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PREVALENCE OF VITAMIN D DEFICIENCY IN HASHIMOTO'S THYROIDITIS AND ITS RELATION TO ANTI-THYROID PEROXIDASE ANTIBODIES

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ABSTRACT

Context: vitamin D deficiency has been considered a risk factor for several autoimmune diseases. Few studies examined prevalence of vitamin D deficiency in autoimmune thyroid disease and have produced conflicting results.

Aims: To study the prevalence of vitamin D deficiency in Hashimoto's thyroiditis (HT) and to assess the correlation between vitamin D and Anti-thyroid peroxidase antibodies (TPO-Ab).

Settings and Design: This is a cross sectional case control study.

Methods and Material: A total of 100 subjects, 50 HT patients and 50 healthy controls who were age and sex matched were included in the study. Serum 25(OH)D, fT4, TSH, TPO-Ab were measured. Subjects were categorized as vitamin D deficient(<12 ng/ml), vitamin D insufficient(12-20 ng/ml) and vitamin D sufficient (>20 ng/ml) based upon recent consensus guidelines. HT patients were categorized as euthyroid, sub clinical hypothyroid and overt hypothyroid based on fT4 and TSH.

Results: The mean 25(OH)D level was 13.19±7.43ng/ml and 13.66±8.61ng/ml in HT patients and healthy controls respectively.Prevalence of vitamin D deficiency was 56% in HT and 50% in controls. Vitamin D insufficiency was observed in 20% of HT and 36% of healthy controls.

There was no significant difference in 25(OH)D levels of overt hypothyroid, subclinical hypothyroid and euthyroid HT patients(p=0.23). Pearson correlation analysis showed no significant correlation between vitamin D and TPO-Ab,TSH and fT4.

Conclusions: The prevalence of vitamin D deficiency in hashimoto's thyroiditis and healthy controls was similar confirming high prevalence of vitamin D deficiency in general population. Vitamin D deficiency did not differ between euthyroid,sub clinical hypothyroid and overt hypothyroid patients of HT.There was no correlation between vitamin D and TPO-Ab.

KEYWORDS : Vitamin D Deficiency, Hypothyroidism, Hashimoto's Thyroiditis

INTRODUCTION:

Vitamin D deficiency have been identified as a risk factor for several autoimmune diseases like type 1 diabetes mellitus, multiple sclerosis, crohn's disease and rheumatoid arthritis.[1-4]

Autoimmune thyroid diseases (AITD) are the most common organ specific autoimmune disorder. Despite of the advancements in understanding the pathophysiology of AITD, its contributing causes are still unknown.[5,6] Like other autoimmune diseases, genetically susceptible factors and various environmental factors contribute to the occurrence of AITD.[5-7] VDR gene polymorphism was found in association with AITD.[8] Vitamin D has also been shown to influence the thyroid follicular cells of rat by directly inhibiting thyrotropin-stimulated iodide uptake in a dose dependent manner.[9]

Some studies found relation between vitamin D and AITD whereas other studies didn't[10-12]In view of these conflicting results and the dearth of published studies, the following study has been done to examine the levels of vitamin D among patients with HT and its correlation to thyroid autoantibodies.

SUBJECTS AND METHODS:

This is a cross sectional case control study conducted in the Department of Endocrinology in a South Indian tertiary care hospital from January to May 2016.

The study included 50 cases with HT and 50 age and sex matched healthy controls.Diagnosis of HT was made by presence of goiter and/or symptoms of hypothyroidism with elevated antithyroid peroxidase antibodies.Subjects with a history of treatment for thyroid disease, history of chronic kidney, liver or cardiac disease, malignancy, epilepsy,history of intake of medications that might alter vitamin D metabolism and thyroid functions were excluded from the study.

Serum fT4, TSH, TPO-Ab, 25(OH)D were measured by electrochemiluminescent immunoassay, Elecsys-2010, Roche Diagnostics.

HT patients were classified into three subgroups according to their thyroid function status.Subjects were considered to have Overt hypothyroidism if they had elevated serum thyrotropin (TSH) (reference interval was 0.30–5.5 mIU/mL) and low free thyroxine (fT4)(reference interval was 0.93–1.7 ng/dL) levels and subclinical hypothyroidism if they had normal serum free T4 and elevated TSH levels and euthyroidism if free T4 and TSH levels were normal (10).

Vitamin D deficiency was defined as a serum level of 25(OH)D of <12 ng/ml(<30nmol/L) and insufficiency as a serum level between 12-20 ng/ml(30-50nmol/L) and sufficiency >20 ng/ml. [13,14]

Statistical analysis was done by using software SPSS version 17 for windows. Results were presented as mean± standard deviation (SD) and with 95% confidence intervals. The independent 't' test, chi-square test, one way annova were used to compare the means between the study groups.Pearson correlation coefficient (r) was computed to find the correlation between vitamin D and TPO-Ab, TSH, fT4.P value < 0.05 was considered significant.

RESULTS:

Characteristics of HT cases and healthy controls were represented in Table 1.

TABLE 1: Characteristics of the HT Cases and Healthy Controls

Parameters	HT cases	Healthy controls	p-value
N	50	50	
Age(years)	27.78±9.23	27.78±9.23	

Sex F/M	44/6	44/6	
BMI (Kg/m^2)	22.68±5.19	22.14±3.59	0.54
TSH (µIU/ml)	41.71±42.63	2.59±1.13	0.001
fT4 (ng/dl)	0.83±0.45	1.31±0.16	0.001
TPO-Ab (IU/ml)	349.32±210.16	22.31±63.22	0.001
25(OH)D3 level (ng/ml)	13.19±7.43	13.66±8.61	0.80
Prevalence of Vitamin D deficiency	56%	50%	0.54
Prevalence of vitamin D insufficiency	20%	36%	0.07

There was no significant difference in 25(OH)D levels in between HT cases and controls and the prevalence of vitamin D deficiency in HT cases was almost similar to that of control group(p= 0.54)(Table 1).

25(OH)D levels among overt hypothyroid, subclinical hypothyroid and euthyroid HT cases were not statistically different(p=0.23) (Table 2).

There was no significant difference in the rates of vitamin D deficiency among patients with overt hypothyroid,sub clinical hypothyroid and euthyroid hashimoto's thyroiditis.

TABLE 2: Vitamin D status in HT subgroups.

	Overt hypothyroid subjects n = 24	**Sub clinical hypothyroid subjects n = 15**	**Euthyroid subjects n =11**	**P value**
25(OH)D3 levels (ng/ml)	12.43±6.55	15.85±8.66	11.2±7.11	0.23
Vitamin D deficiency	62.50%	40%	63.60%	0.32
Vitamin D insufficiency	16.60%	26.60%	18.18%	0.73
Vitamin D sufficiency	20.80%	33.33%	18.18%	0.59

To explore the probable interaction between vitamin D, TSH and thyroid hormones (T3& T4), analysis were performed according to vitamin D tertiles. There was no significant difference between vitamin D deficient, sufficient and insufficient groups in terms of age, BMI, TSH, fT4, a TPO –Ab levels(Table 3).

TABLE 3.Characteristics of Hashimoto's thyroiditis patients according to vitamin D status.

Parameters	**Vitamin D deficient group**	**Vitamin D insufficient group**	**Vitamin D sufficient group**	**P value**
N	28	10	12	
Age(years)	26.39±10.21	29.7±6.92	29.42±8.57	0.49
Sex F/M	25/3	9/1	10/2	
BMI (Kg/m^2)	22.47±5.99	22.87±3.48	23.04±4.69	0.94
TSH (µIU/ml)	42.79±43.10	38.58±43.83	41.79±44.18	0.96
fT4 (ng/dl)	0.81±0.44	0.83±0.52	0.85±0.45	0.96
TPOAb (IU/ml)	331.19±210.27	437.9±349.32	317.82±205.58	0.33
25(OH)D level(ng/ml)	7.74±2.69	15.21±2.21	24.22±3.44	0.0001

Correlation between vitamin D and TPO Ab,TSH,fT4 levels:

When we have investigated the relation between TPO positivity and vitamin D status,we found that there was no significant correlation between vitamin D and TPO-Ab titers,TSH and fT4 levels(Table4).

TABLE 4: Correlation between vitamin D levels and anti-TPO antibodies, TSH,fT4

	fT4	**TSH**	**TPO-Ab**
Vitamin D			
R	0.05	- 0.038	- 0.074
P	0.73	0.79	0.61

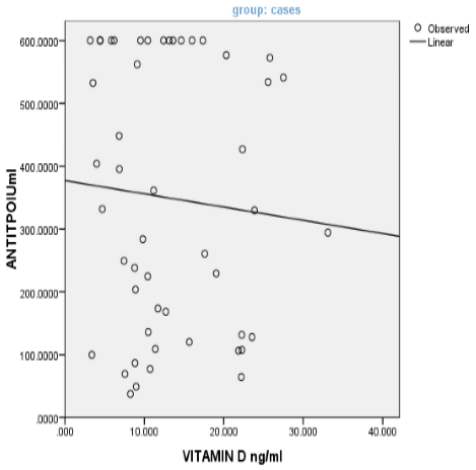

FIG 1 Pearson Correlation analysis of vitamin D and TPO-Ab in HT cases

DISCUSSION:

In the present study, the prevalence of vitamin D deficiency was almost similar in both cases and controls (56% versus 50%).The low vitamin D levels in both HT cases and controls confirms the earlier reports of wide prevalence of vitamin D deficiency in healthy Indians.

Our region lies at a latitude 17.68º N and longitude 83.21º E and receives abundant sunshine throughout the year but our results showed that there was high prevalence of vitamin D deficiency in general population and this may be attributed to skin complexion, traditional clothing, limited outdoor activity, air pollution or other factors leading to inadequate exposure.

With the iodine replacement programme, all over India, the prevalence of iodine deficiency disorders has been decreased but there is an increase in the prevalence of AITD which might be contributed by vitamin D deficiency in general population.

It was also proposed that low levels of vitamin D in hypothyroidism may be due to poor absorption of vitamin D from intestine or the skin may not synthesize vitamin D properly.[8] It is not known whether hypovitaminosis D is a key factor in the pathogenesis of AITD or rather a consequence of the disease.In a study done by Effraimidis et al in genetically susceptible and euthyroid de novo TPO positive individuals found that vitamin D deficiency will not influence development of thyroid autoimmunity. [15]

Vitamin D deficiency may incite AITD which may proceed later to develop subclinical hypothyroidism and overt hypothyroidism. This depends upon the susceptibility of the individual/thyroid gland to autoimmune damage and its subsequent progression to sub clinical and overt hypothyroidism.

In our study, there was no significant difference in vitamin D levels between overt hypothyroid, sub clinical hypothyroid, euthyroid hashimoto's thyroiditis patients (p=0.23) similar to the findings shown in the study by Tamer et al (p=0.84).[11] This suggests that the severity of hypothyroidism may not influence vitamin D levels.

In our study, there was no significant difference in prevalence of vitamin D deficiency between overt hypothyroid (62.5%), subclinical hypothyroid (40%) and euthyroid patients (63.5%; P=0.3) and also there was no difference in prevalence of vitamin D insufficiency within groups (P=0.73) similar to the study by Tamer et al (P=0.063).[11]This infers that thyroid function status will not influence the vitamin D deficiency.

While looking at correlation between TPO antibodies and vitamin D earlier studies showed varied results. A study by kivity et al, Bozkurt et al and Unal et al, showed a significant correlation to TPO antibodies and vitamin D levels.[10,16,17] A study done in North India by Goswami et al showed that serum 25(OH)D values show only weak inverse correlation with TPO-Ab titers whereas Chailurkit et al showed that vitamin D status was not associated with positive TPO-Ab and/or Tg-Ab.[12,18]

Our study showed that there was no correlation of 25(OH)D levels with TPO-Ab titers which is in concordance with study by chailurkit et al.[18]There was no difference in the TPO-Ab titers when compared between vitamin D deficient, insufficient and sufficient groups similar to the findings shown by Goswami et al.[12] This observation indicates that there is no influence of vitamin D status over the titers of TPO-Ab.

Kivity et al showed that vitamin D deficiency correlated with abnormal thyroid function tests(P=0.059) whereas our study didn't. Our study results indicate that there was no influence of vitamin D levels over autoimmunity or related thyroid dysfunction. The putative role of vitamin D over thyroid may be influenced by various genetic polymorphisms and this has to be evaluated further in future studies.

The main limitations of our study were small sample size,lack of information on nutrition and outdoor activity and our study is a cross sectional study so causative role of vitamin D, if any on thyroid autoimmunity could not be readily determined.

In summary, prevalence of vitamin D deficiency in HT patients was almost similar to that of healthy controls and there was no difference in the 25(OH)D levels in euthyroid, sub clinical hypothyroid and hypothyroid HT patients. There was no relation between 25(OH) vitamin D levels and TPO antibody titers,fT4 and TSH.

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