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PREVALENCE OF VITAMIN D DEFICIENCY AND ITS RELATIONSHIP WITH SUBCLINICAL HYPOTHYROIDISM

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ABSTRACT

Vitamin D deficiency has been implicated in various diseases including cancer and auto immune diseases. The present study attempts to establish a relation between vitamin D deficiency, thyroid hormones and TSH in subclinical hypothyroidism.100 newly diagnosed patients with subclinical hypothyroidism were divided into three groups according to vitamin D levels. Mean plasma TSH and T_3 values decreased with increasing vitamin D values and T_4 increased with increasing vitamin D tertiles. However , intergroup comparison showed no statistically significant changes .In females, negative correlation between vitamin D and TSH was statistically significant (p=0.014).The prevalence of vitamin D deficiency, insufficiency and sufficiency in 100 patients was found to be 38%, 38% and 24%. The study indicates the prevalence of vitamin D deficiency in subclinical hypothyroidism, but further studies are needed to determine whether it is a causative factor in the pathogenesis of the disease or a consequence.

KEY WORDS: **Vitamin D, thyroid hormones, subclinical hypothyroidism**

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INTRODUCTION

Vitamin D deficiency is increasing world - wide [1] and has been drawing much attention in the association of various diseases including cancer, cardiovascular diseases, autoimmune diseases, endocrine and metabolic diseases[2, 3]. Vitamin D is an immunomodulator and may affect autoimmune thyroid diseases [4,5]. Subclinical hypothyroidism, most commonly an early stage of hypothyroidism with increased serum TSH levels and normal thyroid hormones, may be caused due to chronic auto immune thyroiditis. Vitamin D has also been shown to influence thyrocytes directly by attenuating TSH stimulated iodide uptake and cell growth [6]. In isolated perfused rat kidney in vitro, synthesis of 24,25 $(OH)_2$ D_3 increased significantly on treatment with T_3,T_4 and TSH suggesting that these hormones have a direct effect on renal vitamin D metabolism[7]. Oral administration of 25(OH) D_3 elevated TSH and slightly decreased T_3 suggesting that 25 (OH) cholecalciferol interferes with the process of hormone secretion probably by altering intracellular calcium of secretory cells[8]. Further thyrocalcitonin and vitamin D control calcium metabolism through their coordinated actions. Hence the present study aims at exploring a relationship between thyroid hormones, TSH and 1,25DHCC in subclinical hypothyroidism.

MATERIALS AND METHODS

A total of 100 freshly diagnosed subclinical hypothyroidism patients aged between 25-55 years both males (n=49) and females (n=51) were considered for the study. Patients whose serum TSH level was more than 4.2μIU/ ml were included for the study. Patients with any liver or kidney diseases or history known to alter vitamin D metabolism, smokers, alcoholics, diabetics were excluded from the study. This study was approved by the institutional ethics committee and informed consent was collected from all subjects. Fasting blood sample was collected in heparinised vacutainer, centrifuged at 4500g for 5 minutes to obtain plasma. Hormones TSH, T_3 and T_4 were estimated by electrochemiluminescence using sandwich principle [9]. 1, 25 dihydroxycholecalciferol (1, 25DHCC) was determined based on the competitive principle by ECLIA [10].

Vitamin D deficiency was defined as plasma 1,25 DHCC concentration less than 20 ng/ml, insufficiency between 21-29 ng/ml and sufficiency $\geq$ 30ng/ml. The study population was thus divided into 3 groups based on vitamin D concentration. Suboptimal vitamin D group included patients having both insufficiency and deficiency. Statistical analysis were performed with SPSS software version 20.Inter group comparison was done by ANOVA, the correlations between 1,25DHCC and other variables were tested by Spearman coefficient and p value less than 0.05 was considered significant.

RESULTS

Mean plasma 1,25DHCC concentration of total samples was 23.5 ng / ml. The prevalence of deficiency, insufficiency and sufficiency in 100 sub clinical hypothyroid patients was 38%, 38% and 24% respectively. There was no significant difference in prevalence of either vitamin D deficiency or insufficiency between sexes. 76% of the adults with subclinical hypothyroidism were in suboptimal vitamin D status. To explore the probable interaction between vitamin D, TSH and thyroid hormones (T_3& T_4), analysis were performed according to vitamin D tertiles. Mean plasma TSH and T_3 values decreased with increasing vitamin D tertiles. T_4 levels increased with increasing vitamin D (Table1). However, intergroup comparison showed no statistically significant changes as p value was greater than 0.05. Mean TSH and T_3 levels were higher in vitamin D deficient and insufficient groups compared to vitamin sufficient group, $p>0.05$ by ANOVA (Table 2). There was a positive correlation between vitamin D and T_4 ($r = 0.101$), and negative correlation between vitamin D and TSH($r = -0.681$) T_3 ($r = -0.150$) respectively (Table3). Gender-wise correlation study showed a statistically significant negative correlation between vitamin D and

TSH (r = -0.763, p = 0.014) in females (Table 4). Further, mean vitamin D in females was much lower (17.83ng/ml) as compared to males (25.26ng/ml).

Table 1
Comparison of TSH and thyroid hormones in vitamin D tertile groups

	Vitamin D tertiles (ng/mL)	TSH (µIU/mL)	T3 (ng/mL)	T4 (µg/dL)
Group I (n= 38)	< 20	7.3± 0.65	2.03±0.45	4.8±0.62
Group II (n= 38)	21-29	5.6±0.63	1.47±0.24	5.10±0.56
Group III (n=24)	> 30	4.36±0.85	1.24±0.19	6.19±0.90
p value		0.185	0.285	0.210

n indicates number of patients

Table 2
Comparison of TSH and thyroid hormones in sub optimal and optimal vitamin D groups

Groups	Vitamin D (ng/mL)	TSH (µIU/mL)	T3 (ng/mL)	T4 (µg/dL)
Sub optimal VitD group (n=76)	<29	6.45±0.34	2.0±0.47	4.2±0.73
VitD optimal group (n=24)	>29	4.36±0.85	1.24±0.19	6.19±0.9
		NS	NS	NS

n indicates number of patients
NS –statistically insignificant

Table 3
Correlation of vitamin D with TSH and thyroid hormones in subclinical hypothyroid patients

		TSH	T3	T4
Vitamin D (n =100)	Pearson correlation Coefficient(r value)	-0.681	-0.150	0.101
	P value (2tailed)	0.205	0.456	0.615

n indicates number of patients

Table 4
Correlation of vitamin D with TSH and thyroid hormones in subclinical hypothyroid female patients

		TSH	T3	T4
Vitamin D (n =51)	Pearson correlation Coefficient(r value)	-0.763	-0.186	0.296
	P value (2tailed)	0.014	0.33	0.230

DISCUSSION

The rapid economic development accompanied by a change in life style behaviours like less exposure to sunlight has increased the incidence and prevalence of vitamin D deficiency in India and other countries[11]. However, data from epidemiologic studies in India are still limited. Though the residents of this area have adequate sunshine, our study shows that more than 75% of adults with subclinical hypothyroidism are in suboptimal vitamin D status. Only 24% had vitamin D sufficiency. Role of vitamin D in bone and mineral homeostasis has been well established, recently 25(OH) vitamin D deficiency is linked with predisposition to autoimmune diseases like type I diabetes and

multiple sclerosis [12] due to its potent immune-regulatory effect. It has been suggested that vitamin D deficiency is related to the pathogenesis of Grave's disease [13]. The presence of receptors of 1, 25 DHCC in the pituitary, pancreas, testis and ovary has raised the question of a possible direct role for 1,25DHCC in the regulation of hormone synthesis and regulation [14]. In the present study, there was a negative correlation between TSH and 1,25DHCC. Plasma TSH decreased with increasing vitamin D tertiles , in agreement with the fact that 1,25DHCC selectively enhance agonist induced TSH release in the rat thyrotroph in vitro [15]. The interaction of 1,25DHCC with T_3 in primary culture of dispersed anterior pituitary cells enhanced TSH release supporting the proposal that 1,25DHCC modulates TSH secretion in vivo. The present study findings are also in the same line, with both 1,25DHCC and T_3 levels being low in patients with high TSH, emphasising the fact that vitamin D deficiency is prevalent in sub clinical hypothyroidism. One of the earlier studies reported low vitamin D level in both hypothyroid and hyper thyroid post-menopausal women [16].However, in the present study, negative correlation between TSH and vitamin D_3 was statistically significant in females probably due to low mean vitamin D values observed in females. High vitamin D status in younger individuals is associated with low circulating thyrotropin[17]. 25(OH) vitamin D_3 insufficiency in thyroglobulin antibody positive subjects was significantly higher than thyroglobulin antibody negative individuals [18]. Further, vitamin D binding protein was found to be increased in hypothyroid subjects [19]. Furthermore, thyroid hormones decrease plasma 1,25vitamin D_3 through transcriptional repression of renal 1 alpha hydroxylase gene [15].

CONCLUSION

The study establishes the fact that 1,25DHCC may play an important role in altering thyroid hormones and TSH levels in subclinical hypothyroidism. Vitamin D insufficiency is associated with subclinical hypothyroidism. Further studies are needed to determine whether vitamin D insufficiency is a causative factor in the pathogenesis of subclinical hypothyroidism or rather a consequence of the disease.

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