Status of vitamin D levels in hypothyroid patients and its associations with TSH, T3 and T4 in north Indian population of Meerut, a cross sectional study

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Abstract

Introduction: Vitamin D deficiency has been identified as a risk factor for several autoimmune diseases, cancers, atherosclerosis, etc. Its deficiency has also been shown to be associated with hypothyroidism with inconclusive results. The present study aims to explore the association of vitamin D deficiency with hypothyroidism.

Materials and Methods: This is a cross sectional study conducted in the department of biochemistry Subharti Medical College, Meerut. A total of 152 clinically suspected hypothyroid subjects in the age group of 20-60 years, from both sexes attending Medicine OPD were included in the study.

All the patients were subjected to complete general physical and systemic examination and findings noted. The vitamin D, T3, T4 and TSH were measured in all by enzyme linked fluorescence assay (ELFA) in Vidas PC auto-analyzer from Biomerieux. The patients were then categorized into euthyroid (TSH=0.25-5µIU/ml), subclinical hypothyroid (TSH >5-7µIU/ml) and overt hypothyroid (TSH>7µIU/ml) based on serum TSH cut off values. The patients were also defined as vitamin D sufficient (>30ng/ml), insufficient (20-30ng/ml) and deficient (<20ng/ml) based upon the recent consensus on vitamin D classification.

Results: The mean value of vitamin D in subclinical hypothyroid (16.73±12.46 ng/ml) and overt hypothyroid (13.23±10.08 ng/ml) were significantly lower than the euthyroid (29.07±19.01 ng/ml) with P value<0.05. Pearson's correlation analysis between vitamin D and TSH (r=-0.314, P<0.01) have shown a significant negative correlation.

Conclusion: Vitamin D deficiency negatively correlates with TSH. Thus we suggest vitamin D supplementation to all hypothyroid patients.

Keywords: Vitamin D, TSH, Subclinical hypothyroid, Overt hypothyroid, Euthyroid

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Introduction

Vitamin D has been known for decades for its role in bone mineral metabolism and development and maintenance of skeletal health, but in recent time effects on extra skeletal tissue has also been observed.[1,2] Vitamin D deficiency has been identified as a risk factor for diabetes mellitus,[3,4] cancers,[5] multiple sclerosis,[6] atherosclerosis,[7] infectious diseases[8] and other autoimmune diseases[9,10] including autoimmune thyroid diseases.[11,12]

It mediates its effects through binding to vitamin D receptor (VDR) and thus activation of respective genes.[13] The VDR are widely distributed in humans, presenting in more than 30 different tissues including pancreas, myocardium, lymphocytes, thyroid gland etc. signifying its importance in humans.[14]

Both vitamin D and thyroid hormones also act through steroid receptors and may affect each other's action as they have similar response elements on gene. So a lower level of vitamin D is likely to aggravate the systemic abnormalities associated with hypothyroidism.[15,16]

The prevalence of thyroid disease is on the rise. It has been estimated that there are about 42 million people in India suffering from thyroid diseases[17] and the prevalence of hypothyroidism has risen markedly in the last few decades affecting even younger age groups in the form of congenital hypothyroidism.[18]

Vitamin D is present in the serum in either of its two forms: 25 hydroxycholecalciferol [25(OH) D] or 1, 25 dihydroxycholecalciferol [1, 25(OH) D]. The measurement of 25(OH) D was preferred to 1, 25(OH) D in many studies as it has fairly long circulating half-life of 15 days,[19] and reflects the total vitamin D content of the body.[20]

It is not clear if any association exists between vitamin D deficiency and hypothyroidism. There are few reports with inconclusive results. Therefore we undertook the present study with aim to examine the association of vitamin D deficiency with hypothyroidism and to find out its relations with thyroid stimulating hormone (TSH), triiodothyronine (T3), tetraiodothyronine (T4) in north Indian population of Meerut.

Materials and Methods

This is a cross sectional study conducted in the department of biochemistry, Subharti Medical College,

Meerut during the periods from Mar 2014 to Feb 2015 after obtaining ethical clearance by the institutional ethical clearance committee. A total of 152 clinically suspected hypothyroid subjects in the age group of 20-60 years from both sexes attending Medicine OPD were included in the study. Informed consent was obtained from each participant.

Any known case of hyperthyroidism or hypothyroidism on treatment, supplementation with calcium or vitamin D or patients on medications which can affect thyroid functions such as, oral contraceptives, estrogen, glucocorticoids and iodine were excluded from the study after taking proper medical history.

Sample collection: After 12-14 hours of fasting, venous blood sample was collected under all aseptic conditions in plain vial and processed within 24 hours. Serum T3, T4, TSH and vitamin D were measured by enzyme linked fluorescence assay (ELFA) in Vidas PC auto-analyzer from Biomerieux. In our study we measured 25(OH) D as it has longer circulating half-life.

Patients were then categorized into euthyroid (TSH=0.25-5μIU/ml), subclinical hypothyroid (TSH >5-7 μIU/ml) and overt hypothyroid (TSH>7 μIU/ml) based on TSH cut off values. Patients were also categorized as vitamin D sufficient (>30ng/ml), insufficient (20-30ng/ml) and deficient (<30ng/ml) based upon recent consensus of vitamin D classification.[21,22]

Statistical Analysis

The data were subjected to statistical analysis using software SPSS version 16 for windows. Results were presented as mean± standard deviation (SD) and with 95% confidence intervals. The independent 't' test was used to compare the means between the study groups. Pearson correlation coefficient (r) was computed to find the correlation between vitamin D groups with different thyroid function profiles.

Results

It was observed that 53.94% (82) of subjects were vitamin D deficient, 21.05% (32) were insufficient and 25% (38) of subjects had sufficient vitamin D levels (Table 1). In this study 65.78% (100) subjects were euthyroid, 13.15% (20) were subclinical hypothyroid and 21.05%(32) were overt hypothyroid (Table 2).

Biochemical analysis shown in Table 2 revealed that serum TSH levels were significantly higher in both subclinical (6.05±.54 μIU/ml) and overt hypothyroidism (17.34±15.16) as compared to Euthyroid (2.06±1.27μIU/ml) with P value <0.05. Mean serum levels of vitamin D in subclinical hypothyroid (16.73±12.46 ng/ml) and overt hypothyroid (13.23±10.08ng/ml) patients were highly significant when compared to controls (29.07±19.01ng/ml) with P value<0.05.

Pearson's correlation analysis depicted a significant negative correlation between levels of Vitamin D and TSH (r= -0.314, P < 0.01) in vitamin D deficient group. In the insufficient and sufficient vitamin D groups, the Pearson's correlation analysis for Vitamin D and TSH were insignificant, (r= -0.044, P > 0.01) and (r= -0.037, P > 0.01) respectively. Most of the hypothyroid patients had serum Vitamin D levels below 20ng/ml.

Table 1: TSH, T3, T4, and mean Age of the study population in different vitamin D groups

Vitamin D groups	Age (yrs)	TSH (μIU/ml)	T3 (nmol/L)	T4 (nmol/L)
Deficiency, n=82 (53.94%) <20ng/ml	37.63±11.82	7.81±10.12	1.52±1.52	72.61±33.42
Insufficiency, n=32 (21.05%) 20-30ng/ml	39.62±14.37	2.40±2.32	2.47±2.31	98.17±46.34
Sufficiency, n=38 (25%) >30ng/ml	40.60±13.40	1.62±10.00	3.23±4.79	95.78±28.62

Legend 1: Vitamin D deficiency group has lower mean age, higher TSH and T3 but normal T4 inclined towards lower reference range. In insufficiency and sufficiency group, TSH and T4 were normal but T3 was slightly elevated.

Table 2: Comparison of vitamin D and TSH in euthyroid, subclinical hypothyroid and overt hypothyroid groups expressed as Mean±SD

Parameters	Euthyroid (100), TSH=(.25-5)	Sub clinical hypothyroid (20), (TSH >5-7)	Overt hypothyroid (32), (TSH >7)
Vit D (ng/ml)	29.07±19.01	16.73±12.46	13.23±10.08
TSH (μIU/ml)	2.06±1.27	6.05±.54	17.34±15.16
T3 (nmol/L)	2.80±3.38	1.11±0.77	0.77±0.69
T4 (nmol/L)	98.79±33.01	62.48±25.98	50.22±26.28

Vitamin D: Euthyroidvs subclinical hypothyroid (P=0.006), Euthyroidvs overt hypothyroid(P=0.000), Subclinical hypothyroid vs Overt hypothyroid(P=0.272)
TSH: Euthyroidvs subclinical hypothyroid(P=0.000), Euthyroidvs overt hypothyroid(P=0.000), Subclinical hypothyroid vs Overt hypothyroid(P=0.002)
P<0.05 is considered significant.

Legend 2: Degree of deficiency progressing from subclinical to overt hypothyroidism, with progressive increase in TSH level from subclinical to overt hypothyroidism.

Table 3: **Correlation of *Vitamin D status* with TSH, T3 and T4**

		TSH	T3	T4
Vitamin D <20	Pearson Correlation	-.314**	.225*	.277*
	Sig. (2-tailed)	.004	.043	.012
Vitamin D 20-30	Pearson Correlation	-.044	.124	.112
	Sig. (2-tailed)	.807	.492	.535
Vitamin D >30	Pearson Correlation	.037	-.041	.208
	Sig. (2-tailed)	.832	.811	.224

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Legend 3: Vitamin D deficiency showing significant negative correlation with TSH and positive correlation with T3 and T4.

Discussion

About 5-6 decades back vitamin D deficiency was thought to be uncommon in India as it is located between 8.4°N and 37.6°N latitude with abundant sunshine.[23] Later on, several epidemiological studies have revealed that there is widespread prevalence of vitamin D deficiency of varying degrees (50-90%) in Indian population with low dietary intake of calcium.[2] We observed vitamin D deficiency in 53.94% of subjects irrespective of thyroid hormone status. It was also observed that vitamin D deficient group had higher serum TSH levels as compared to vitamin D insufficient and sufficient groups (Table 1). These findings were in accordance with the findings of many authors.[24,25] It suggested that vitamin D does have a role to play in hypothyroidism, although a causal relationship could not be established. But there are some studies that reported both normal and decreased concentrations of vitamin D in patients with thyroid disorders.[26,27]

It was observed that none of the groups had sufficient vitamin D levels (>30ng/ml) as shown in Table 2. Subclinical hypothyroid patients (13.15%) had vitamin D<20ng/ml and overt hypothyroid patients (21.05%) had vitamin D <15ng/ml. Euthyroid group (65.78%) had vitamin D levels in between >20-<30ng/ml with mean value 29.07±19.0 which was close to the upper side of the spectrum. This could be due to high prevalence of vitamin D deficiency in the general population from where the sample was drawn. But the degree of deficiency was corresponding to the severity of disease as shown in Table 2. A recent hospital based study from north India reported that 56% of hypothyroid patients had vitamin D levels below 20ng/ml whereas only 10% had sufficient levels.[28] Although no separate account of statistics for subclinical and overt hypothyroidism were given in their study. Another study reported that more than 75% of adults with subclinical hypothyroidism had vitamin D levels below 29ng/ml and only 24% had vitamin D levels above 29 ng/ml.[29]

Both subclinical and overt hypothyroid patients had significantly lower levels of serum vitamin D as compared to euthyroid (P<0.001). One possible explanation for these reduced levels of vitamin D in subclinical and overt hypothyroidism can be the sluggish intestines which lead to reduced absorption of vitamin D. Since the primary source of vitamin D in body is its synthesis from cholesterol in skin with the help of sunlight, there seems to be other factors as well leading to its insufficient levels. A recent study suggested that vitamin D deficiency may lead to Grave's disease and its deficiency has also been associated with auto-immune thyroid disorders and its protective role has been mentioned due to its immune regulatory effect.[30,31]

We observed a significant negative correlation between vitamin D in deficient group and TSH on pearson's correlation analysis (r=-0.314, p<0.01) suggesting the existence of inter relationship between vitamin D deficiency and hypothyroidism. It also states a putative role of vitamin D as a potential modifiable risk factor for hypothyroidism. In order to function, vitamin D must bind to VDR which is found in several cell types including thyroid gland.[13,32] Studies have shown that patients of autoimmune thyroid disease have several VDR polymorphisms that affect its expression and activation.[33] So vitamin D plays a role in maintaining a euthyroid state by interacting with its receptor in the thyroid gland. Although a causal relationship could not be established.

Conclusion

Vitamin D deficiency negatively correlates with TSH and the severity of vitamin D deficiency

corresponds to the severity of thyroid disease, with progressive increase in TSH level from subclinical to overt hypothyroidism. Thus it may be suggested that vitamin D be supplemented to all hypothyroid patients including the subclinical cases. We hypothesize that the Subclinical cases might progress to overt hypothyroid if not timely supplemented with vitamin D.

Limitations of the study

Control subjects were not taken separately.

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