-OHD levels, and proportion of 25-OHD deficiency did not differ significantly across various seasons, but there was only a

significant difference between mean serum levels taking in spring and autumn (25.6 ± 41.6 vs 16.9 ± 15.1 ng/ml, p=0.03).

There was a positive correlation between mean serum 25-OHD and age (r=0.300, P=0.001, R^2=0.09). In linear regression analysis, for each one year increase in age serum 25-OHD increased by 0.43 ng/ml (SE=0.05, P=0.001) (Figure 1). Proportion of serum 25-OHD deficiency was inversely related with age decades (P=0.0001). There was no correlation between serum vitamin D and weight (Spearman's correlation coefficient= 0.121, P=0.331) and seasons (Spearman's correlation coefficient=0.029, P=0.43).

Discussion

The findings of this study indicated high prevalence of vitamin D deficiency across all age groups of women presented to rheumatology clinic particularly young women aged less than 30 years. Proportion of vitamin D deficiency in this study was conversely related with age. In older women vitamin D deficiency was surprisingly higher than premenopausal women whereas, the levels of serum 25-OHD was expected to be lower due to impaired synthesis of vitamin D by skin in older population [29].

High prevalence of vitamin D deficiency among patients referring to rheumatology or primary care clinics has been reported in several studies but its relation with age has not been investigated [18-20]. Studies from other geographic regions of Iran have also shown high proportion of vitamin D deficiency in women and lower serum 25-OHD in young and middle aged females compared with older women [3,10,30]. Similar observations have been reported from other countries [31,32]. Relationship between serum vitamin D and age seems to be important because physiological effects of vitamin D on bone mass varies according to age [4-6]. Serum vitamin D has been recognized as an independent determinant of bone mass attainment and body composition during adolescence [9].

Vitamin D deficiency in young women may be associated with compromised bone mass acquisition. Whereas greater bone mass attainment at the time of puberty may provide further bone mass for later cycles of life particularly postmenopausal state [8,9].

In addition, most of autoimmune diseases that are supposed to be linked with vitamin D deficiency develop during premenopausal period particularly in young women. Vitamin D status has been considered as an environmental risk factor of several rheumatic

Age groups	No	Serum 25-OHD Mean ng/ml + SD (Median)	Serum 25-OHD <10 ng/ml N(%)	25-OHD<20 ng/ml N(%)	25-OHD ≥20-29ng/ml N (%)	25-OHD ≥ 30 ng/ml N(%)
<30	118	19.3 ± 16 (13.7)	42(35.6)	85(72)	16(13.6)	17(14.4)
30-39	131	19.1 ± 16 (14)	41(31.3)	84(64.1)	22(16.8)	25(19.1)
40-4	170	23.1 ± 27.6 (16)	48(28.2)	105(61.8)	29(17.1)	36(21.2)
50-59	230	30 ± 30.4 (20.6)	55(23.9)	105(45.7)	53(23)	72(31.3)
60-69	114	38 ± 34.9 (25.5)	13(11.4)	46(40.4)	17(14.9)	51(44.7)
≥ 70	80	45.5 ± 41.1(35)	8(10)	20(25)	15(18.8)	45(56.3)
Total	843	28 ± 29.8 (18.8)	207(24.6)	445(52.8)	152(18)	246(29.2)

*Severe deficiency=serum 25-OHD <10 ng/ml
Insufficiency=serum 25-OHD ≥ 20-29 ng/ml=Sufficiency=serum 25-OHD ≥ 30 ng/ml

Table 1: Serum 25-hydroxyvitamin D (25-OHD status, in study population, mean ± SD (Median) and N(%).

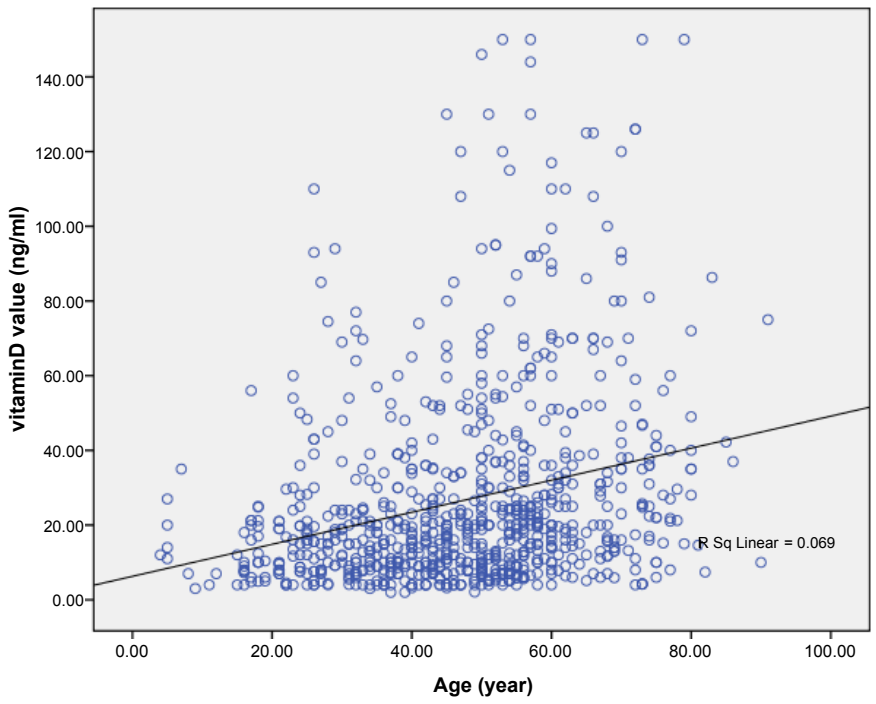

Figure 1: Linear relationship between serum 25-OHD concentration and age in women presenting a rheumatology clinic in northern Iran.

diseases and therefore, its deficiency may predispose young women to the development or progression of these disorders [13-16,25,33].

Several factors including low intake of vitamin D, inadequate sunlight exposure, clothing were shown to be associated factors of low vitamin D in women [3,10,30,34].

These factors enclose all age groups and cannot solely explain the observed differences in serum 25-OHD across various age decades.

Based on available knowledge older women are expected to be at greater risk of vitamin D deficiency because of greater duration of indoor activities and its consequence of lower sunlight exposure. Additionally lower ability of vitamin D synthesis in the elderly subjects can lead to lower serum 25-OHD [29].

Unexpectedly, our study indicated higher level of serum 25-OHD in older women which may be attributed to lower ability of kidney in synthesis of 1,25 dihydroxyvitamin D by aging which results in lower serum 1,25 dihydroxyvitamin D level and lower catabolic activity of serum 25-OHD. Consequently serum 25-OHD level remains higher in older compared with younger subjects [28].

Young females have more active reproductive system and probably greater production of sex hormones than older women. Serum level of estrogen and progesterone in young women was shown to be inversely related with serum 25-OHD levels [35].

There is a physiologic increase in serum Parathyroid Hormone (PTH) levels in adolescents for their growing skeleton. Serum PTH concentration is inversely associated with serum 25-OHD concentrations [36]. In young women greater bone metabolism and remodeling may demand greater vitamin D consumption compared with older women and consequently can lead to lower serum 25-OHD [2,29,36].

The findings of this study should be considered with limitations. Data in regard to duration of sunlight exposure, dietary intake of vitamin D, life style, were not collected. However, the study patients comprised of population with uniform life styles including dietary habits, eating pattern and so these factors are expected to have less confounding effects on results. In particular, variations in sunlight exposure should be minimal, because the conventional Islamic clothing in all age groups of adult women, cover all parts of the body except face and hands, and therefore do not seem to affect the results. Similarly, the effect of seasonal changes on serum 25-OHD affects all age groups equally with minimal confounding effect. Particularly, in our earlier study, we have found no seasonal variations in serum vitamin D regarding sex and age [37].

These findings may not be applicable to general population because the participants have been selected among rheumatology patients.

However, a proportion of vitamin D deficient women may be at early stage of a vitamin D associated rheumatologic or metabolic diseases which might be prevented by raising serum to sufficient levels.

In conclusion, the findings of this study indicate high prevalence rate of vitamin D deficiency particularly in young women presenting to rheumatology clinic in north of Iran. Regarding to possible contributive role of vitamin D deficiency in the development or progression of several skeletal and extra skeletal conditions particularly in young women, the results of this study suggest early recognition as well as correction of serum 25-OHD deficiency. However, the relationship between serum 25-OHD and age requires further studies.

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