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A STUDY OF VITAMIN D LEVELS IN HYPOTHYROID PATIENTS, A CASE CONTROL STUDY IN A TERTIARY CARE HOSPITAL OF CENTRAL INDIA

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Abstract:

Background: Role of vitamin D in bone and mineral homeostasis has been well established. Both Vitamin D and thyroid hormone act through steroid receptors and may affect each other's action as they have similar response elements on genes. It is still unclear if any association exists between hypothyroidism and Vitamin D insufficiency.

Aim: The aim of the study was to estimate the levels of vitamin D in the hypothyroid patients so as to establish a correlation between TSH and Vitamin D levels in hypothyroidism.

Methods: A total of 90 subject's age group between 25-65 years were included in the study. Levels of Vitamin D and Thyroid Stimulating Hormone (TSH) were measured. Statistical analysis was done by suitable SPSS software. Mean ± SD of Vitamin D and TSH were calculated in all cases. Quantitative data was assessed using independent sample student's t-test. An association between study variables was assessed using Pearson's correlation analysis. Differences were considered statistically significant at $p<0.05$.

Results: We observed that 25(OH) Vitamin D levels were significantly lower in hypothyroid patients (19.2 ± 1.40 ng/ml) compared to controls (28.4 ± 1.36 ng/ml), $p < 0.001$. A negative and significant correlation was observed between 25(OH) Vitamin D and TSH levels ($r= -0.45$, $p < 0.001$). In females, negative correlation between vitamin D and TSH was statistically significant ($p=<0.01$).

Conclusion: Our study concludes that patients of hypothyroidism suffered from hypovitaminosis D which encourages the supplementation of Vitamin D supplements in hypothyroid patients and screening of Vitamin D levels in hypothyroid patients.

Key words: - Vitamin D; Thyroid Stimulating Hormone (TSH); Hypothyroidism.

Introduction

Vitamin D deficiency is a global health problem. Over a billion people worldwide are vitamin D deficient or insufficient.[1] Though initially thought to be uncommon, the reported prevalence of Vitamin D insufficiency in India is around 50-90 %.[2] Despite enough sunshine, this unexpected insufficiency of Vitamin D levels among Indians has become a matter of concern.[3] Besides the well known role in skeletal system, its role has recently been implicated in cardiovascular system, cancer and several autoimmune disorders including Diabetes mellitus.[4-6] Vitamin D is a steroidal hormone,

introduced in the body through food, but major synthesis occurs through exposure of skin to solar ultraviolet light. Vitamin D obtained from skin or diet, is converted by the liver to 25(OH) D and is metabolized in the kidneys by the enzyme 25-hydroxyvitamin D-1α-hydroxylase (CYP27B1) to its active form 1,25-dihydroxyvitamin D.[7] Vitamin D mediates its effect through binding to vitamin D receptor (VDR), and activation of VDR-responsive genes.[8,9] Initially thought to be vitamin just regulating calcium homeostasis, research has shown that this steroid hormone affects more than 36 cell types which possess VDR including thyroid gland, it also has a role in regulating cell proliferation and differentiation.[10] Vitamin D exerts its metabolic effects on skeletal, cardiovascular and reproductive systems. So, a lower level of Vitamin D is likely to aggravate the systemic abnormalities associated with hypothyroidism.[11,12]

Hypothyroidism is defined as a deficiency of thyroid activity. It results from reduced secretion of both T4 and T3. Biochemically decrease in T4 and T3 concentrations lead to hyper secretion of pituitary TSH and an amplified increase in serum TSH levels.

Serum concentration of 25(OH) D is the best indicator of vitamin D status. It has a half life of 15 days. Whereas, circulating 1,25(OH)D is not a good indicator of Vitamin D status due to its short half life of 15 hours and its level being regulated by parathyroid hormone, calcium and phosphate.[13]

Levels of vitamin D more than 30ng/ml is considered to be normal, levels of 20-29ng/ml (< 50nmol/L) is insufficient and if it is less than 10ng/ml (12.5nmol/L) signifies severe deficiency.[14] It is still unclear if any association exists between hypothyroidism and Vitamin D insufficiency. The aim of the present study was to estimate serum 25(OH) Vitamin D concentrations in newly diagnosed hypothyroid patients & healthy controls and correlate their levels with serum Thyroid stimulating hormone in a central Indian population.

Material and Methods

This analytical study to evaluate the vitamin D levels of hypothyroid patients was conducted in the Department of Clinical Biochemistry of a tertiary care hospital & Central Lab Indore (M. P.). We enrolled 90 subjects after an informed written consent. This study was approved by institutional ethics committee. Case group was formed by 45 patients (age group: 20-65 yrs) of recently diagnosed hypothyroidism selected from the hospital medical OPD with patients from different regions of central India. Clinically newly diagnosed hypothyroid patients of both sexes, ages between 20 to 65 years, with no history of thyroxine and hypolipidemic drugs in the last 3 (three) months were included in the study. Patients with chronic renal failure, diabetes mellitus, liver diseases, pregnancy and age less than 20 and more than 65 years were excluded. Subjects receiving drugs known to affect lipid metabolism were also excluded from the study.

Control group consisted of apparently healthy volunteers of comparable age group and gender (n=45). None of them had any history of intake of dietary supplements or thyroid disorder related drugs. All subjects underwent the same protocol.

Table 1
Biochemical characteristics in study population

Parameters	Case	Control	p value
Vitamin D (ng/ml)	17.2±1.40	28.4±1.36	< 0.001*
TSH (µIU/ml)	11.21±0.84	3.05±0.16	<0.001*

*p value < 0.05 is considered statistically significant

Table 2:
Correlation of vitamin D with TSH in hypothyroid patients

		TSH (µIU/ml)
Vitamin D (ng/ml)	Pearson correlation Coefficient(r value)	-0.45
	P value	<0.001

Gender-wise correlation study showed a statistically significant negative correlation between vitamin D and TSH (r = -0.57, p = < 0.01) in females.

Table 3:
Correlation of vitamin D with TSH in hypothyroid female patients

		TSH (µIU/ml)
Vitamin D (n=28)	Pearson correlation Coefficient(r value	-0.57
	P value	<0.01

Collection and preparation of sample

Fasting venous sample was collected under sterile conditions. Fresh serum samples were taken, Serum was checked for hemolysis and if hemolyzed then that serum was discarded. There after the samples were analyzed for TSH using chemiluminescence immunoassay by (Architect I 1000 SR Abbott.) and Vitamin D levels were assayed using ELISA (Enzo Life Sciences) with a sensitivity of 1.98 ng /ml & inter assay CV of less than 10%.

Statistical analysis

Data was maintained on excel spread sheet. Analysis was performed using SPSS software. Descriptive data were expressed as mean and standard deviation of all variables. Quantitative data was assessed using independent sample student's t-test. An association between study variables was assessed using Pearson's correlation analysis. Differences were considered statistically significant at $p<0.05$.

Results

The baseline characteristics of the two groups were comparable with respect to age and sex. Biochemical analysis shown in Table 1: revealed that serum TSH levels were significantly higher in cases (11.21±0.84 µIU /ml) as compared to controls (3.05±0.16 µIU/ml). Mean levels of serum 25 (OH) vitamin D in hypothyroid patient group was (19.2±1.40 ng/ml) compared to controls (28.4±1.36 ng/ml).

As observed in Table: 2, Pearson's correlation analysis depicted a significant and negative correlation between levels of 25(OH) Vitamin D and TSH ($r= -0.45$, $p < 0.001$). Most of the hypothyroid patients had serum 25(OH) Vitamin D levels below 20ng/ml.

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.[15] However, data from epidemiologic studies in India are still limited.

Low levels of 25(OH) Vitamin D is now a commonly accepted finding in central Indian population and overt deficiency has often been associated with a number of clinical disorders. We observed in this study that vitamin D does have a role to play in hypothyroidism as a significant correlation was found between serum TSH levels and serum 25(OH) Vitamin D levels even though a causal relationship could not be established. In this study, the hypothyroid patients had significantly lower levels of serum 25(OH) Vitamin D as compared to controls ($p <0.001$). One of two mechanisms may explain the low levels of vitamin D in patients with hypothyroidism. First, low levels of vitamin D may be due poor absorption of vitamin D from the intestine. Secondly, the body may not activate vitamin D properly.[8] The study by Amal Mackway et al also goes in favour of our study.[16] In the developing country like India, females generally suffer from hypovitaminosis, in which vitamin D deficiency is more frequently seen. 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.

We observed a negative correlation of serum 25(OH) Vitamin D levels with TSH in hypothyroid patients on Pearson's correlation analysis ($r= -0.45$, $p<0.001$) suggesting an inter relationship that exists between vitamin D insufficiency and hypothyroidism. It also states of a putative role of vitamin D as a potential modifiable risk factor for hypothyroidism. In order to function, vitamin D must bind to its receptor VDR which is found in several cell types including thyroid gland.[17] Studies have shown that patients of autoimmune thyroid disease have several VDR polymorphisms that affect its expression and activation.[18] So probably vitamin D plays a role in maintaining a euthyroid state by interacting with its receptor in the thyroid gland.

In an experimental study by Byron Richards (2008) studied the effect of vitamin D deficiency on thyroid gland, he reported that a lack of vitamin D contributed to the possibility of low thyroid hormones.[19] The significant negative correlation between Vitamin D and TSH indicates the association between TSH and Vitamin D.

Conclusion

Our study concludes that patients of hypothyroidism suffered from hypovitaminosis D which encourages the supplementation of Vitamin D supplements in hypothyroid patients and screening of Vitamin D levels in hypothyroid

patients. Further, large scale prospective studies will be required to establish a cause and effect relation of vitamin D deficiency in pathogenesis of hypothyroidism.

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