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Original Article

The Relationship between Thyroid Hormones, Vitamin D and Fasting Blood Glucose Level During Summer and Winter in Nondiabetic Adults

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ABSTRACT

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Key words
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Background and Aims: 25-hydroxy vitamin D3 is recognized to be an essential element for healthy body; however, its deficiency has been identified as a risk factor for thyroid disease, diabetes mellitus and other autoimmune diseases and infectious diseases. Thyroid disease is common in the general population that its prevalence increases proportional to age. Subjects with poorly controlled diabetes, with or without its complications, may experience some changes in their thyroid function tests. The present study aimed to evaluate the association between thyroid hormones, vitamin D3 and fasting blood glucose (FBS) level during summer and winter in nondiabetic adults.

Materials and Methods: A total of 1093 Caucasian adults without diabetes were chosen for study. The serum levels of 25-hydroxy vitamin D3, thyroxin (T4), thyroid stimulating hormone (TSH) and FBS were measured in these samples and the association of these factors during summer and winter were evaluated.

Results: The study results demonstrated a significant association in T4 and TSH with 25-hydroxy vitamin D3. The significantly lower serum level of T4 and no significant difference in TSH level were determined in impaired fasting glucose subjects as compared to normal fasting glucose subjects. No significant association was detected between serum level of 25(OH) D3, TSH, T4 and FBS in winter and summer.

Conclusions: 25-hydroxy vitamin D3 may play a role on thyroid hormone regulation. In addition, thyroid hormones can affect FBS level. As a result, lifestyle and diet may have possible effects on thyroid hormones and blood glucose regulation.

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Introduction

Vitamin D3 has an important role in bone health through maintaining calcium and phosphorus homeostasis. There is an increasing prevalence of hypovitaminosis D in the world [1]. The prevalence of hypovitaminosis D in tropical countries such as China, Turkey, India and Iran was estimated between 30% and 93% [2]. The significant role of such factors as sunlight exposure, low daily intake of vitamin D and low consumption of supplements has been suggested as the main cause of low prevalence of 25-hydroxy vitamin D3 or 25 (OH)D3 (active metabolite of vitamin D) serum level in the tropical countries [2, 3]. Accumulating research suggests that circulating concentrations of 25 (OH)D3 may be inversely related to the pathogenesis of several endocrine conditions such as type 1 diabetes, type 2 diabetes, adrenal diseases, polycystic ovary syndrome and thyroid disease [1, 4].

Thyroid disorders are regarded as one of the common glandular disorders. The role of thyroid disorders has been investigated and described in diabetes [5, 6]. Two key metabolic, thyroid hormones production such as Triiodothyronine (T3) and Thyroxin (T4) are stimulated by thyroid stimulating hormone (TSH) secreted by the pituitary gland [7]. Elevated levels of free circulating thyroid hormones (hyperthyroidism) and reduced levels (hypothyroidism) may cause hyperglycemia and hypoglycemia, respectively. Thyroid disease is found in both types 1 and 2 diabetes. The prevalence of type 2 diabetes (T2D) is increasing dramatically in the world, which has reached epidemic proportions in some areas. This increase in prevalence is primarily being driven by the environmental factors, through 'modern age' dietary and exercise habits [8]. Diabetic patients have a higher prevalence of thyroid disorders compared with the general population [9]. The prevalence of thyroid disorder in diabetic population was reported to be 13.4% with higher prevalence in female T2D patients as compared to the male T2D patients [10]. Since thyroid hormones regulate metabolism and diabetes, they can alter metabolism of foodstuff, the metabolism of the organism may be further affected by the combination of thyroid disease and diabetes. These interactions need to be recognized for the clinical management [11].

The present study aimed to analyze the association between 25 (OH) D3, T4 and TSH concentration as well as fasting blood glucose (FBS) level in non diabetic adults during summer and winter.

Materials and Methods

This cross-sectional study population consisted of 1093 subjects, carried out on samples referred to Buoali laboratory, Yazd-Iran, from 1st February, 2013 to 31st January, 2015. Five milliliter fasting blood samples were taken from volunteers. The sera were separated by centrifugation and used for measurement of 25 (OH) D3, thyroxin (T4), TSH concentration and FBS level. The study group was clinically assessed by a medical doctor. Moreover, the estimation of serum 25 (OH) D3, T4 and TSH

was made using a chemiluminescence assay (LIAISON DiaSorin SpA, Italy). The reference values of serum 25 (OH)D3 were higher than 74.88 nmol/l (30 ng/ml), T4 was 4.4-12.6 ng/dL and TSH was 0.3-3.6 mIU/L. Subjects who did not report having thyroid disease, goiter, or taking thyroid medications were selected. FBS was measured by the Prestige auto analyzer (Tokyo, Japan) and Biosystem kit (Spain). The participants' glucose was classified based on the latest American Diabetes Association criteria: normal FBS≤5.6 mmol/l (100 mg/dl), impaired FBS 5.6–6.9 mmol/l (100–125 mg/dl) and diabetes ≥7 mmol/l (126 mg/dl) [12]. Those with all types of diabetes had been excluded from this study. The data collected in the present study were analyzed using SPSS Ver. 16 software. The means and standard deviations of the serum levels of 25 (OH) D3, T4 and TSH were calculated, and compared via applying independent t-test. Linear regression analysis was also used to assess correlations of the serum levels of 25 (OH) D3, T4 and TSH with the blood glucose level. P values of statistical significance were set at P≤0.05. Seasonal variation of serum 25 (OH)D3 was defined as the difference between winter and summer values based on time points of the first visit to the laboratory and blood sampling: winter (December 1- February 28), spring (March 1- May 31), summer (June 1- August 31) and autumn (September 1- November 30). The Ethics Committee of Shahid Sadoughi University of Medical Sciences approved this Study.

Result

The study sample consisted of 251 males and 842 females with mean age of (38.1±13.6) and (37.5±10.79) years, respectively. The total mean of 25 (OH) D3, TSH concentration and T4 were reported as 24.73±18.1 ng/ml, 2.17±1.26 µIU/ml and 9.27±1.80 µIU/ml, respectively, and the average concentration of FBS was 91.11±10.20 mg/dl. Demographic characteristics of subjects are demonstrated in Table 1. The results of the present study revealed a significant association between increased TSH level, 25 (OH) D3 deficiencies, and increased T4 level within subjects with 25 (OH) D3 sufficiencies in the study population.

Table 1. Demographic characteristics of subjects

Sex	Age (yr)	FBS (mg/dl)	T4 (µIu/ml)	TSH (µIu/ml)	Vitamin D3 (ng/ml)
Male (N=251)	38.1±13.6	91.08±10.69	8.95±1.69	2.10±1.18	25.58±18.59
Female (N=842)	37.5±10.79	91.11±10.12	9.34±1.81	2.18±1.27	19.07±14.37

All data are presented as Mean±SD.

Furthermore, the subjects were divided into two groups based on the FBS <100 mg/dl as a normal group and level of FBS between 100 until 125 mg/dl as an impaired glucose group. While the serum levels of T4 were significantly lower in impaired fasting glucose subjects as compared to normal fasting glucose subjects (p=0.002). No significant difference was

observed in regard with TSH concentration between the two groups (p=0.671). Moreover, there was no significant association between 25 (OH) D3 and fasting blood glucose in the study population (p=0.439). No significant association was detected between serum level of 25 (OH) D3, TSH, T4 and FBS in winter and summer (Fig.1).

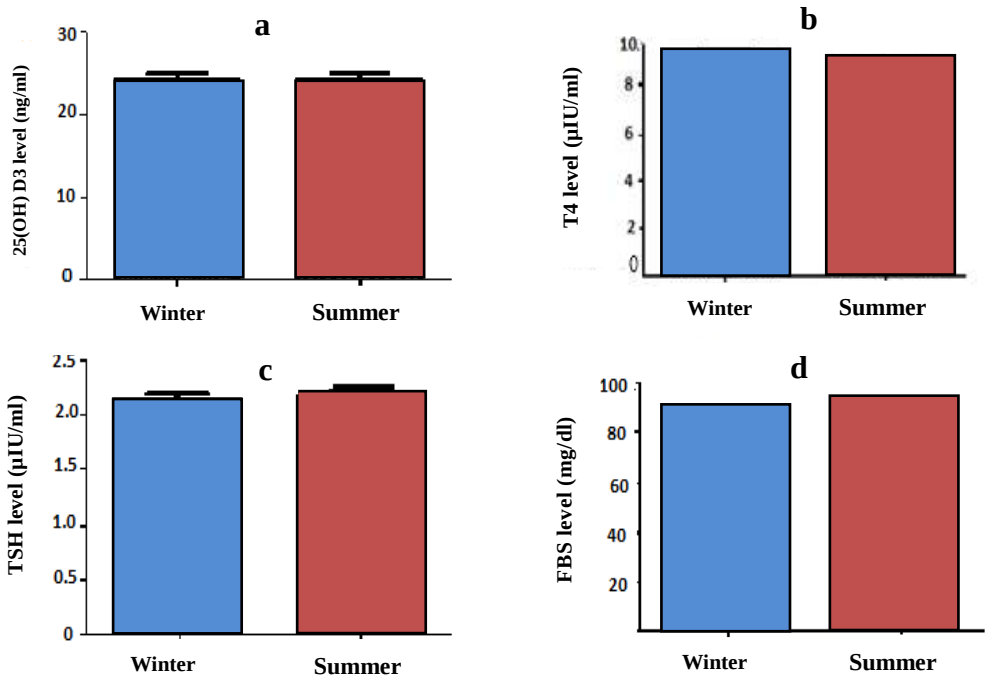

Fig. 1. The effect of winter and summer on vitamin D (a), T4 (b), TSH(c) and FBS (d) serum levels on samples Values are presented as mean ± SEM.

Discussion

Vitamin D3 can be mentioned as a fat-soluble metabolite which has been the focus of keen interest since there is a growing awareness of its role in cancer, cardiovascular diseases, thyroid diseases, type 1 and 2 diabetes, neurodegenerative diseases, multiple sclerosis, bone/ calcium homeostasis, immunity and chronic inflammation [1, 13-15]. In the present study, TSH levels were demonstrated to be associated with 25 (OH) D3 statuses, yet not in a season-dependent manner. The findings of the current study demonstrated increased TSH levels in subjects with vitamin D deficiency in euthyroid population, which are in agreement with those of Barchetta et.al and Leonard et al. studies [16]. Furthermore, increased T4 levels were shown in subjects with 25 (OH) D3 sufficiencies in euthyroid population that it is conceivable due to the increased TSH levels in euthyroid population with 25 (OH) D3 deficiencies. In contrary, Konno et al. [17] demonstrated serum seasonal variation of TSH and its response to Thyrotropin-releasing hormone, with a peak in winter, without any

significant changes in serum T4, free T4 (FT4), T3, FT3 levels. In another study, the effect of vitamin D was investigated on anterior pituitary cells of the rat and TSH secretion [18]. Hence, hypothalamus-pituitary-thyroid axis may be affected by the amount of 25 (OH) D3 circulating, which may be regulated by sex hormones, genetic susceptibility, or environmental factors mentioned in Zhang et.al's study [19]. Sun irradiation can be mentioned as one of the environmental factors affecting serum levels of 25 (OH) D3 due to its UV-mediated activation [20]. In the current study, a significant association was not observed between serum level of 25 (OH) D3, T4 and TSH in winter and summer, whereas the solar climate of Iran with the natural high sunshine duration in summer should have positive effects [21]. This non-significant association may be related to the type of Muslim women's hair and bodies clothing as well as lack of sun exposure due to the long periods of time spent indoors by Muslim women in this study.

There was no association between 25 (OH) D3 and FBS within the study population. The results of the present study have revealed conflicting results compared to those of Pittas et al. [22], who reported daily supplementation with 500 mg of calcium citrate and 700 IU of vitamin D3 for three years prevented increases in plasma glucose. In another study, the relation of vitamin D and intake was evaluated in type 2 diabetes within women [23]. However, according to a study by Lind et al. [24], subjects with impaired glucose tolerance without vitamin D deficiency do not benefit from vitamin D supplementation. The mechanisms by which risk of high serum glucose may be affected seem not to be clear. The present study enjoys several strengths, including large size, and the same population that included Caucasian Iranian samples.

Thyroid dysfunctions are more frequent in diabetic patients than in the general population [25]. Current knowledge of thyroid hormone signaling suggests a relationship between thyroid hormones and diabetes. Thyroid hormone produces changes in the hormone levels and gene profiles that can put the body in a situation like fasting, and thus, reduced insulin signaling, which stimulates liver gluconeogenesis, and increases blood glucose levels [7]. Several studies have demonstrated that different prevalence of the association between thyroid dysfunction and diabetic populations [26-29]. In the present study, the subjects with high blood glucose levels had lower levels of T4 compared with the normal group, though no significant differences were detected in TSH level. The results of Moura Neto et al.'s [30] study showed that patients with T2DM had higher levels of FT4 and similar TSH levels compared to the control group. In another study by Lambadiari et al., TSH levels were not different between groups including impaired glucose tolerance, type 2 diabetes (T2DM) and control group, FT4 levels were lower in controls than in DM subjects [31]. These findings are in contrary to findings of a study carried out by Singh et.al who reported higher level of TSH in T2DM and lower level of T4 compared to the control group [9]. In another study, diabetic women were demonstrated to

have higher mean serum TSH levels and lower FT4 concentration than diabetic men [25]. Since several studies have reported conflicting results based on the type of thyroid disease and diabetes, environmental factors and culture of study population, the results of present study with the statistically significant non diabetic population can influence future decisions.

Conclusion

In conclusion, according to the relation of 25 (OH) D3 with thyroid hormones, which is also visible in the current study as well as the possible role of thyroid hormones in the regulation of blood glucose levels, the lifestyle and diet may have possible effects on thyroid hormones and blood glucose regulation. As a result, they will present a cheap and easy way to enhance the public health.

Conflict of Interest

The authors declare no conflict of interest.

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