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Original Research Article

Serum Vitamin D profile in overt hypothyroid patients: A case-control study from a tertiary care hospital

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Abstract

Introduction: Vitamin D receptors present in the thyroid tissue have a direct regulatory role in thyroid hormone synthesis and function. This study is to compare the levels of Vitamin D3 in hypothyroid and euthyroid subjects.

Materials and Methods: After obtaining ethical clearance, 65 subjects with a definite diagnosis of hypothyroidism from medicine or surgery outpatient departments and 65 euthyroid subjects underwent Vitamin D3 estimation at a tertiary care hospital."Endocrine Society Clinical Practice Guidelines" defines vitamin D deficiency (VDD) as levels<20 ng /ml. Statistical analysis was done using SPSS software and mean values of both groups were compared with student T test and correlation using Pearson's coefficient.

Results: Group-1 consisted of 65 hypothyroid subjects (20 males and 45females) with thyroid stimulating hormone (TSH) values over 10 µIU/ml with mean age of 42.66 ± 9.40 years. Group-2 consisted of 65 euthyroid subjects (23males and 42 females) who were matched for age and sex with mean age of 41.41 ± 9.02 years. T3, T4 and Vitamin D3 levels were significantly lower while TSH levels were significantly higher in the case group. On analyzing the correlation between the thyroid profile and vitamin D3 levels, it was found that there was significant negative correlation between TSH and Vitamin D3 levels. (Pearson's correlation coefficient -0.491, with p value <0.001).

Conclusion: The statistically significant low levels of Vitamin D3 in the case group emphasizes the need to routinely do Vitamin D3 estimation in hypothyroid subjects as well as to check thyroid function tests in all cases with low Vitamin D3 levels

Keywords: Vitamin D3, Hypothyroidism, Thyroid Stimulating Hormone (TSH)

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1. Introduction

Cholecalciferol, or vitamin D3 is synthezised from cholesterol found beneath the skin upon sun exposure.[1] Vitamin D receptors present in various human organs play a significant role in ion homeostasis, cell division, proliferation and immunological responses.[2] The receptor for 1, 25 (OH) 2D (VDR) is a transcription factor that regulates gene expression and mediates biological activity. VDR is a member of a large family of nuclear hormone receptors which includes the receptors for glucocorticoids, mineralocorticoids, sex hormones, thyroid hormone, and vitamin A metabolites or retinoids.[3]

A level of 25(OH) D3 > 30 ng/ml is considered adequate; however, a level of 20–29 ng/mL is considered inadequate and a level of less than 20 ng/ml is considered evidence of deficiency of vitamin D3.[4] Low serum 25-hydroxy vitamin D3 levels are common in both industrialized and developing nations.[5]

One of the most vital organs in the body, the thyroid gland, also has vitamin D receptors. The thyroid hormone receptor and the thyroid-vitamin D receptor are members of the large class of receptors known as nuclear receptors.[6] Autoimmune diseases including rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, type 1 diabetes mellitus and autoimmune thyroid diseases are closely linked with low vitamin D levels.[6]

The main thyroid hormones in circulation are triiodothyronine, thyroxine, and their free versions, free T4 and free T3.[8] Hypothyroidism can clinically manifest with no obvious symptoms to potentially fatal issues.[9]

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Iodine deficiency causes hypothyroidism which is more common in areas with low iodine content in the soil. Iodine-rich areas are more likely to have autoimmune diseases such as Hashimoto's thyroiditis.[10] A variety of clinical presentations, including euthyroid, subclinical and frank hypothyroid states with or without visible goitre are seen in individuals with Hashimoto's thyroiditis.[11]

According Goswami etal, autoimmune hypothyroidism was estimated to be the most common endocrine condition affecting the Indian population.[12] Other causes include previous thyroid surgery, medication like radioactive iodine treatment or nonfunctioning thyroid since childhood.[13]

According to a meta-analysis that assessed vitamin D levels in autoimmune thyroid diseases, low vitamin D levels were observed in Hashimoto's thyroiditis and Grave's disease.[14]

On the other hand, some studies failed to reveal any conclusive link between vitamin D and autoimmune thyroiditis.[15]

The present study aims to explore the correlation of Vitamin D3 levels in patients with hypothyroidism.

2. Materials and Methods

The study included patients attending the Medicine and Surgical Outpatient departments of a tertiary care centre. The study was conducted over a 3-month period after obtaining ethical clearance from the Institutional Ethics Committee of the concerned hospital. The study design was of cross sectional case control type on a sample size of 130 patients with the study tool being a pre-designed, semi-structured questionnaire taking into account the demographic details and complete medical history. Vitamin D3 and Thyroid Function tests (TFTs) in cases and controls were estimated using the Chemiluminescent Microparticle Immunoassay (CMIA) technique on the Abbott ARCHITECTi8200 system.

After obtaining written consent from the patient(s), the research related laboratory investigations were conducted and the data entered in Microsoft Excel. Further the statistical analysis was conducted using SPSS version 26.

The study was conducted in case control manner by analyzing 65 cases of hypothyroidism and 65 control samples of euthyroidism. The following inclusion and exclusion criteria were followed:

2.1 Inclusion criteria

Cases included patients with a diagnosis of hypothyroidism and controls were euthyroid subjects who gave consent to take part in the study.

2.2 Exclusion criteria

Patients who had other medical illnesses, those on Vitamin D supplements, corticosteroids, anticonvulsants or other medication affecting Vitamin D metabolism were excluded. In addition bedridden patients, deaf and mute persons, pregnant women, subjects below 18 years and those who refused to give consent were excluded.

For this study, "Endocrine Society Clinical Practice Guidelines" were followed, which defines vitamin D deficiency (VDD) as levels<20 ng /ml.[16] Serum vitamin D3 levels equivalent to or over 30 ng/ml were considered adequate. However serum vitamin D3 levels between 20 and 30ng/ml were considered insufficient and levels under 20 ng/ml. as Vitamin D deficient. Serum vitamin D level under 4.2 ng/ml was considered as Severe Vitamin D deficiency.[16]

3. Results

The study population consisted of 130 individuals divided into 2 groups. Group-1 consisted of 65 hypothyroid subjects (20males and 45 females) with TSH values over 10 µIU/ml who had mean age of 42.66 ± 9.40 years and Group-2 consisted of 65 euthyroid control subjects who were matched for age and sex (23 males and 42 females) who had a mean age of 41.41 ± 9.02 years. (**Table 1**).

Table 1: Demographics *(*Age and Sex) of the study population

	Group 1 (n=65)	**Group 2 (n=65)**	**p value**
Age (years)	42.66 ± 9.40	41.41 9.02	0.348
Sex (M/F)	20 / 45	23 / 42	0.576

It was found that females were predominant in the hypothyroid group with M:F ratio of 1:2.25. (**Figure 1**). It was noted that the age and sex difference in the case and control population were not statistically significant.

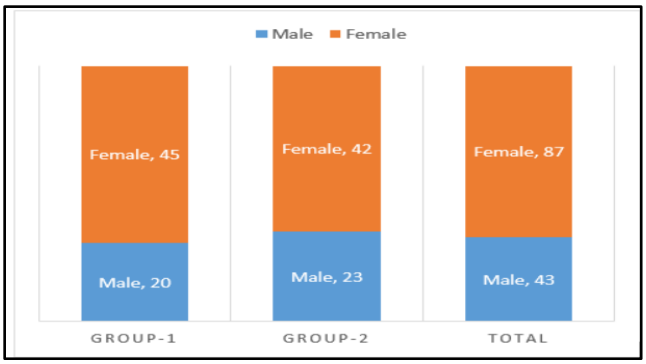

Figure 1: Sex distribution of study subjects.

The distribution of the study subjects based on their Serum Vitamin D levels are shown in **Figure 2**.

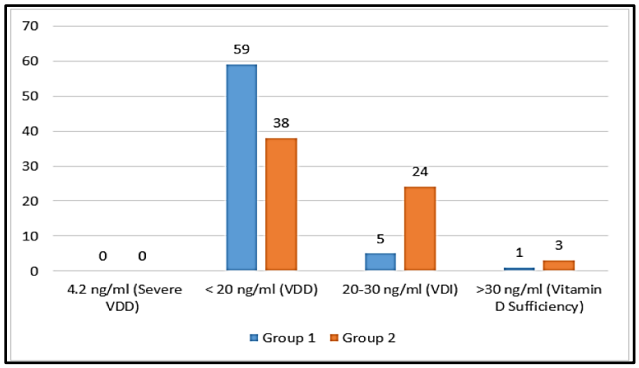

Figure 2: Stratification of cases (Group1) and controls (Group2) as per Vitamin D levels.

The subjects were divided into 4 categories based on their serum Vitamin D levels. It was found that there were statistically significant differences between the case and control groups with regard to their serum vitamin D levels (**Table 2**).

Table 2: Serum Vitamin D levels in cases and controls

Vitamin D level (ng/ml)	Group 1 (Case, n=65)		Group 2 (Control, n=65)	
	Frequency	%	Frequency	%
≤ 4.2 (Severe VDD)	0	0.00	0	0.00
<20 (VDD)	59	90.77	38	58.46
20-30 (VDI)	5	7.69	24	36.92
>30 (Vitamin D Sufficiency	1	1.54	3	4.62

It was noted that the hypothyroid case population had a statistically significantly lower mean vitamin D level than the euthyroid control population as shown in **Figure 3**. Independent sample t-test showed p value- <0.001 (Highly significant).

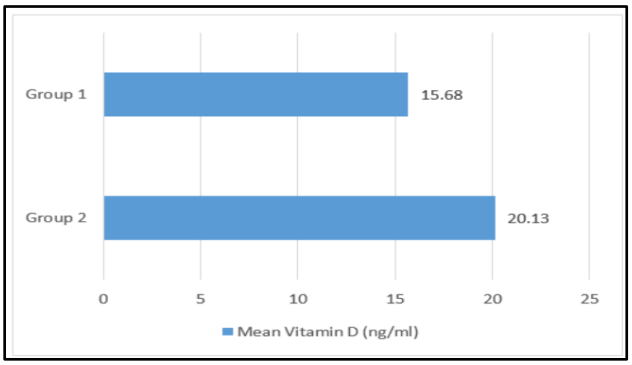

Figure 3*:* Mean value of Vitamin D in *hypothyroid and euthyroid groups.*

Table 3: Comparison of thyroid profile and Vitamin D levels in case and control groups

	Group 1 (Case, n=65)	Group 2 (Control, n=65)	p value
	Mean ± SD	Mean ± SD	<0.001
T3 (ng/ml)	0.75 ± 0.31	1.11 ± 0.28	<0.001
T4 (µ/dl)	5.29 ± 1.96	8.57 ± 1.82	<0.001
TSH (µIU/ml)	29.88 ± 30.75	2.74 ± 1.32	<0.001
Vitamin D (ng/ml)	15.68 ± 5.07	20.13 ± 5.88	<0.001

On analysing the correlation between the thyroid profile and vitamin D levels (**Table 4**), it was found that there was significant negative correlation between TSH and Vitamin D levels. (Pearson's correlation coefficient -0.491, with p value <0.001). T3 and T4 showed positive correlation with Vitamin D levels but were not statistically significant.

Table 4: Correlation between Vitamin D level with thyroid profile in hypothyroid group

TSH (µIU/ml)	Pearson Correlation	-.491**
	Sig. (2-tailed)	.000
	N	65
T3 (ng/ml)	Pearson Correlation	.015
	Sig. (2-tailed)	.906
	N	65
T4 (µ/dl)	Pearson Correlation	.185
	Sig. (2-tailed)	.140
	N	65
**. Correlation is significant at the 0.001 level (2-tailed).		

The correlation between TSH and Vitamin D level has been shown in **Figure 4**.

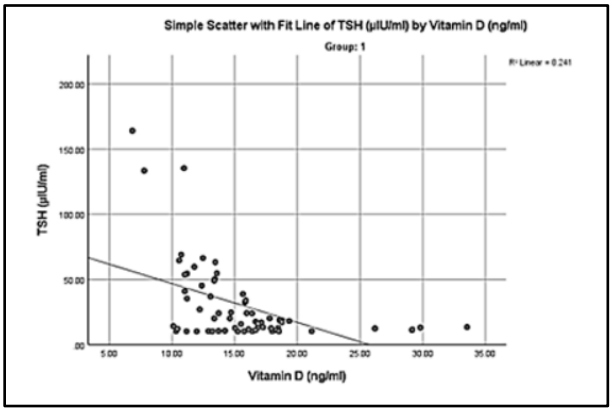

Figure 4*:* Correlation between Vitamin D and TSH levels in Hypothyroidism.

4. Discussion

The mechanisms underlying the correlation between vitamin D and hypothyroidism are multifaceted. Additionally, vitamin D deficiency has been linked to insulin resistance and metabolic syndrome which are risk factors for thyroid dysfunction. Conversely, thyroid hormones are crucial for the activation and metabolism of vitamin D, potentially exacerbating deficiency in hypothyroid patients.[17]

The current study was conducted on a sample size of 130 individuals split up into case and control groups with preselected hypothyroid patients as case group. In the present study, the hypothyroid case population had a statistically significant lower mean vitamin D level than the euthyroid control population.

Similarly, in the study by Mackawy et al, serum 25(OH) D3 levels were tested in 30 hypothyroid patients and 30 healthy individuals. It was observed that hypothyroidism substantially correlated with decreased vitamin D3 levels and hypocalcaemia.[18]

The current study has not focused on subclinical hypothyroid cases and only overt hypothyroid cases were taken into consideration, Ucaret al. in a study conducted in Turkey showed that serum 25(OH) D3 levels in elderly patients with subclinical hypothyroidism were lower than in healthy controls.[19] This gives an added perspective that not only overt hypothyroidism can cause decreased serum vitamin D levels but also sub clinical hypothyroidism.

Present study found a positive correlation between T3 and Vitamin D levels though statistically not significant. However, in a cross-sectional case-control study by Aljohani et al, showed a negative correlation between FT3 and vitamin D levels.[20]

In the study by Mirhosseini et al, serum 25 (OH) D levels above 125 nmol/L showed a 32% lower risk of increased anti-thyroid antibodies and a 30% lower risk of hypothyroidism.[21]

In 2020, Pezeshki et al carried out a pilot randomized clinical trial to examine the effectiveness of vitamin D treatment for subclinical hypothyroidism. The use of vitamin D supplements was found to dramatically lower TSH mean levels by the researchers, highlighting the importance of vitamin D treatment and screening for subclinical hypothyroid people.[22] The findings in the current study also points to an increase in risk factor for decreased vitamin D levels in patients with hypothyroidism. This can be an indicative factor for prophylactically managing expected hypovitaminosis in this risky category of patients.

Vitamin D supplementation is found to reduce antithyroid antibody levels, improve thyroid function and improve other markers of autoimmunity, such as cytokines, e.g., IP10, TNF-α, and IL-10, and the ratio of T-cell subsets, such as Th17 and Tr1.Vitamin D may help control autoimmunity and improve thyroid function by impacting various immunological mechanisms.[23] Current study did not incorporate the causes of hypothyroidism including autoimmune thyroiditis.

4.1 Limitations of the study

A detailed analysis of confounding factors like metabolic syndrome, obesity, sun exposure could not be incorporated in this study. Being a cross-sectional study, the exact onset and duration of hypothyroidism and Vitamin D deficiency also could not be ascertained. However an age and sex matched control group is the major strength of this study

5. Conclusion

The study has been able to further support the correlation between reduced Vitamin D levels and hypothyroidism. Given the critical role that vitamin D plays in preserving health homeostasis, it is imperative that all patients with hypothyroidism undergo routine vitamin D screening. For hypothyroid individuals, regardless of gender, the recommended course of action is to screen for vitamin D deficiency and take vitamin D supplements to raise their blood levels of the vitamin, which in turn helps to improve their thyroid profile levels. Further studies, by taking into account the limitations of this study can help achieve further correlation for medical care improvement in patients with hypothyroidism.

6. Ethical Statement

This protocol was reviewed and approved by the Institutional Ethics Committee. Written informed voluntary consent was obtained from all participants and they were assured of confidentiality and the anonymity of their identity.

7. Funding and Financial

None.

8. Conflict of Interest

None.

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