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Original Research Article

Study of Vitamin D Deficiency in Hypothyroidism in a Tertiary Care Centre in Southern Bihar

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Abstract

Aim: To Study vitamin D deficiency in hypothyroidism in a tertiary care centre in southern Bihar.

Methods: This observational study was carried out over a period of 6 months in the Department of General Medicine, Narayan Medical College and Hospital, Sasaram, Bihar, India. This research comprised of 100 patients. They were classified as hypothyroid if their TSH level was greater than 5.0 mU/L and their T3 and T4 levels were lower than normal. Thyroid dysfunction patients' serum T3, T4, and TSH levels with reference ranges (1.2 – 4.4 pg/ml for T3), (0.8 – 2.0 ng/dl for T4), and (0.5 – 5.0 mU/l for TSH).

Results: The mean of all studied parameters, age and sex distribution in all studied groups. Overall mean age of the study population was 47.1 ± 7.29 years. Majority of the patients reported were female (60%). On comparing serum 25 (OH) vit. D levels according to the sex distribution, they were insignificantly decreased in females than those of male hypothyroid patients (t=-0.18, and t=-1.42, P >0.05) respectively.

Conclusion: The patients with hypothyroidism suffered from hypovitaminosis D

Keywords: T3, T 4 , TSH, vitamin D, thyroid dysfunction

Introduction

Vitamin D is a steroid molecule that is mostly generated in the skin and controls the expression of many genes. [1] The vitamin D receptor (VDR) may be found in nearly all tissues and cells in the body. Vitamin D's primary function is to regulate bone metabolism as well as calcium and phosphorus balance. Recent research shows that vitamin D insufficiency, which is widespread throughout the world, may also have a role in autoimmune disorders, malignancies, metabolic syndromes, cardiovascular disease, infection, and all-cause mortality. [1-3] Low vitamin D levels have also been linked to autoimmune thyroid disorders (AITD) including Hashimoto's thyroiditis (HT) and Graves' disease (GD). Thyroid

tumorigenesis has been linked to impaired vitamin D signalling. [4-6] Vitamin D comes in two forms: vitamin D3 (or cholecalciferol) and vitamin D2 (or ergocalciferol). The former is mostly generated in the skin by 7-dehydrocholesterol reductase in response to UVB light and may also be acquired from a few dietary sources (primarily fatty fish), whereas the latter is created by plants and fungi. [7,8] Both forms of vitamin D are taken to the liver and transformed by 25-hydroxylase to 25-hydroxyvitamin D (25(OH)D or calcidiol) (CYP27A1 and CYP2R1). The primary circulating and stored form of vitamin D is 25(OH)D, and blood levels of this form are thought to be the best marker for measuring whole-body vitamin D status. [5,7-9] Although this is debatable, vitamin D deficiency is typically described as a 25(OH)D level of less than 50 nmol/L, and vitamin D insufficiency as 50–75 nmol/L of 25(OH)D. [1,2,10] At normal quantities, 25(OH)D is biologically inactive and must be transformed by 1-hydroxylase (CYP27B1) in the kidneys to the physiologically active form 1,25-dihydroxyvitamin D (1,25(OH)2D or calcitriol). The activity of the 1-hydroxylase enzyme is tightly regulated by PTH and is inhibited by high levels of 1,25(OH)2D and fibroblast growth factor 23. (FGF23). Furthermore, 24-hydroxylase deactivates 1,25(OH)2D. (CYP24A1). [5,7-9] Other cell types, including immune cells, express 1-hydroxylase and can convert dormant 25(OH)D into active 1,25(OH)2D in an autocrine or paracrine way without the aforementioned feedback control. 8 It has been hypothesised that serum 25(OH)D levels are the most important determinant of extra renal 1,25(OH)2D production. Indeed, rather than serum 1,25(OH)2D concentrations, several correlations have been discovered between vitamin D status (reflected by serum 25(OH)D concentration) and extra skeletal health outcomes. 5 Vitamin D is stored in fat cells and released from them, and it is bound to the vitamin D binding protein (DBP). DBP binds around 88 percent of 25(OH)D and 85 percent of 1,25(OH)2D, while albumin binds 12–15 percent of circulating vitamin D, with the free from having better accessibility to target cells. [5] To exercise its effects, the active 1,25(OH)2D form binds to the nuclear vitamin D receptor (VDR), which then acts on the vitamin D response element (VDRE) of target genes. 5 1,25(OH)2D regulates the expression of nearly 200 genes, including those involved in the regulation of cellular proliferation, differentiation, death, and angiogenesis. [2] VDR is expressed and responds to 1,25(OH)2D in a variety of organs, including the brain, prostate, breast, and colon, as well as immune cells. In addition to being a powerful immunomodulator, 1,25(OH)2D inhibits cellular growth in both normal and malignant cells and causes terminal differentiation. [2] A membrane bound VDR may also exist, allowing 1,25(OH)2D to exert more rapid, non-genomic effects. [9,10]

Material and methods

The current prospective study was carried out over the period of 6 months in the Department of General Medicine, Narayan Medical College and Hospital, Sasaram, Bihar, India, with the agreement of the protocol review committee and the institutional ethics committee. This research includes 100 patients.

Routine investigations: Serum T3, T4 and TSH for thyroid dysfunction patients with reference range (1.2 – 4.4 pg/ml for T3) , (0.8 – 2.0 ng/dl for T4) and (0.5 – 5.0 mU/l for TSH). [11]

Research investigations: Estimation of serum 25 (OH) D levels using spectrophotometric method. This method is based on that vit D forms with antimony trichloride in chloroform a pink color that can be read at 500 nm wavelength. [12] Vitamin D deficiency was defined as a serum level of 25OHD of < =20 ng/ml and

insufficiency as a serum level between >20 ng/ml and <30 ng/ml and normal >or=30 ng/ml. [13,14]

Statistical Analysis

SPSS 21.0 for Windows was used to do statistical analysis on the results. For each variable, the mean and standard deviation (SD) were computed. The F test for analysis of variance (ANOVA) was performed to compare the outcomes of all investigated cases in all researched groups. The differences in mean values for each examined variable were assessed using the student's "t" test. Correlation coefficients were used to show the relationships between serum Vit. D, calcium, and TSH (r2). When P> or 0.05, the results are judged significant or non-significant.

Results

Table 1: Demographic profile

Parameters: Mean ± SD		**N=100**	**Age (%)**
Sex	**Male**	40	40%
	Female	60	**60%**
Age (Years)		**47.1 ± 7.29**	

Table 1: The mean of all studied parameters, age and sex distribution in all studied groups. Overall mean age of the study population was 47.1 ± 7.29 years. Majority of the patients reported were female (60%).

Table 2: Mean± SD of serum 25(OH) vit D, Calcium and TSH levels in hypothyroid patients according to sex

Parameters Mean ±SD	**Male =40**	**Female=60**	**t-test /p- value**
25(OH) vit D ng/ml	16.58 ± 2.37	15.27 ±1.99	t= -1.42/p=0.223
Calcium levels (mg/dl)	7.82 ± 2.23	7.79 ±1.45	t= 0.018/p= 0.888
TSH (mU/L)	6.70 ± 1.12	7.15 ± 0.86	t=- 0.525/p=0.587

Table 2 On comparing serum 25 (OH) vit D levels according to the sex distribution, they were insignificantly decreased in females than those of male hypothyroid patients (t=-0.18, and t=-1.42, P >0.05) respectively.

Discussion

Vitamin D is well-known for its major function in bone and mineral homeostasis, and it has recently been shown that a lack of it is linked to a variety of illnesses including cardiovascular disease, cancer, infection, obesity, and osteoporosis. [15] Surprisingly, it has recently been demonstrated that vitamin D has powerful immunomodulatory effects and plays key roles in the development of autoimmune disorders. (12) The greatest measure of vitamin D status is serum 25(OH)D concentration. It has a circulation half-life of 15 days and represents vitamin D generated cutaneously as well as vitamin D acquired through diet and supplements. [16] In contrast to 25(OH)D, circulating 1,25(OH)2D is not a reliable indication of vitamin D status since it has a short half-life of 15 hours and blood concentrations are influenced by parathyroid hormone, calcium, and phosphate. [17] Typically, levels of 1, 25(OH)2D do not fall until vitamin D insufficiency is severe. [18-19] As a result, in the current investigation, we evaluated serum 25(OH)D rather than 1,25(OH)2D to assure more precise findings. Few studies have been done to establish if there is a substantial relationship between vitamin D levels and hypothyroidism and whether vitamin D insufficiency is involved in the aetiology of hypothyroidism or is a result of the condition, and those that generated contradictory results.

Some scholars studied the incidence of vitamin D insufficiency in Saudi communities, but our study was one of only a few that looked at the relationship between vitamin D and calcium levels and hypothyroidism in Saudi Arabia, specifically the Qassim region.

Our findings indicated that females had lower serum 25 (OH) vit D levels than male patients; otherwise, this reduction was non-significant; nevertheless, we can attribute this non-significant decrease to the limited sample size of our study.

Previous research has found that serum 25(OH)D levels do not differ considerably between males and females, which is consistent with our findings. [20,21]

Furthermore, Hashemipour et al. [22] investigated the prevalence of vitamin D in Tehran and discovered no significant differences between males and females, as well as no connection between vitamin D and sunshine exposure. In contrast to our findings, Sedrani, [23] Al-Jurayyan et al., [24] Fida, [25] Naeem et al, [26] reported that vit D serum levels are substantially lower in females than in males. Although some writers have found greater blood levels of 25(OH)D in normal males than in normal women, [27,28] evidence for hypothyroid individuals is lacking. In Saudi Arabia, the incidence of vitamin D insufficiency was lower in the elderly than in young students of both sexes, and it was greater in females than in men. [29] However, a Japanese study of 200 euthyrotic Graves' disease patients revealed vitamin D insufficiency in 40% of women and about 20% of males (p 0.005). [30] The disparities between these studies can be explained by changes in patient selection, dietary vitamin D intake, sunshine exposure, and seasonal fluctuations.

When compared to TSH levels, vitamin D and calcium serum levels exhibited a negative connection. These findings showed that there may be a link between vitamin D deficiency and hypothyroidism. Our findings were consistent with earlier research, which found that the prevalence of vitamin D deficiency in Hashimoto's patients (92%) was substantially greater than in healthy controls (63%) (p 0.0001). [31,32]

In an experimental research, Byron Richards (2008) [33] investigated the effect of vitamin D shortage on the thyroid gland and discovered that a lack of vitamin D led to the likelihood of low thyroid hormones.

One of two processes might explain low vitamin D levels in hypothyroid individuals. First, low vitamin D levels may be related to inadequate absorption of vitamin D from the gut. Second, the body may not effectively activate vitamin D. Other studies have found that people with Graves' illness had low levels of Vitamin D. [34] Importantly, both vitamin D and thyroid hormone bind to steroid hormone receptors, which are found on the skin. A distinct gene in the Vitamin D receptor has been linked to autoimmune thyroid illness, such as Graves' disease and Hashimoto's thyroiditis.

Vitamin D suppresses the synthesis of the Th1 polarising cytokine (IL-12), therefore indirectly changing T cell polarisation from Th1 to Th2. Vitamin D directly suppresses Th1 cytokine (IL2 and IFN-c) production while increasing Th2 cytokine (IL-4) production in the CD4+ T cell response. [35]

Furthermore, several recent researches have revealed a link between vitamin D and a variety of autoimmune disorders. Polymorphisms in the vitamin D receptor (VDR) gene and vitamin D status are linked to a variety of autoimmune disorders. [36,37] Furthermore, vitamin D supplementation has been shown to reduce the start and/or progression of a variety of autoimmune disorders in people and animal models. [35] These findings showed that vitamin D insufficiency may

contribute to the start and/or progression of a variety of autoimmune disorders.

Recent research has shown that vitamin D has a function in Graves Disease (GD). First, polymorphisms in vitamin D-related genes, such as the VDR gene and the vitamin D binding protein gene, have been linked to GD. Second, in BALB/c mice, vitamin D deprivation modifies Graves' hyperthyroidism caused by thyrotropin receptor vaccination. Third, vitamin D analogue suppresses inflammatory responses in human thyroid and T lymphocytes. [38,39]

Research done in the Netherlands, on the other hand, found that vitamin D insufficiency is not related with the early phases of thyroid autoimmunity. [40-42]

Conclusion

Our results indicated that patients with hypothyroidism suffered from hypovitaminosis D. Moreover, the positive significant correlation between each of serum vit D and calcium with thyroid hormones and that negative significant correlation with TSH levels, suggested that deficiency of serum vit D were significantly associated with degree and severity of the hypothyroidism which encourage the advisability of vit D supplementation. Screening for Vitamin D deficiency recommended for all hypothyroid patients.

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