

A Study on Association of Hypothyroidism and Vitamin D Deficiency

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Abstract

Background and Aim: Hypothyroidism is an important endocrine disorder due to the deficiency of thyroid hormones. Vitamin D (Vit D) a steroid pro-hormone (Cholecalciferol). Both the hormone Thyroxin and Vitamin D shares a common steroid receptor. Vitamin D deficiency is prevalent globally nowadays. Various autoimmune disease also associated with Vitamin D deficiency and Hypothyroidism may be one of them.

Objective: The purpose of this present study was to examine the association of hypothyroidism and vitamin D deficiency or insufficiency in the local population and to find out the relation of Vitamin D level deficiency or insufficiency in relation with Thyroid stimulating hormone (TSH), free T3 (FT3) and free T4(FT4) level.

Method: A one year cross sectional prospective observational study was conducted from June 2021 to May 2022 at Tripura Medical College, Tripura. A total of 100 previously diagnosed adult hypothyroid patients between the age group of 18 to 65 years were included in the study. Serum FT3, FT4, TSH I and serum Vitamin D level were assayed. Results were documented and statistically analyzed.

Result: A statistically significant no of elderly females were found to had Vitamin D deficiency or insufficiency in hypothyroid individual. There is a positive correlation with FT3 and FT4 level with vitamin D and a negative correlation was found between Vitamin D and serum TSH level.

Conclusion: The etiology of hypothyroidism is multi-factorial where vitamin D deficiency may be one of the causes which may be picked up easily and can be corrected.

Keywords: Hypothyroidism, Vitamin D insufficiency, Deficiency.

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Introduction

Hypothyroidism is an important endocrine disorder due to the deficiency of thyroid hormones. This may cause subtle symptoms without any signs or may lead to a very

serious complication like myxedema coma [1]. Permanent loss or destruction of the thyroid, through processes such as autoimmune destruction or irradiation

injury, is described as primary hypothyroidism. Central or secondary hypothyroidism, caused by insufficient stimulation of a normal gland, is the result of hypothalamic or pituitary disease or defects in the thyroid-stimulating hormone (TSH) [2].

Hypothyroidism is defined as high level of serum Thyroid stimulating hormone (TSH) > 5 mIU/L and low level of serum free T4 < 0.8 ng/dl and free T3 hormone < 1.2 pg/ml [3]. The pathophysiological effect of hypothyroidism affects the basic metabolism of human body. Vitamin D (Vit D) a steroid pro-hormone (Cholecalciferol) which is synthesized from cholesterol under the skin of human being on exposure to sun light converted to active form of 1,25, dihydroxycholecalciferol in the kidney. The precursor of active Vitamin D is 25-hydroxyvitamin D {25(OH) D} which can be measured in the serum. Vitamin D deficiency is defined as a serum level of 25(OH) D of ≤ 20 ng/ml and insufficiency as a serum level between > 20 ng/ml and < 30 ng/ml and normal ≥ 30 ng/ml.³ Vitamin D deficiency is globally prevalent nowadays.

Vitamin D plays an important role as immuno-modulator and has anti-inflammatory property apart from its primary function on bone and muscles. Different autoimmune diseases like type 1 diabetes mellitus, SLE, Rheumatoid arthritis are associated with Vitamin D deficiency or insufficiency. Even Hashimoto's thyroiditis also behaves in similar way [4]. Vitamin D and thyroid hormones also bind to a common steroid receptor. Hence, again hypothetically, there may be a common association of Vitamin D deficiency with Hypothyroidism. Furthermore, it was reported by Tamer *et al* in 2011 that patients with Hashimoto's thyroiditis, an autoimmune thyroid disease, had lower Vitamin D levels [5]. Only, few studies were

conducted to find any significant association between the levels of Vitamin D and hypothyroidism and its pathogenesis but yielded conflicting results. The purpose of this present study was to examine the association of hypothyroidism and vitamin D deficiency or insufficiency in the local population and to find out the relation of Vitamin D level deficiency or insufficiency in relation with TSH, free T3 and free T4 level.

Methodology

A one year cross sectional prospective study was conducted from June 2021 to May 2022. A total of 100 previously diagnosed adult hypothyroid patients between the age group of 18 to 65 years were included in the study. Patients with other chronic illness, chronic kidney disease (CKD) and patients who are on Vitamin D supplements were excluded from the study.

A detailed history and clinical examination was performed to identify the signs and symptoms related to hypothyroidism and/or VDD (Vitamin D Deficiency). Thyroid-stimulating hormone (TSH), free T4 (FT4), and 25 hydroxy Vitamin D levels were assayed for each patient. Serum FT3, FT4, TSH estimation of patients were done keeping in mind the normal reference range (1.2 – 4.4 pg/ml for FT3), (0.89 – 2.3 ng/dl for FT4) and (0.5 – 5.0 mIU/L for TSH). Hypothyroidism was defined as high level of serum Thyroid stimulating hormone (TSH) > 5 mIU/L and low level of serum free T4 < 0.8 ng/dl and free T3 hormone < 1.2 pg/ml. Estimation of serum 25 (OH) D levels was done using spectrophotometric method. Vitamin D deficiency (VDD) was defined as a serum level of 25(OH)D of ≤ 20 ng/ml and insufficiency as a serum level between > 20 ng/ml and < 30 ng/ml and normal ≥ 30 ng/ml. The biochemical parameters were assayed in the Department of Biochemistry attached in the institution

itself. Chemiluminescence enzyme immunoassay (CLIA) was used for TSH, FT4 FT3, whereas enhanced CLIA (E-CLIA) was utilized for assaying Vitamin D (total 25 hydroxy-Vitamin D).

Data was analyzed using Statistical Package for social sciences (SPSS INC Illinois, Chicago) version 21.0. Univariate analysis was done and presented as percentage, proportions and figures. The differences between mean values for each tested variable have been tested by student "t" test. The association between serum Vitamin D and TSH level were tested by Chi square

test. p value

<0.05 was considered as statistically significant.

Results

A Total of 100 patients were included in the study. The baseline values of Serum FT3, FT4, TSH and serum 25 (OH) D levels in this current study is presented in the Table-5. Females (n=67 i.e. 62.2%) were more in number than the males (n=37 i.e. 38.8%). Elderly age group of 55 to 65 years (24.5%) were more affected than the younger age group of 25 to 35 years (13.3%) (Table-1).

Table 1: Gender distribution

Gender	Frequency	Percentage
Female	61	62.2%
Male	37	37.8%

Prevalence of vitamin D deficiency was 67.3% with frequency of 66. Prevalence of vitamin D insufficiency was 29.6% with frequency of 29. Only 3.1% of hypothyroid subjects had normal level of vitamin D (Table-2).

Table 2: Age distribution

Age group	Frequency	Percentage
25 – 35	13	13.3%
36 – 45	18	18.4%
46 – 55	22	22.4%
56 – 65	24	24.5%
66 - 75	21	21.4%

In female hypothyroid individuals, vitamin D deficiency was more common in 68.2% (n=45) than insufficiency which was 55.2% (n=16). Again, in male hypothyroid individuals, vitamin D deficiency was 31.8% (21) in comparison to vitamin D insufficiency 44.8% (n=13) (Table-3).

Table 3: Level of Vitamin D

Vitamin D	Frequency	Percentage
Deficiency	66	67.3%
Insufficiency	29	29.6%
Normal	3	3.1%

Vitamin D deficiency and insufficiency both were more common in elderly hypothyroid individuals than to younger age group. (Table-4)

Table 4: Gender and age wise distribution of Vitamin D

Demographic Parameters	Vitamin D		
	Deficiency	Insufficiency	Normal
Gender			
Female	45 (68.2%)	16 (55.2%)	-
Male	21 (31.8%)	13 (44.8%)	3 (100%)
Age group	Deficiency	Insufficiency	Normal
25 – 35	9 (13.6%)	4 (13.8%)	-
36 – 45	8 (12.1%)	9 (31.0%)	1 (33.3%)
46 – 55	15 (22.7%)	6 (20.7%)	1 (33.3%)
56 – 65	15 (22.7%)	8 (27.6%)	1 (33.3%)
66 - 75	19 (28.8%)	2 (6.9%)	-

Baseline values of Thyroid hormones and serum Vit D were depicted in Table 5. Statistically significant correlations of Serum Vit D with Thyroid hormones was observed. (Table 6)

Table 5: Baseline values of Thyroid hormone and 25(OH)D3{Vitamin D}

	Mean	Standard deviation	95% CI
T3	2.33	0.691	2.19 – 2.46
T4	1.38	0.388	1.30 – 1.46
TSH	10.4	8.94	8.65 – 12.2
Vit D	19.4	4.46	18.5 – 20.3

Table 6: Correlation of Vit D with FT3, FT4, TSH level

		FT3 level	FT4 level	TSH
Vit D level	Pearson correlation coefficients	0.622	0.588	- 0.589
	p value	<0.01	<0.01	<0.01

A scatter diagram was plotted which depicted the relation between serum vitamin D and FT3 level which had a moderate positive correlation ($r=0.622$). Again, the relationship between serum vitamin D and FT4 level also had a moderate positive correlation ($r=0.588$) with P value <0.01 which was again statistically significant. (Figure1)(Table 7).

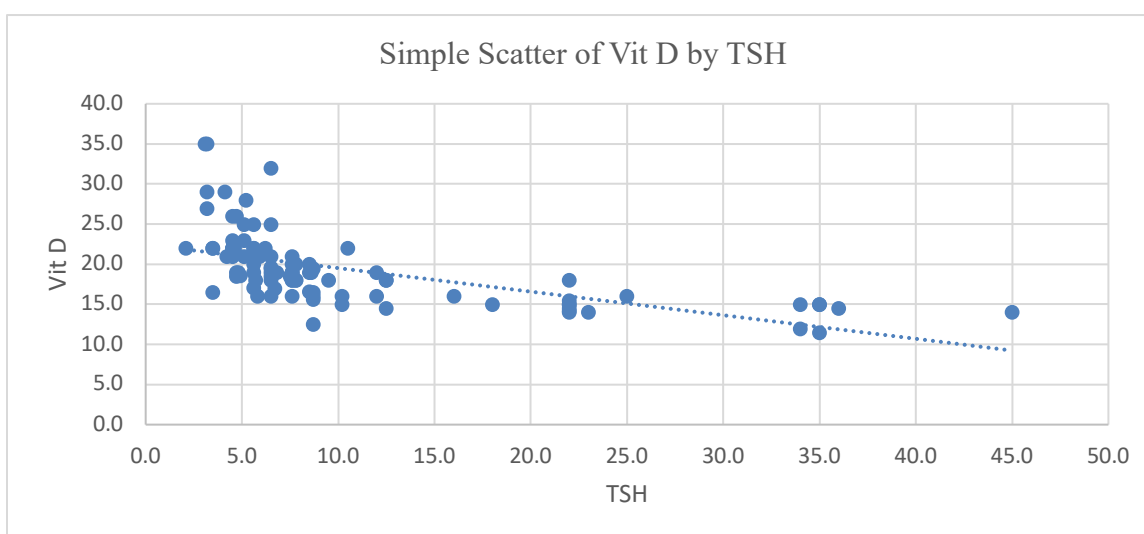


Figure 1: Relation between serum vitamin D and FT3 level

Table 7

Vit D	TSH
Pearson Correlation coefficient	- 0.589
p value	0.00

Another scatter diagram was plotted which showed the relation between serum Vitamin D and TSH had a negative correlation ($r=0.589$) with a P value of <0.01 which was also statistically significant. (Figure 2)(Table8)

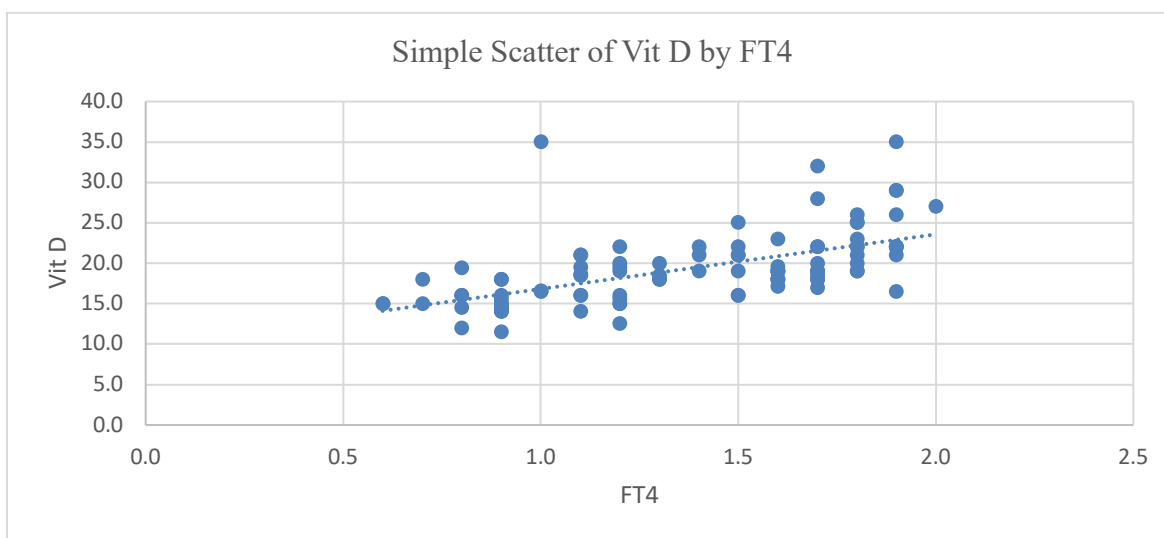


Figure 2: Relation between serum Vitamin D and TSH

Table 8

Vit D	FT4
Pearson Correlation coefficient	+ 0.588
p value	0.00

Discussion

Hypothyroidism remains an important endocrine disorder which causes spectrum of various clinical manifestation and metabolic derangement. It is more prevalent in the elderly individuals and in Sub-Himalayan region. In our study, elderly groups are identified to be more affected by hypothyroidism compared to young subjects. Unlike our study, females' predominance of Hypothyroidism was observed in various studies compare to male [6-10]. So elderly females should be screened

at their middle age for their thyroid hormone status so that it can be corrected promptly.

Vitamin D deficiency or insufficiency is a recognized problem starting from young generation to elderly individuals all over the world probably due to lack of sunlight exposure since young age. It is considered as endocrine disorder and may be associated with other endocrine insufficiency also [11]. Vitamin D plays a pivotal role in human immunity also. Many autoimmune disorders

may have causal association with vitamin D deficiency [4]. Apart from pituitary insufficiency or Iodine deficiency autoimmune disorder also plays an important role in hypothyroidism [4].

Low serum vitamin D level may predispose to autoimmune destruction of thyroid gland [5]. Like other studies, the prevalence of vitamin D deficiency and insufficiency in hypothyroid individuals was comparable in the present study. Again, vitamin D deficiency was more common in females compared to the male counterpart in our study as well as in other studies. This may be because of the fact that females are less exposed to the Sun light compared to the male population since their childhood [11].

Vitamin D deficiency and insufficiency was more common in elderly hypothyroid individual than to younger age group [10]. There is a positive correlation of vitamin D deficiency and insufficiency with serum free T4 level in this present study which was similar to the other Asian and Indian study [8]. Also, there is negative correlation of vitamin D deficiency with serum TSH level in this current study which is observed in other studies [8]. In vitamin D receptor (VDR), and in thyroid receptor an individual gene has been discovered that predisposes individuals to autoimmune thyroid disease [9]. Autoimmune destruction of the thyroid gland, like in Hashimoto's thyroiditis may be one of the important causes for hypothyroidism in elderly people [7]. At the same time, serum vitamin D deficiency is also prevalent in the elderly people [9]. This may lead to the close association of the vitamin D deficiency in this subgroup of population with hypothyroidism. A further study, however, is required to establish the autoimmune mechanism as an etiology for the vitamin D deficiency and hypothyroidism.

The limitation of our study is that it is not a comparative study. This is only an observational study and the sample size is also very less. To know the relationship of autoimmune thyroiditis and vitamin D deficiency in this study, we could not include anti thyroid peroxidase antibody level for better evaluation as the facility was not available in the institution. A large comparative study is required to explore the fact of hypothyroidism and vitamin D deficiency which can be corrected very easily.

Conclusion

The etiology of hypothyroidism is multifactorial where vitamin D deficiency may be one of the causes which may be picked up easily and can be corrected. There is a statistically positive association of Hypothyroidism and vitamin D deficiency.

Correction of vitamin D deficiency in earlier stage may prevent autoimmune thyroiditis and also can prevent various systemic complications out of hypothyroidism.

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