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Vitamin D Insufficiency and Thyroid Capacity in Postmenopausal Women

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Abstract: ***About half of the world's population suffer from Vitamin D inadequacy. Although there are reports of Vitamin D insufficiency in immune-mediated hypothyroidism, an association between Vit. D and thyroid stimulating hormone (TSH) levels has yet to be revealed. This prospective study was conducted at Al-Karama Teaching Hospital in Baghdad from January to December 2016 on (150) post-menopausal women whose average age was (62.2±5.3) years, and their records during routine maintenance visits were reviewed. All patients were examined for the symptoms related to thyroid function and osteoporosis. Participants were divided into three subgroups according to their TSH levels (below <0.5 mIU/L, 0.51-4.0 mIU/L and >4.0 mIU/L). Patient characteristics and Vit. D levels were compared between these subgroups. Multivariate linear regression model was constructed using serum Vit. D and serum TSH as the dependent variables to identify factors independently associated with these laboratory values. Vitamin D was insufficient (10-30 ng/mL) in 20(17.2%) and deficient (<10 ng/mL) in 90(54.8%), while it was normal in 40(27.2%) of the participant women. In 17(11.3%), TSH was low and in 12(8.0%) of women TSH was high, while the remaining 121(80.6%), had normal TSH levels. Subjects with low TSH had significantly higher Vit. D concentrations (37.9±18.4 ng/mL) compared to the other two groups (P-value 0.016). In multivariate regression analysis, TSH was not a contributing factor, as age was the only significant predictor of Vit. D levels. Meanwhile, no predictor (including age and Vit. D) was identified for TSH levels in linear regression analysis. It can be concluded that age was the only independent predictor of serum Vit. D in this study population. Though suppressed TSH was associated with higher Vit. D levels, the association was not linear between TSH and Vit. D in postmenopausal women.***

Keywords: Vitamin D insufficiency, TSH, Menopausal women

1. Introduction

Vitamin D insufficiency is present in over half of population all over the world [1]. It has been long known that Vit. D inadequacy contributes to development of osteopenia and osteoporosis [2-4].

As the Vit. D receptors are present in all human cells regardless of their different embryologic origins, many studies have concentrated on the extra-skeletal effects of Vit. D and the way it affects general health of patients [5].

In addition to the limited oral intake and age-related decline in its absorption, decreased exposure to sunlight is among the leading causes of Vit. D insufficiency in women [6].

Age-related changes that contribute to the reduced serum levels of this vitamin are mediated through the attenuation of hypodermal synthesis of Vit. D precursor, as well as reductions in alimentary absorption of cholesterol-based provitamin molecules in daily nutritional intake [7].

Vit. D insufficiency has been implicated in increasing prevalence of autoimmune diseases, including type I diabetes mellitus [8], rheumatoid arthritis [9] and systemic lupus erythematosus [10-12].

On the other hand, immune- mediated pathophysiology comprises the major etiology of hypothyroidism in iodine-replete areas [13]. Moreover, aging is linked to the increased prevalence of subclinical forms of hypothyroidism [14-16]. Interestingly, low Vit. D levels is reported in patients with hyperthyroidism presumably due to the acceleration of its metabolism [17].

Studies have yielded conflicting results on the frequency of Vit. D insufficiency among patients with an ongoing autoimmune process in humans. Vit. D levels have been found to be lower in patients with autoimmune thyroid disorders compared to the healthy volunteers in one study [18]. Yet, other studies have not yielded similar results [19]. Vit. D insufficiency is very common among women in the geographic region where this study is conducted [20].

In view of these conflicting reports, our aim of this study was to examine the association between serum levels of Vit. D and thyroid stimulating hormone (TSH) among postmenopausal women.

2. Materials and Methods

This prospective study was conducted at Al-Karama Teaching Hospital in Baghdad from January to December 2016 on (150) menopausal women. The clinical records of all post-menopausal women who presented to the primary care clinic for routine checkup visits between January to December 2016 were screened by a member of research teams for the availability of serum levels of Vit. D and TSH. Patients who had simultaneous measurements during this period were considered for enrollment, and enrolled only if they had been postmenopausal for at least past 48 consecutive months. Patients older than 80 years, and those with diabetes mellitus, rheumatoid arthritis, chronic kidney disease with an estimated glomerular filtration rate < 60 mL/min/1.73 m2, hypo or hyperparathyroidism, cirrhosis, malnutrition and malabsorption were excluded. TSH levels between 0.5-4.0 mIU/L were regarded normal [21]. Subjects with serum 25-OH VitD levels below 10 ng/ml were considered ‘deficient’, whereas those with levels between 10-30 ng/ml were considered ‘insufficient’. VitD levels > 30 ng/ml were considered ‘sufficient’. Participants were divided to three subgroups according

to their TSH level (below <0.5 mIU/L, 0.51-4.0 mIU/L and >4.0 mIU/L) [22].

Statistical Analysis

All pertinent clinical and laboratory information were entered to SPSS version 17.0. Categorical data were analyzed using chi square test (degree of freedom = 2) and reported with 95% confidence interval (CI). Numerical variables were analyzed using two-tailed one-way analysis of variance (ANOVA) with Bonferroni correction for post hoc inter-group comparisons. These data were presented as mean ± standard deviation (SD). Linear regression analyses were performed to examine the factors that predicted serum concentrations of Vit. D. Null hypotheses were rejected where p values were less than (0.05).

3. Results

A total of (150) participants were included in this study. The average age of the study population was (62.5 ± 5.3) years. Only 40(27.32%) of the population had normal serum Vit. D level. Overall, 20(17.2%) had Vit D insufficiency and 90(54.8%) had Vit. D deficiency. In 17 (11.3%) of the cases, TSH was lower than 0.5 mIU/L and in 121 (80.6%), TSH was within normal reference range, while abnormally high levels of TSH (>4.0 mIU/L) were reported in 12(8.0%) subjects. Serum Vit. D levels were significantly different among the study subgroups (P = 0.016). It was determined that subjects with TSH levels <0.5 mIU/L had significantly higher Vit. D concentrations (37.9 ± 18.4 ng/mL) compared to subjects with normal TSH levels (23.9 ± 21.9 ng/mL) and those with elevated TSH concentrations (17.5 ± 11.0 ng/mL) as shown in table (1). The second linear regression analysis using serum TSH concentrations as the dependent variable was performed with age, age at menopause, serum Vit. D, current smoking, BMI and number of pregnancies as independent variables. In the constructed model, neither age nor Vit. D was found to be independent predictors of serum TSH level as illustrated in table (2). In order to identify the independent factors affecting Vit. D levels, a multivariate linear regression model was constructed using the serum Vit. D concentrations as the dependent factor. The constructed model is shown in Table 2. Age was the only independent predictor of Vit. D levels (correlation coefficient: 0.51, CI: 0.19-1.11; p-value= 0.012), whereas serum TSH levels were not found to be an independent predictor of Vit. D concentrations as shown in table (3).

Table 1: Serum Vit. D levels among the three TSH subgroups

	TSH<0.5 N = 17	TSH0.51-4.0 N = 121	TSH>4.0 N = 12	Total N = 150	P-Value
Age (year)	61.9±6.2	62.1±5.2	63.4±4.5	62.5±5.3	0.698
Age at Menopause (year)	46.7±5.3	46.1±5.3	47.1±4.6	46.6±5.1	0.876
Normal Vitamin D	9(52.9%)	31(25.6%)	1(8.3%)	40(27.2%)	0.070
Vitamin D Insufficiency	4(23.5%)	14(11.5%)	2(16.6%)	20(17.2%)	
Vitamin D Deficiency	6(35.2%)	76(62.8%)	8(66.6%)	90(54.8%)	
Serum Vitamin D ng/mL	37.9±18.4	23.9±21.9	17.0±11.7	25.1±20.6	0.016

Table 2: Linear regression analysis using serum concentrations of thyroid stimulating hormone (TSH) as the dependent variable

Model	Coefficients	Std. Error	P-Value	95.0% Confidence	Interval
Age (year)	0.09	0.18	0.19	-0.07	0.26
Age at Menopause (year)	0.04	0.11	0.95	-0.21	0.27
Current Smoking	0.49	4.02	0.67	-7.12	7.15
Serum Vitamin D3 (ng/mL)	0.01	0.01	0.88	-0.11	0.12
Body Mass Index (Kg/M2)	0.02	0.07	0.95	-0.24	0.09
Number of Pregnancies	-0.09	0.23	0.64	-0.29	0.31

Table 3: Linear regression analysis using serum vitamin D3 concentrations as the dependent variable

Regression Model	Coefficients	Std. Error	P-Value	95.0% Confidence	Interval
TSH (mIU/L)	-0.13	0.24	0.90	-0.23	0.41
Age (year)	0.51	0.27	0.01	0.19	1.11
Age at Menopause (year)	-0.28	0.29	0.51	-0.57	0.37
Frequent Sun Exposure	-18.84	11.31	0.34	-34.92	6.03
Current Smoking	-17.13	10.98	0.23	-37.45	8.12
Calcium Supplementation	2.54	3.68	0.33	-4.91	11.11
Dairy Product used at least once a day	0.59	2.37	0.95	-3.19	3.91

4. Discussion

Vitamin D inadequacy was found to be very common in the current study. As the main finding of this study, suppressed levels of TSH have been associated with higher Vit. D levels, though no linear association between TSH and Vit. D has been noticed in postmenopausal women.

Accordingly, the linkage between Vit. D and the function of thyroid gland is best to be examined among the postmenopausal women. TSH is a physiologic indicator of thyroid function and its elevated level is particularly the most sensitive screening test for hypoactive thyroid function [23].

Vit. D is an omnipotent regulator of the innate immunity, and inadequate serum levels of this vitamin have been linked to autoimmune reactions [24].

In patients with systemic lupus, a decrease in the amount of immunoglobulin produced by B cells once the cells are pre-incubated with Vit. D have been observed [25].

Moreover, the association between autoimmune thyroid disorders such as Hashimoto's disease and Grave's disease with low levels of VitD has been described [26, 27].

Metabolism of Vit. D is also reciprocally regulated by thyroid hormones. Provitamin D3 is synthesized from 7-dehydrocholesterol and the enzymatic reaction takes place principally in keratinocytes located in the basal and spinous strata of the epidermis layer [28].

On the other hand, thyroid hormone exerts important effects on skin. Histologic examination of the skin in hypothyroid patients has shown changes indicative of epidermal thinning and hyperkeratosis [29].

There is a strong suggestion that the epidermal barrier function is probably impaired in hypothyroidism with a speculation that synthesis of Vit. D is decreased in patients with overt hypothyroidism and high TSH [30].

In the multivariate linear regression model constructed using serum Vit. D and serum TSH as the dependent variables, age is identified as the only independent predictor of Vit. D level in the present study. It has been shown that serum levels of Vit. D decrease with age.

The decrease in serum Vit. D level is more pronounced in women and the decline is noticed to start in premenopausal phase [31]. Unexpectedly, age has shown a positive correlation with Vit. D levels in our population. As such as the study population grow older the serum concentrations of Vit. D increase. We speculate that the observation is due to the fact that our population consists of post-menopausal women with a tendency to include subjects in the seventh decade of their lives (average 62.5±5.3 years old). Interestingly, in two other reports from the same region as the current study, higher levels of Vit. D have been reported in older women in comparison with their younger counterparts [32, 33]. This could be due to the higher rate of consumption of Vit. D supplements in this age group.

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