

ORIGINAL RESEARCH

Association between Vitamin D, Calcium and Thyroid Hormones Levels in Hypothyroid Patients in Tertiary Care Hospital

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ABSTRACT

Background and Objective: Deficiency of Vitamin D is very common and same applies to Hypothyroidism in Indian population, Impact of Vitamin D deficiency on Thyroid functions and data on its effect on patients with hypothyroidism is limited. The present study was conducted in hypothyroid patients to know the relationship between serum Vitamin D and calcium levels with Thyroid hormones. **Materials and Methodology:** Tertiary Care Hospital based study was conducted to estimate and correlate the levels of Serum Vitamin D, Calcium and Thyroid hormones in 30 cases of hypothyroid and controls. Analysis was done using SPSS version 14.0 statistical software. **Results:** There was statistically significant correlation seen between low Vitamin D levels and Low TT3 levels. Serum Calcium levels were low in patients with hypothyroidism. **Conclusion:** Estimation of serum Vitamin D levels and serum calcium levels in Hypothyroid patients may be of significant help as it may suggest requirement of prophylactic supplementation with Vitamin D to reduce the cardiovascular and other risk causing increased morbidity in these patients.

Key Words: Serum Calcium, Vitamin D, Thyroid Hormones, Hypothyroidism

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INTRODUCTION

Vitamin D deficiency is a major global public health problem in all age groups.^[1] Vitamin D plays a very important role in regulating bone metabolism and calcium and phosphorus homeostasis. Vitamin D also has a multitude of non-calcaemic actions and has proven to be not just a simple vitamin but a prohormone with multiple functions in various tissues. This is due in part to the presence of the Vitamin D Receptors in most tissues and cells including the skin, skeletal muscle, adipose tissue, endocrine pancreas, immune cells, blood vessels, brain, breast, many cancer cells, and placenta. Vitamin D is a steroid molecule, mainly produced in the skin, which regulates the expression of many genes. It has immunomodulatory and protective effects against cardio-metabolic disorders.^[2] Vitamin D is necessary for the normal functioning of many organs, including the thyroid gland. Vitamin D deficiency has been linked with autoimmune disease and thyroid cancer.^[3]

Hypothyroidism affects up to 5% of the general population, with a further estimated 5% being undiagnosed. Over 99% of affected patients suffer from primary hypothyroidism. The clinical hypothyroidism occurs in 1.5-2% of women and 0.2% of men.^[4,5]

Most importantly, both vitamin D and thyroid hormone bind to similar receptors called steroid hormone receptors. A different gene in the Vitamin D receptor has been shown to predispose people to autoimmune thyroid disease including Graves's disease and Hashimoto's thyroiditis. For these reasons, it is important to understand the relation between thyroid hormones and vitamin D. Though there are many studies showing association between the thyroid hormones and vitamin D levels, Association with many autoimmune diseases like Hashimoto's thyroiditis, Graves's disease, Rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), inflammatory bowel disease

(IBD), multiple sclerosis (MS) and type 1 diabetes (T1DM) is well known.^[2] However Conclusions have not been drawn about their association. Hence many studies from different centres may be required to draw the conclusion. The current study was therefore undertaken to study the association of hypothyroidism with Vitamin D levels in our population in a tertiary care centre having known that it is a public health problem and carries risk for cardiovascular and many more diseases.

AIM AND OBJECTIVES

The aim and objective of our study was to understand the relationship between thyroid hormones and serum vitamin D levels and to know if association between serum calcium levels and hypothyroidism.

MATERIALS AND METHODOLOGY

The study was conducted from January to April 2024. All the subjects were enrolled from out-patient section at Kamineni Hospitals Ltd, Hyderabad. The present study (case-control) was conducted on 30 patients who were diagnosed as hypothyroid clinically (Group 1). They were compared with 30 age and sex matched controls (Group 2) who underwent routine health check-up. All patients and controls were > 15yrs age. Cases included patients newly diagnosed as hypothyroidism based on clinical and laboratory diagnosis. Controls included health check-up patients without any known chronic illness or family history of thyroid diseases. Any individual who is already on treatment for hypothyroidism or diagnosed with diabetes, hepatic or renal disorders, metabolic bone disease, malignancy, pregnancy, lactation, or having medications altering bone metabolism and joint

diseases were excluded from study. Informed consent was obtained from all the individuals who were enrolled and institutional ethical committee approved the study.

The main objective of the study was to compare the serum Vitamin D levels and calcium levels between cases and controls and to correlate the levels of thyroid hormones with Vitamin D and calcium levels. Serum samples were obtained to perform the thyroid function tests including T3, T4 and TSH along with 25 Hydroxy vitamin D and calcium levels under aseptic precautions. Thyroid function tests and 25 OH Vitamin D were tested with CLIA Method on Beckman Coulter Access 2 Immunoassay analyser and Serum Calcium was performed by Arsenazo III method Beckman Coulter AU 480 Chemistry analyser. The socio demographic data obtained were tabulated. The data was statistically analysed using SPSS version 14.0. The correlation between various parameters in the groups was analysed using student's T test and p value was considered statistically significant if <0.05.

RESULTS

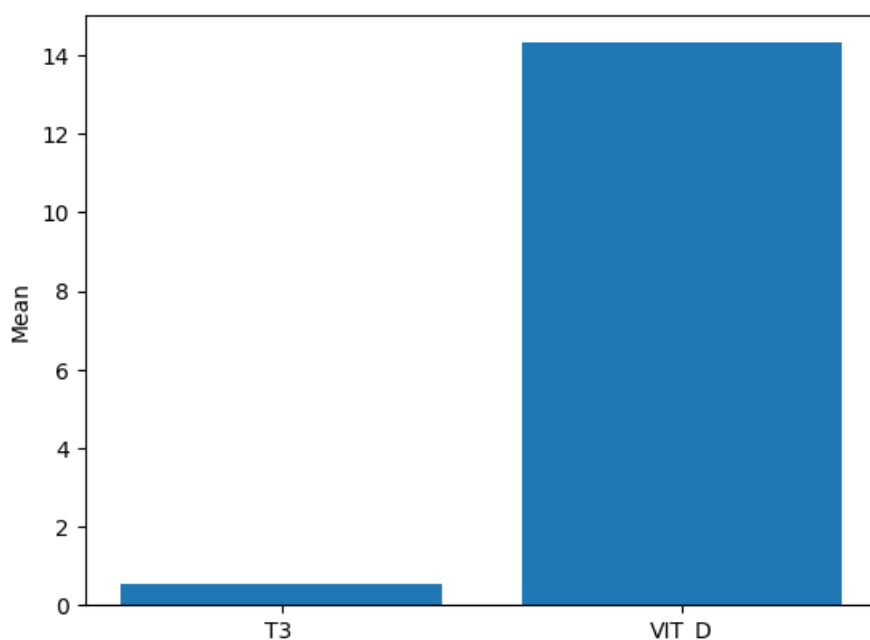
The mean age of study population was 44.9± 8.5 years in Group 1 (Case) and 45.7±7.2 years Group 2 (Control). The Mean values of T3, T4 and TSH among controls were 1.22±0.36, 9.53±3.56 and 2.49± 2.08 respectively and in hypothyroid cases it was 0.55±0.32, 4.22±1.8 and 9.54±5.0 respectively. The serum 25 OH Vitamin D levels and serum calcium levels among controls was observed to be 44.7±20 and 9.67±1.0 respectively and among cases it was 14.3±6 and 7.56±1.0 respectively (Table 1).

Table 1: Showing Comparison between cases and controls demographic and biochemical parameters

Parameters	Group I (n=30)	Group II (n=30)	t value, p value
Age (in years)	44.9±4.25	45.73±3.63	t = -0.81, p= 4.18
Gender	Male:12 (40%) Female :18 (60%)	Male:16 (53%) Female:14 (47%)	t = 0.25, p= 7.97
T3 (ng/ml)	0.55±0.16	1.22±0.18	t = -14.71, p= 3.03
T4 (µg/dl)	4.22±0.9	9.53±1.78	t = -14.54, p= 5.22
TSH (mIU/mL)	9.54±2.5	2.49±1.04	t = 14.21, p= 1.50
Calcium (mg/dl)	7.56±0.53	9.67±0.53	t = -15.35, p= 4.24
25 OH Vit D (ng/ml)	14.31±3.73	44.71±10.56	t = -14.85, p= 1.96

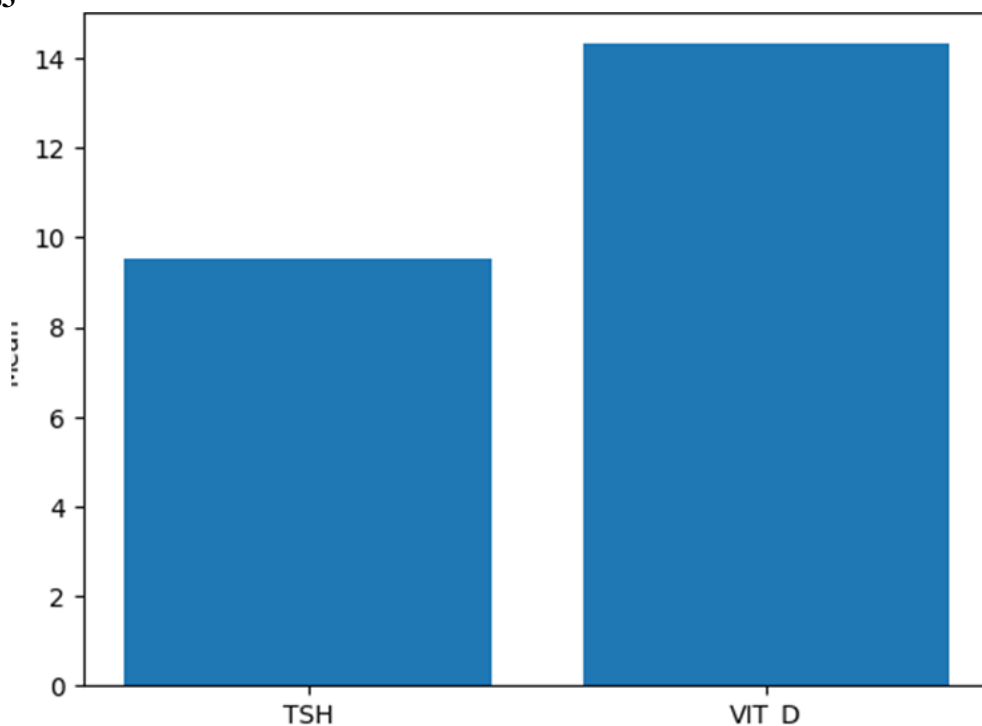
This showed that mean calcium and vitamin D levels were significantly low in cases of hypothyroid as compared to controls. The comparison and correlation between the Thyroid function tests and Vitamin D as well as Calcium was analysed using students independent 2 sample t test to know the association between the variables. It was observed that statistically significant correlation (p <0.05) was seen between low Total T3 and low Vitamin D levels with positive correlation (Graph 1).

Graph 1: Showing comparison between Total T3 and 25 OH Vitamin D levels Correlation coefficient:0.38, p value:0.04



Low Total T3 was associated with low serum calcium levels but it was not statistically significant. Low Vitamin D levels as well as low calcium levels positively correlated with low Total T4 levels but was not found to be statistically significant. High TSH levels negatively correlated with low Vitamin D levels but was not statistically significant (Graph 2).

Graph 2: Showing comparison between TSH and 25 OH Vitamin D levels Correlation coefficient: -0.04, p value:0.83



DISCUSSION

Vitamin D is a fat-soluble vitamin mainly synthesised in the body on exposure to UV light as vitamin D3. Vitamin D is a fat-soluble nutrient that is canonically converted *in vivo* to active hormone (calcitriol or 1,25-dihydroxycholecalciferol) following two

hydroxylation steps, first in the liver (calcitriol or 25-hydroxy vitamin D), and second in the kidneys. Many studies have shown vitamin D deficiency with autoimmune thyroiditis. In one of the studies, 72% of subjects with autoimmune thyroid disease were deficient in vitamin D, whereas just under 31% of

healthy subjects had low levels of vitamin D. In another study^[6] people in Greece with Hashimoto's thyroiditis revealed that more than 85% of them had low levels of vitamin D, as well as high levels of anti-thyroid antibodies. In yet another study^[7,15,16] people with hypothyroidism who took extra vitamin D supplements for 12 weeks had improvements in blood levels of thyroid stimulating hormone (although the extra vitamin D did not affect levels of the actual thyroid hormones triiodothyronine, T3, and thyroxine, T4). Analogous to many other studies we observed that in our patients with hypothyroidism, Low vitamin D levels were observed and its association with Low Total T3 was statistically significant indicating low active form.

There are two main reasons for decreased vitamin D levels in hypothyroidism. Firstly, poor absorption of vitamin D from the intestine may be the cause. Second, the body may not activate vitamin D properly.^[8] Vitamin D deficiency has also been associated with clinical atherosclerosis in coronary calcification as well as with cardiovascular events such as myocardial infarction, stroke, and congestive heart failure.^[9] Thyroid hormones have a variety of effects on the cardiovascular system that can greatly impact cardiac function. We also observed a significant difference in serum calcium levels between the studied groups with lower level seen in hypothyroid patients in comparison to others. Low calcium may be due to altered calcium homeostasis due low vitamin deficiency. However, it is still not sure if Vitamin D deficiency is due to hypothyroidism or low vitamin D affects thyroid function. This requires larger population studies to understand the molecular basis of its association. A study^[10] showed significant changes in ionized Ca, but not total Ca means that the physiologically active form of Ca is affected, while the overall concentration of Ca is still significantly unchanged.

In observational studies, significant inverse associations of blood pressure with dietary intake of magnesium (Mg), potassium, Calcium (Ca), fibre and protein have also been reported. Several experimental and clinical studies suggest that Ca depletion elevates blood pressure. Although the changes in these analytes may not be severe in acute stages but it is possible that these disturbances will affect patient in the long term.^[10,14] Serum Calcium in hypothyroidism is believed to be connected with hypertension and heart muscle. In our study we observed high TSH and low T3 and T4 were associated with low serum calcium levels. Segal study has provided conclusive evidence for two central issues: That Calcium is the first messenger for the plasma membrane-mediated action of thyroid hormone to increase cellular sugar uptake, and that thyroid hormone produces an acute increase in Calcium uptake by the heart, an effect that is demonstrable at physiological concentrations and, therefore, points to a physiological relevance for this action. Calcium influences hypertension through the

fact that, Calcium load leads to the increment in Na excretion and a reduced sodium intake reduces Ca excretion and vice versa and hence decrease in hypertension.^[10-13]

Limitations: A larger sample size would yield better information as to whether vitamin D deficiency is a casual factor in the pathogenesis of hypothyroidism or rather a consequence of the disease. reflecting the population. Analysis of other parameters like Parathyroid hormone and magnesium and Free thyroid hormones would be helpful in concluding. Also, it is ideal to do prospective experimental clinical studies by follow-up of patients on vitamin D and calcium supplementation and observe the Thyroid hormonal changes.

CONCLUSION

The results of our study on hypothyroid patients suggested association with Vitamin D deficiency and hypocalcaemia. This association warrants the prophylactic treatment in the form of vitamin D supplementation for all hypothyroid patients as it carries cardiovascular and other risk, thereby increasing the morbidity. Screening for Vitamin D deficiency and serum calcium levels recommended for all hypothyroid patients.

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