

Hypovitaminosis D in Iraqi Hashimoto Thyroiditis Patients

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Abstract:

The association of abnormal levels of vitamin D with autoimmune thyroid disease including Hashimoto's thyroiditis has been somewhat controversial. The study aimed to investigate whether there is a correlation between vitamin D deficiency and Hashimoto's thyroiditis in Iraqi patients. This study is a cross-sectional study involving patients who visited the outpatient clinic in Baghdad teaching hospital for thyroid evaluation and follow-up during the period from December 2018 until April 2019. Out of those patients, 36 patients (24 females and 12 males) were diagnosed with Hashimoto's thyroiditis. Diagnosis of the patients was based on clinical symptoms and the results of thyroid function, and anti-thyroid antibody tests. In addition, 20 healthy individuals (age and gender matched) were also recruited in the study as a control group. Age distribution of patients showed that the majority of patients (52.8 %) were between the ages of 20 and 40 years. On the other hand, 2.8%, 25% and 19.4% were in the age groups <20, 40-60 and >60 years respectively. The data of the present study showed that Hashimoto's thyroiditis was more prevalent in females than males (67% females vs 33% males). Comparison between patient and control group by measuring serum vitamin D revealed a highly significant decrease in patients (10.18 ± 6.78 ng/ml) when compared to the control (68 ± 8 ng/ml) ($P < 0.001$). No significant difference in the level of vitamin D was found between male and female patients (7.2 ± 3.1 and 10.35 ± 6.2 ng/ml respectively). In conclusion, Hashimoto's thyroiditis is associated with a significant decrease in vitamin D status.

Keywords: Hashimoto disease, Vitamin D, Autoimmune.

1.Introduction

Autoimmune thyroiditis or Hashimoto's thyroiditis (HT) is a chronic hypothyroid disease characterized by the presence of thyroid antibodies (thyroglobulin antibodies (Tg-Ab)) and thyroid peroxidase antibodies (TPO-Ab)) [1, 2]. Discovered more than one hundred years ago, HT is now reported to be the most common autoimmune disease. In addition to clinical features, the demonstration of antibodies directed against thyroid cells (predominantly thyroglobulin and thyroperoxidase) is detrimental in the diagnosis of HT [3]. This disease is characterized by gland invasion by lymphocytic cells accompanied by follicular atrophy which subsequently results in gradual atrophy of thyroid tissue and hypothyroidism. Although the pathogenesis of HT is not fully understood, but excessively stimulated T CD4⁺ cells are thought to be major players in this autoimmune disease. Furthermore, Th17, T-regulatory cells and apoptosis are of most importance in TH development [4]. Current evidence suggests that genetic susceptibility and environmental factors, in addition to immune dysfunction contribute to the development of HT. Since its discovery in the beginning of the 20th century, the role of vitamin D has evolved from a vitamin to a steroid pro-hormone. Vitamin D is player in several immune functions [5]. The effect of vitamin D on various immune cells is suggestive of vitamin D prominent role in immune-mediated disorders in autoimmunity. Systemic Lupus Erythematosus, multiple sclerosis and Type 1 Diabetes Mellitus are examples of Autoimmune diseases that have been reported to be associated with vitamin D deficiency. Researchers have revealed that Vitamin D can suppress

Th17 cytokine production, enhance T-regulatory cells activation, induce natural killer cell functions, promote Th2 cytokine production and suppress Th1 which skew T cells toward Th2 polarization [6]. A number of studies have observed an association between thyroid autoimmunity and hypovitaminosis D in all age groups [7, 8, 9]. Bozkurt and co-workers have even suggested that vitamin D may potentially have a role in the development of HT and its subsequent progression into chronic hypothyroidism [9, 10]. Nevertheless, others have reported normal levels of vitamin D in HT patients [11]. The current study was aimed at investigating the level of vitamin D in a sample of Iraqi HT patients, and whether vitamin D levels could correlate with the level of autoantibodies and thus to disease severity

2. Materials and Methods

The present study investigated patients visiting Baghdad teaching hospital for thyroid evaluation and follow-up during the period from December 2018 to April 2019. Out of those patients, 36 patients (24 females and 12 males) were diagnosed with HT and the others were excluded. The HT patients were diagnosed by a physician based on clinical symptoms and the results of laboratory investigations (low thyroid hormone levels, increased TSH level and the presence of Thyroglobulin antibodies (TgAb): more than 20 IU/mL. The age of HT patients ranged from 17 to 77 years (mean age 43.38 ± 16.3 years). This study also recruited 20 apparently healthy individuals (age and gender matched) as a control group. The level of total Vitamin D (ng/ml) was measured in sera of HT patients and control using a competitive electrochemiluminescence assay (Roch Diagnostics, Germany). This assay employs a capture protein (vitamin D binding protein) that binds to both 25-OH D3 and 25-OH D2. Measurement of Vitamin D level in the sera of patients and control was done according to the manufacturer's instructions. Statistical analysis; The software Graphpad prism 5.0 (GraphPad Software, Inc, USA) was used for statistical analysis. Mean values and Standard deviation (SD) were calculated. Mann-Whitney test was used to compare between patients and control groups, while Sperman's correlation coefficient was used to test the strength of a relationship between data sets. P values above 0.05 were considered non-significant, while P values less than 0.05 were considered as significant

3. Results and Discussion

The Age distribution of patients showed that the majority of patients were in the age group 20-40 years, followed by the age groups 40-60 years and more than 60 years (52.8, 25 and 19.4% respectively). On the other hand, only 1 patient (2.8%) was less than 20 years old. The mean age of the HT patients included in this study was 43.38 ± 16.3 years. Out of the 36 patients in the study, 24 (67%) were females and 12 (33%) were males (Table 1).

Table 1. Basic Characteristics of HT patients included in the study.

Character	Patients
Age (mean \pmSD)	43.38 \pm 16.3
Age groups (years)	N (%)
< 20	1 (2.8)
20-39	19 (52.8)
40-59	9 (25)
> 60	7 (19.4)
Gender	N (%)
Female	24 (66.7)
Male	12 (33.3)

Measurement of the level of total vitamin D in HT patients and control showed that that former had 10.18 ± 6.78 ng/ml, while the latter had 68 ± 4 ng/ml with a highly significant difference ($p=0.001$) as shown in Table 2 and Figure 1.

Table 2. the level of total vitamin D in HT patients and control.

Group	level of total vitamin D ng/ml	P value
HT patients	10.18 ±6.78	0.001
Control	68±4	

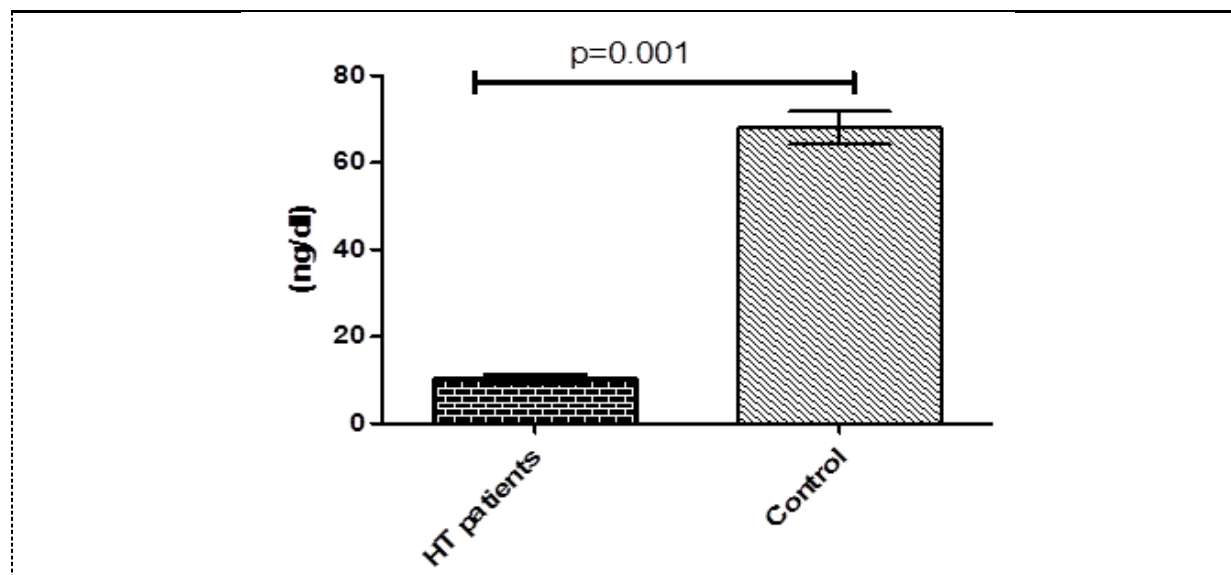


Figure 1. Serum vitamin D level in HT patients and control.

Comparison of the level of vitamin D between male (7.2 ± 3.1 ng/ml) and female HT patients (10.35 ± 6.2) showed no significant difference between the two genders as shown in table 3.

Table 3. Comparison between male and female HT patients using serum vitamin D concentration (ng/ml).

Parameter	Male		Female		P value
	Mean	(±) SD	Mean	± (SD)	
Vitamin D level in serum (ng/ml)	7.2	3.1	10.35	6.2	0.43

Furthermore, correlation analysis revealed no association between the concentration of Thyroglobulin antibodies (TgAb) and the level of vitamin D in TH patients ($r=-0.14$, $p=0.4$).

4. Discussion

Iraq has observed an increase in thyroid disorders during the last three decades. Hashimoto's thyroiditis was reported in 6.3% of patients in a cohort of 79 Iraqi individuals suffering from thyroid nodules [12]. Furthermore, HT was prevalent in 11.1% of patients diagnosed with Childhood Hypothyroidism during a 10 years period in Baghdad [13]. [14] studied the frequency of thyroid disease of autoimmune origin in Duhok (North of Iraq) and concluded that a considerable number of subjects are prone to deranged thyroid functions and thus are susceptible to autoimmune thyroid disorders. Published data have reported that the occurrence of HT increased with age and the peak was between 45 to 65 years which contradicts the results of the current study [4, 15]. This disagreement could be attributed to the difference in sample size between the studies. Consistent with previous studies [3, 16, 17], the majority of HT patients included in this study were females with a female to male ratio of 2:1. In general, autoimmune diseases tend to occur more in females. This higher susceptibility in females is partly attributable to the X chromosome, which has many genes relating to the immune system. Nevertheless, the occurrence of HT in a population could result from the interaction

between both genetic and environmental factors [18]. Deficiency in vitamin D is a worldwide problem. Due to its immunomodulatory role, vitamin D has been the focus of a growing number of studies which have proposed a potential protective role in immune mediated disorders. A recent clinical trial investigated the effect of vitamin D supplementation (in the form of cholecalciferol) on HT patients. Preliminary data showed a change in CD4⁺ T-cell subsets balance and thus improved disease control [19]. The results of the present study agreed with a number of clinical studies which have shown low vitamin D levels in patients with HT, implying of the presence of an association between vitamin D deficiency and thyroid autoimmunity [10, 20]. Nevertheless, the present study did not manage to find an inverse correlation between vitamin D levels and serum anti- thyroid antibodies reported by others who have suggested that vitamin D could contribute to the pathogenesis of HT [7, 20]. However, there is a controversy whether low vitamin D level is a cause or a result of HT (1). As no correlation was observed between vitamin D level and the concentration of Tg-Abs in HT patients included in the present study, it can be predicted that this deficiency in vitamin D is the result of HT rather than a cause. The result of the present study was inconsistent with other studies which have reported no difference in vitamin D levels between HT patients and the healthy control group [11]. These discrepancies in the level of vitamin D in HT patient could be attributed to factors such as the method used for estimating vitamin D levels, sample size, severity of the disease in addition to biological characters of the studied sample such as BMI [21]. No significant difference in vitamin D status was found between male and female patients which is consistent with other studies [22].

5. Conclusion

In conclusion, vitamin D deficiency was found in HT patients with no difference between genders. Further studies focusing on the effect of vitamin D supplements on the management of HT patients are recommended.

6. References

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