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Vitamin D Deficiency as a Contributing Factor in Hypothyroidism

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ABSTRACT

Vitamin D Deficiency is a major global health problem affecting over one billion people around the world. Recent evidence has shown that vitamin D plays a vital role not only in bone metabolism but also in the immune system and endocrine function. This study was conducted to find the association of vitamin D deficiency with hypothyroidism, and to see if there is any gender-based difference. An analytical study was carried out at AL-Hujaa Hospital in Karbala Between November and January. A total of 100 hypothyroidism patients (50 males and 50 females) were included in the study. Serum levels of thyroid-stimulating hormone (TSH) and vitamin D3 were assayed by standard laboratory methods. Statistical analysis was done to check the correlations between the different variables. The results showed that females had higher and more variable TSH levels than males indicating more thyroid malfunction. Males, on the other hand, had lower mean vitamin D3 levels which might correspond to a higher prevalence of deficiency. There was a negative correlation between levels of TSH and of vitamin D3 in both groups. However, in females, this correlation was statistically significant ($r = -0.505$, $p = 0.002$) and in males, it was not ($r = -0.432$, $p = 0.095$). These results indicate that vitamin D deficiency is associated with increased levels of TSH, particularly in females, and therefore, it may be a possible indicator of the role of vitamin D in thyroid function. The association could be explained by many mechanisms at the immunological, molecular, and metabolic levels including the role of vitamin D in regulation of autoimmunity and hormone signaling pathways. In summary, vitamin D deficiency can be considered as a contributing factor in the development and progression of hypothyroidism, particularly in women. The detection and correction of vitamin D could prove beneficial as an add-on to standard thyroid hormone therapy in improving the outcome of patients.

1. Introduction

Vitamin D deficiency is a major global public health problem. Over a billion people worldwide have deficient or insufficient levels of vitamin D. However, no government agency or global health organization has declared a pandemic to inform the public of the critical need to raise vitamin D levels in the blood. Since its discovery in the early 20th century, our understanding of the role of vitamin D has evolved from that of a simple nutrient to that of a steroid pro-hormone.

It is known for its role in many immune functions as well as for the growth of bone and muscle (3). Studies have shown that a deficiency of Vitamin D is associated with autoimmune diseases, including rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel disease.

Vitamin D Supplementation May Halt Onset/Progression of IBD, MS, and T1DM. Vitamin D supplementation can stop the onset and/or progression of autoimmune diseases such as inflammatory bowel disease (IBD), multiple sclerosis (MS), and type 1 diabetes (T1DM) (4). In this regard, many patients diagnosed with hypothyroidism, particularly those having Hashimoto's thyroiditis, have been found to be deficient in vitamin D. Such deficiency is often linked to immune system malfunction and chronic inflammation (5).

Vitamin D is essential for calcium homeostasis and for the development and maintenance of the skeletal system (6). Hypothyroidism is a condition characterized by decreased function of the thyroid gland; when this decrease becomes very severe, it is referred to as myxedema. It is the most common disorder of thyroid function. The low thyroid hormone usually results from inadequate dietary intake of iodine. In some cases, the

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antibodies may block the TSH receptor and cause hypothyroidism to begin. The condition is marked by a general slowing of all metabolic activities; it usually shows as a decrease in all physical and mental processes. It is interesting to note that both vitamin D and thyroid hormones function through similar receptors, known as steroid hormone receptors. A polymorphism in the gene encoding the Vitamin D receptor has been associated with susceptibility to autoimmune thyroid disorders, including Graves' disease and Hashimoto's thyroiditis (7).

Hypothyroidism refers to a chronic disorder in which the levels of thyroid hormones (T4, thyroxine and T3, triiodothyronine) are insufficient. This disease of the thyroid gland affects mainly women; its prevalence is about 5% in the general population. Many thyroid diseases occur in women after menopause. Therefore, diagnosis is difficult because symptoms of thyroid disorders and ovarian dysfunction overlap (8). Infertility, cardiovascular disease, and neurological and musculoskeletal problems are some of the consequences of untreated or inadequately treated hypothyroidism.
Symptoms: (9).. The predominant cause of thyroid disorders, including hypothyroidism, globally ranges from environmental iodine deficiency (10). In regions where iodine levels are sufficient, autoimmune thyroiditis, also known as Hashimoto's disease, emerges as the leading cause of primary hypothyroidism. Levothyroxine is the cornerstone of treatment for hypothyroidism and is recognized as one of the essential medicines necessary for basic health care by the World Health Organization. (11). (12).

2. Data Collection

The analytical Study of TSH and Vitamin D level of Data collected from11/23 to 1/29 at AL-Hujaa Hospital in Karbala Governorate. 50 infecteddate of male and 50 infected data of Female with hypothyroidism.

Clinical Profile Test

Estimation of Thyroid Stimulating Hormone (TSH)

The forms of an antibody sandwich complex. Collecting Serum Sample volume: ~20–50 µL in collection tube: then centerfuge to obtain serum/plasma, then analyzer pipepettes sample +biotinylated antibody+ruthenium-labeled antibody. Streptavidin-coated microparticles are added. The complex binds to microparticles. then reaction mixture moves to the measuring cell. Magnet holds microparticles on the electrode surface, and nbound substances are washed away. With Voltage applied , Electro chemiluminescent reaction produces light. Photomultiplier measures light intensity. Then analyzer calculates TSH concentration using the calibration curve. were performed directly by the Elecsyes TSH (USA) device. (13), (14).

Estimation of VItamin D (25-hydroxyvitamin D)

The Elecsys Vitamin D Total Assay is a laboratory test to measure the total Vitamin D (25 hydroxyvitamin D) levels in the blood. This test is commonly performed in hospital laboratory settings using automated analyzers such as the Roche Cobas e analyzer(15)..

A sample volume of about 15-30 µL is collected from the patient in a specified tube and then centrifuged to remove serum. The sample is then mixed with Vitamin D binding protein for the release and binding of 25-OH Vitamin D. Biotinylated Vitamin D analog and ruthenium-labeled reagents are added. Here, patient Vitamin D is made to compete with the labeled Vitamin D for binding to the antibody. A complex of biotinylated streptavidin is captured by microparticles coated with streptavidin. Unbound substances are washed away while a magnet holds the microparticles on the electrode surface. At the end of the process, a voltage is applied to generate electro chemiluminescent light. The signal is then measured to determine the Vitamin D concentration.

Statistical Analysis

Descriptive statistics showed a marked increase in TSH hormone levels over the male cohort, with the mean ± SD for females at 17.5. This would indicate a higher prevalence of thyroid dysfunctions, probably including cases of overt hypothyroidism. On the other hand, Vitamin D3 levels for males had a mean ± SD of 16.08 ng/mL, which shows that most male patients are deficient in Vitamin D3.

TSH hormone levels showed a significant association with Vitamin D3 by Pearson correlation. This was true for the entire group and males, where a strong negative correlation was observed ($r = -0.432$), indicating that as TSH levels increase, Vitamin D3 levels tend to decrease. For females, the correlation was also strong and negative ($r = -0.505$). A t-test was applied for comparing the mean of quantitative variables between two groups. The statistical analysis of clinical biological indicators was performed using SPSS version 27 (SPSS Inc., Chicago, IL, USA)..

3. RESULTS AND DISCUSSION

The levels of Vitamin D3 seem to be related inversely with TSH more sharply in females than in males, indicating that higher TSH may be associated with lower levels of Vitamin D3. It is possible that in males, the relationship between thyroid function and metabolism of Vitamin D3 is less pronounced or influenced by other physiological or lifestyle factors. This vitamin, whether obtained from sunlight, food, or supplements, is biologically inactive and requires two hydroxylations in the body for its activation. 25-hydroxyvitamin D or calcidiol represents the first product of hydroxylation which takes place mainly in the liver. The second hydroxylation is mainly a renal process that generates the physiologically active compound 1,25-dihydroxyvitamin D or calcitriol. In females, higher levels of TSH were significantly associated with lower levels of Vitamin D3. This is in line with previous studies that indicated a possible relationship between Vitamin D deficiency and thyroid dysfunction, especially in women. Hormonal factors, such as the influence of estrogens on thyroid metabolism and Vitamin D pathways, could also contribute to this gender-specific association (17).

Deficiency of Vitamin D3 prevails in both males and females; however, females have slightly higher average levels than males, yet most remain below sufficiency (18).
Vitamin D has effects on the immune system, thus being able to affect the autoimmune processes that may lead to dysfunction of the thyroid. There is evidence showing that low levels of Vitamin D are associated with autoimmune diseases of the thyroid, such as Hashimoto's thyroiditis, which is the most common cause of hypothyroidism.
In patients with hypothyroidism, several mechanisms may explain the decreased levels of Vitamin D3. First, hypothyroidism may reduce metabolic activity and hence intestinal absorption, which may affect Vitamin D metabolism.
Secondly, autoimmune processes that take part in thyroid malfunction may change immune regulation and Vitamin D receptor action (21). Thirdly, patients with hypothyroidism may have reduced physical activity and sunlight exposure, which can further lower endogenous Vitamin D synthesis in the skin (22).
In men, hypothyroidism happens less and less often; however, Vitamin D deficiency may still be there and may go along with high TSH levels. The TSH levels go up and Vitamin D levels tend to go down. This link reflects the job of Vitamin D in immune control and endocrine work (17).
Vitamin D and thyroid hormones share a common pathway at the molecular level in their effects on gene expression by nuclear receptors, which are members of the superfamily of steroid hormone receptors. Binding to specific response elements on DNA, these receptors regulate the transcription of genes responsible for metabolism as well as cell differentiation and proliferation. A hypothesis has been put forward that Vitamin D deficiency may impair the signaling of thyroid hormones, either through changes in receptor expression or by effects on downstream gene transcription, which would reduce tissue responsiveness to T_3 despite normal or near-normal circulating levels (23),(24).
In terms of metabolism, the characteristics of hypothyroidism include lowered basal metabolic rate, reduced activity of oxidative mitochondria, and an impairment in the metabolism of lipids and carbohydrates. It has been shown that Vitamin D deficiency leads to insulin resistance, increased adipogenesis, and chronic low-grade inflammation (25).
The presence of these conditions may interact synergistically to worsen metabolic dysfunction, manifesting clinically as weight gain, fatigue, and reduced physical performance. Additionally, both conditions negatively impact mitochondrial ATP production, contributing to the generalized lethargy observed in the patients (26).
Vitamin D has a role in the interaction with calcium homeostasis, and therefore, implications in hypothyroid patients. It is known that Vitamin D is necessary for the absorption of calcium in the intestine and for keeping the serum level of calcium. (27)
Although hypothyroidism is typically associated with reduced bone
turnover rather than big changes in calcium levels, along with Vitamin D deficiency, may mess with how you absorb calcium — and that could up the risk of osteopenia over time. This underlines the value of good Vitamin D status for keeping your bones strong in people with thyroid problems. (28).
Neuromuscular and neuropsychiatric manifestations form another area of similarity between hypothyroidism and Vitamin D deficiency. Muscle weakness, depressive symptoms, and cognitive impairment are related to both conditions (29).
These effects can be accounted for by changes in the synthesis of neurotransmitters, the signaling of neuronal calcium, and the availability of energy at the cellular level. Vitamin D receptors are widely distributed in the brain, which supports its role in neurocognitive function and further emphasizes its contribution to the clinical picture of hypothyroidism (30).
Vitamin D may also have an effect on peripheral metabolism of thyroid hormones by deiodinase enzyme activity modulation. The deiodinases are a group of enzymes that catalyze the conversion of thyroxine (T_4) to the biologically active T_3 (31). A deficiency in Vitamin D levels may disturb the conversion process, leading to low intracellular T_3 availability and worsening hypothyroid symptoms at the tissue level (32).
In clinical terms, many studies have shown a high prevalence of Vitamin D deficiency in hypothyroid patients. Some studies have shown that Vitamin D supplementation can lower thyroid antibody titers and improve certain clinical symptoms, mainly fatigue and mood disturbances. However, Vitamin D supplementation should not replace standard thyroid hormone replacement therapy. It can only be an adjunct that improves the overall outcome of the patient. (33), (34).

4. Tables and Figures

Table 1. Result of TSH hormone test of Mean.ST

Parameter	*Male*	*female*
TSH	8.42 ± 5.58	10.19 ± 17.5
Vitamin D3	16.08±9.47	18.69±6.33

The table 1, describes the features of participants by contrasting 50 males with 50 females concerning their TSH and Vitamin D3 levels. In males, the mean level of TSH is 2.5, while in females, it is 3.9, and the values of TSH in females show wide variability (SD = 17.5). This variability indicates a higher prevalence of thyroid dysfunctions, perhaps including cases of overt hypothyroidism. The mean level of Vitamin D3 in males is 16.08 ng/mL, which means that most males are deficient in Vitamin D3.

TABLE 2. Pearson Correlation between parameters in Male group

Parameter	*TSH*	*Vitamin D3*
TSH (μlU/ML)	1	-0.432
Vitamin D3(ng/mL)	-0.432	1

The study results on table 2 showed a significant relationship between TSH hormone and Vitamin D3 notably in male group, the significant negative correlation between TSH that increase and Vitamin D3 tend to decrease.

TABLE 3. Pearson Correlation between parameters in male**.**

Parameter	TSH	Vitamin D3
TSH (µlU/ML)	1	-0.505
Vitamin D3(ng/mL)	-0.505	1

The study results, as shown in Table 3, revealed a significant relationship between TSH hormone and Vitamin D3, notably in the female group. A moderate negative correlation between Vitamin D3 and TSH hormone tends to decrease.

5. CONCLUSIONS

Gender disparities have been noticed in the association of hypothyroidism with Vitamin D3 levels. In general, females are more prone to hypothyroidism compared to males, mostly due to hormonal and immunological factors. Estrogen is believed to impact immune responses and may enhance the susceptibility to autoimmune thyroid diseases. Therefore, in most cases, women present higher prevalence rates of both hypothyroidism and Vitamin D deficiency.

Hypothyroidism and Vitamin D_3 have a complex relationship, involving pathways that are interconnected at the immune, molecular, and metabolic levels. Vitamin D deficiency can contribute to the development of hypothyroidism and its progression, especially the autoimmune forms of the disease; it also amplifies the clinical manifestations..

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AUTHERS DECLARATION

We confirm that all the tables in the manuscript belong to the current study.

CONFLICTION OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of the study.

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