Vitamin D Deficiency & Low Serum Calcium Levels in Hypothyroid Patients

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ABSTRACT

Introduction: Vitamin D deficiency prevails in epidemic proportion all over Indian sub continent. The role of vitamin D as a immune modulator has been emphasized in recent years. Low levels of Vitamin D were observed in several autoimmune diseases including multiple sclerosis, rheumatoid arthritis, SLE, Type I diabetes mellitus. Thyroid diseases are among the most common endocrine abnormalities. Currently there is no consensus regarding role of Vitamin D deficiency in hypothyroid patients. In present study we explored the probable interaction between vitamin D and Hypothyroidism and also tried to find any correlation between Serum Ca^{2+} levels and Thyroid disorder.

Material and Methods: The present study was a cross sectional study conducted in the department of Internal medicines, ASCOMS Hospital Jammu. It was conducted from April to October (2017).We enrolled a total of 60 subjects in the study. Venous samples were collected from all patients. The quantitative determination of 25 (OH) vitamin D and Serum Ca^{2+} was done using spectrophotometer method. Levels of TSH, T3 T_4 were estimated using fluorescence array. Statistical analysis were performed using SPSS software. All data presented as frequency and mean $\pm$ SD, unpaired t-test was used to compare between two means of all parametric continuous variable. Chi-square test statistic was used to test association between categorical variables.

Results: The following observations were deduced for the 60 subjects enrolled in the study. The mean levels of serum 25(OH) vitamin D was 16.20 ng/ml in hypothyroid group versus 49.93ng/ml in control group. This was statistically significant P = 0.001. There was significant negative correlation between 25 (OH) vitamin D and TSH levels in the hypothyroid group (r = -0.37 P = < 0.05).We also observed significant difference in levels of serum ca^{2+} between the two groups. Hypothyroid group serum ca^{2+} (7.29 $\pm$ 0.40 mg/dl), control group serum ca^{2+} (9.92 $\pm$ 0.43mg/dl) (t= -24.816 P= 0.000).A positive correlation was observed between 25 (OH) vitamin D and FT_3 levels in hypothyroid groups though it was insignificant (r = 0.008 P =0.966).

Conclusion: The study concluded that in hypothyroid patients, levels of 25 (OH) vitamin D and Serum ca^{2+} were significantly decreased. There may be a rationale for recommendation of vitamin D and calcium supplementation for hypothyroid patients.

Keywords: Vitamin D, Hypothyroid, Serum ca^{2+}, AITD's (Autoimmune Thyroid Diseseas)

INTRODUCTION

Vitamin D plays a major role in physiological processes that modulate mineral metabolism and immune function with probable link to several chronic and infectious conditions [1]. Vitamin D is a steroid molecule, mainly produced in the skin, which regulates the expression of a large number of genes [2]. Vitamin D is recognized to be an essential element of bone metabolism and skeletal health; however its deficiency can cause rickets in children as well as an increased propensity of osteoporosis. Vitamin D deficiency is a global health problem. Over one billion people worldwide are vitamin D deficient or insufficient. The role of Vitamin D as an immune modulator [3] has been emphasized in recent years, and low levels of hormone were observed in several autoimmune diseases including multiple sclerosis and systemic lupus erythematosus. Vitamin D mediates its effect through binding to vitamin D receptor (VDR)[4], and activation of VDR-responsive genes.VDR genes polymorphism was found to associate with autoimmune thyroid diseases (AITDs) [5].Vitamin D plays a significant role in modulation of immune system, enhancing the innate immune response while exerting an inhibitory action on the adaptive immune system. Several studies have revealed low serum levels in patients with Hashimoto's thyroiditis (HT) indicating association between vitamin D deficiency and thyroid autoimmunity. Animal studies [6] have shown that the administration of 1, $25(OH)_2$ Vitamin D in addition to cyclosporine to effectively prevent the induction of experimental autoimmune thyroiditis (EAT) with a synergistic effect in the CBA mice [7]. Thyroid diseases are among the most common endocrine abnormalities [8]. Few past studies have reported the impact of vitamin D deficiency on thyroid diseases. Currently there is no consensus regarding the optimal role of vitamin D deficiency in hypothyroid patients and its association with hypothyroidism. In the present study we explored the probable interaction between vitamin D status and hypothyroidism and also tried to find any correlation between serum calcium levels and thyroid disorder.

MATERIAL AND METHODS

The present study was a cross sectional study conducted in ASCOMS hospital, Jammu from April to October 2017. A total of 60 subjects were enrolled into the study. They were recruited from the out patients department and the indoor

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wards of the department of Internal medicine of ASCOMS hospital. They had their complete history taken and clinical examination done. Structured questionnaires were administered to them to obtain demographic information including age, gender, BMI. The study populations were classified in two main groups; group I consisted of 30 healthy controls and group II included 30 hypothyroid patients. Ethical approval for this study was obtained from ethics committee of the institute. All participants gave their written informed consent after the aim and the objectives have been explained to them.

BIOCHEMICAL ASSAY

Venous samples was taken from all the patients from the antecubital vein. The quantitative determination of 25 –OH vitamin D was carried out by using *UV 2005 spectrophotometer method,* A serum level of 0-20ng/ml was considered as deficient, level 21-29 ng/ml was considered insufficient and > 30ng/ml was considered sufficient. Determination of serum Calcium levels using Spectrophotometer method. This method is based on formation of Ca^{+} ions violet complex with o-cresol-pthalein complex in alkaline medium. Serum T_3, T4, andTSH levels were assessed using fluorescence array with reference range (1.2-4.4 pg/ml for T_3) (0.8-2.0 ng/dl for T_4) and 0.3- 5.0 m u/l for TSH).

STAISTICAL ANALYSIS

All statistical analysis was performed using SPSS software. All data presented as frequency (percentages) and mean ± SD and median (interquartile range) were appropriate. Unpaired t-test was used to compare between two means of all parametric continuous variable. The Chi-square test statistic was used to test association between categorical variables. Linear regression analysis was performed to test association between biochemical parameter.A P-value <0.05 was considered statistically significant.

RESULTS

The demographic characteristic of study participants including mean value ± S.D are shown in Table. 1.The mean age of hypothyroid group was (42.6 years) and was not significantly different from the control group (45.1 year) P> 0.05.There were more females 17 (57%)than males patients 13(43%) in hypothyroid group, though it was statistically non significant P>0.05.The mean levels of serum 25(OH) Vitamin D ng/ml was as follows: 49.93ng/ml in the control group and 16.29ng/ml in hypothyroid group. Using t-test to compare the levels between two group showed a significantly lower levels of 25(OH)vit D, in the hypothyroid group (t= -36.6 P=0.001).However in the hypothyroid group, when we compared the levels of 25(OH)vit D between the male and female patients we observed insignificant difference (t= 0.023 P=0.98).

TSH Status among hypothyroid and control group participants are shown in table 1.The levels of TSH was significantly raised in hypothyroid patients when compared to controls (t= 10.023 P=0.000).When analyzing for association and

Parameters	Control group I Healthy controls Mean ± SD	Cases group II Hypothyroid Cases Mean ± SD	t- value p value
Age	45.1 ±8.90	42.6 ± 16	2.8 0.008
Sex	15 F (50 %)	17 F (57 %)	
	15 M (50 %)	13 M (43 %)	>0.05
Serum 25(OH) Vit D ng/ml	49.93± 4.95	16.29 ± 1.70	-36.36 0.001
Serum Calcium mg/dl	9.92 ± 0.43	7.29 ± 0.40	-24.816 0.001
Serum TSH mU/L	3.65± 0.53	9.45 ± 3.06	10.023 0.000
Serum fT3 pg/ml	2.09 ±0.47	2.61 ± 0.70	3.419 0.002
Serum fT4 ng/dl	1.20 ± 0.36	1.19 ± 1.53	-0.46 0.96

Table-1: Parameters

Hypothyroid cases group II			
Parameters	**Female 17**	**Male 13**	**t test/ p value**
25(OH) vit D	16.28 ± 1.70	16.29 ± 1.65	P =0.98
ng/ml			t = 0.023
Serum calcium mg/dl	7.29 ± 0.40	7.27 ± 0.39	P = 0.84
			t= 0.196
TSH mU/L	9.45 ± 3.06	9.66 ± 3.10	P = 0.79
			t = 0.267

Table-2: Parameters

correlation, following observations were made: In the hypothyroid group there was significant negative correlation between 25 (OH)vit D levels and TSH (r= -0.37 P=<0.05). There was significant positive correlation between serum 25(OH) vitD and serum Ca^{2+} in both the case and the control group (r= 0.328 P=0.07).A positive correlation was observed between 25(OH)vit D and FT_3 levels in hypothyroid group (r=0.008 P=0.966); though it was insignificant. We also observed a significant difference (*Table 1.)* in the levels of serum calcium between hypothyroid group(7.29± 0.40 mg/dl) and control group (9.92 ± 0.43 mg/dl) (t= -24.816 P=0.000).The intragroup levels of serum Ca^{2+} between male and female hypothyroid patients did not show significant difference (Table 2.) (t=0.196 P=0.84).

DISCUSSION

Vitamin D deficiency prevails in epidemic proportion all over Indian subcontinent. With prevalence [9] of 70% -90% in general population in India. This prevalence is remarkably high. Several studies have shown that vitamin D may play a role in many biochemical mechanisms in addition to bone and calcium metabolism [10]. The role of vitamin D as an immune modulator has been emphasized in recent years, and low levels of hormone were observed in several autoimmune diseases including multiple sclerosis [11], SLE [12], type1 diabetes mellitus, rheumatoid arthritis. Most effects of vitamin D are mediated via vitamin D3 receptor (VDR).The immune modulator properties of vitamin D are ascribed to its effect on T and B lymphocytes, all of which harbors VDRS. Low vitamin D may increase the degree of autoimmunity and subsequently increase the prevalence of autoimmune diseases (AITDs) [13]. Thyroid diseases are among the most common endocrine abnormalities. The pathogenesis of AITDs, like other autoimmune diseases are multifactorial, combining genetic, immune, environmental and hormonal influences such as vitamin D. As few studies have focused on investigating the correlation between vitamin D status and hypocalcaemia in hypothyroid patients, we proposed in this study to investigate the prevalence of vitamin D and calcium deficiency in hypothyroid patients. In our study population the mean age was 42.6 years and there were more females (57%) than males (43%) though the difference was statistically non significant. Other studies Dong yebo shin etal [14] did show the fact that vitamin D deficiency and AITD are predominantly found in women and it do signifies a certain association between these two condition. However R Heshmat et al [15] studied the prevalence of vitamin D in Tehran and found non significant difference between males and females. We also reported statistically significant negative correlation between 25(OH) vit D levels and levels of TSH. The patients in hypothyroid group showed markedly lower levels of 25(OH) vit D compared to healthy controls. The levels of serum calcium in hypothyroid group was also markedly lower when compared to controls. The results are in agreement with previous studies of kivity"s et al [6] that reported a correlation in vit D deficiency to presence of abnormal thyroid function and significantly low levels of vitamin D in patients of AITDs. The findings are also in harmony with the results of AMH Mackawy et al [16] (2013) in which they noted the association of lower levels of serum calcium along with vit D deficiency in hypothyroid patients. Following mechanism may explain low levels of vit D in patients with hypothyroidism. Active forms of vitamin D prevent the development of autoimmune diseases. It suppresses autoimmune disease pathology by regulating the differentiation and activity of CD 4+ T cells resulting in a more balanced T1/T2 response favouring less development of self reactive T cell and autoimmunity. As immune modulator[17] vitamin D reduces activation of the acquired immune system. In a study in Theran, Mansournia et al [18] showed that 5 ngm/ml increase in levels of vitamin D. The risk of occurrence of Hashimotos thyroiditis would be decreased by 17%.We also noted in our study that the levels of serum calcium were lower in hypothyroid group when compared to controls. Studies Hassan et al [19] have also shown such result. Thyroid hormones are believed to influence calcium metabolism. In hypothyroid patient there can be decrease in blood calcium levels because of impaired mobilization of calcium into bones. A significant decrease in ionized calcium and normal total calcium levels in hypothyroid cases were seen in study done by Al- hakeim et al [20].

CONCLUSION

This study concluded that in hypothyroid patients levels of vitamin D and serum Ca^{2+} was decreased compared to control group. These findings may suggest a potential role of 25 OH vitamin D in development of hypothyroidism. This study recommend that patients with hypothyroid disorder need to regularly checked for levels of vitamin D and serum Ca^{2+}. There may be a rationale for recommendation of vitamin D and Ca^{2+} supplementation for hypothyroid patients.

Limitations

Our study population of 30 subjects in each group is comparatively small and the study can be extended to a larger population. The levels of phosphorous, parathyroid hormone and thyroid antibodies were not investigated. Ongoing and future long term randomized control trials are required to determine the role of vitamin D in pathogenesis of hypothyroidism.

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