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ROLE OF VITAMIN D IN HYPERTHYROIDISM AND HYPOTHYROIDISM

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Abstract:
The fundamental function of vitamin D is to keep the balance of calcium and phosphorus, which protects the health of bones. According to recent research, vitamin D may also play a function in several non-skeletal conditions, including endocrine diseases like type 1 and type 2 diabetes, adrenal disorders, and polycystic ovarian syndrome. Inadequate vitamin D levels are linked to thyroid conditions such as Hashimoto's thyroiditis. Similarly, it was found that patients with newly diagnosed Graves disease had lower concentrations of 25-hydroxyvitamin D. Thyroid cancer has been linked to faulty vitamin D signalling, according to research. Studies on vitamin D supplementation in thyroid disease patients are carried out. Randomized controlled trials are required to shed light on the effectiveness and safety of vitamin D as a therapeutic tool for this dysfunction, even if observational studies suggest a positive role for it in the therapy of thyroid disease.

Aim of the study:
This review will describe the effects of vitamin D supplementation and concentrate on the role of vitamin D in thyroid diseases such as hyperthyroidism and hypothyroidism.

Methodology:
The literature review is comprehensive research on the role of vitamin D in thyroid disease management. PUBMED is the search engine that was the mainly database used for the search process, and articles were collected from 1990 to 2022. The term used in the search were: Vitamin D, thyroid disorder, hyperthyroidism, hypothyroidism.

Conclusion:
Although several findings support the role of vitamin D in the pathogenesis of thyroid diseases and the strong association in the treatment plan, there is a lack of evidence, and a dearth of intervention studies and clinical trials suggest that vitamin D insufficiency or deficiency may be associated with increased risk of thyroid disease. Therefore, no guidelines or recommendations are currently available for or against recommending vitamin D by the Endocrine Society.

Keywords: *Vitamin D, thyroid disorder, hyperthyroidism, hypothyroidism, etc.*

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INTRODUCTION:

Vitamin D is a steroid molecule mostly made in the skin and controls the expression of several genes. Most body tissues and cells include the VDR. Vitamin D's major functions are controlling calcium and phosphorus balance and bone metabolism. According to recent research, vitamin D deficiency, which is widespread worldwide, may also have an important role in autoimmune disorders, metabolic syndromes, cancer, cardiovascular disease, infections, and all-cause mortality. Moreover, AITD, such as HT and GD, have been linked to low vitamin D levels. Thyroid tumorigenesis has been linked to faulty vitamin D signalling. [1, 2]

2 types of vitamin D are vitamin D2 and vitamin D3 (also known as cholecalciferol) (or ergocalciferol). Vitamin D2 can be derived from food sources such as fatty fish and is primarily created in the skin by 7-dehydrocholesterol reductase upon exposure to ultraviolet B (UVB) radiation, whereas plants and fungi produce the latter. Both vitamin D forms are delivered to the liver, where 25-hydroxylase converts them into calcifediol, also known as 25(OH)D3 (CYP27A1 and CYP2R1). [3]

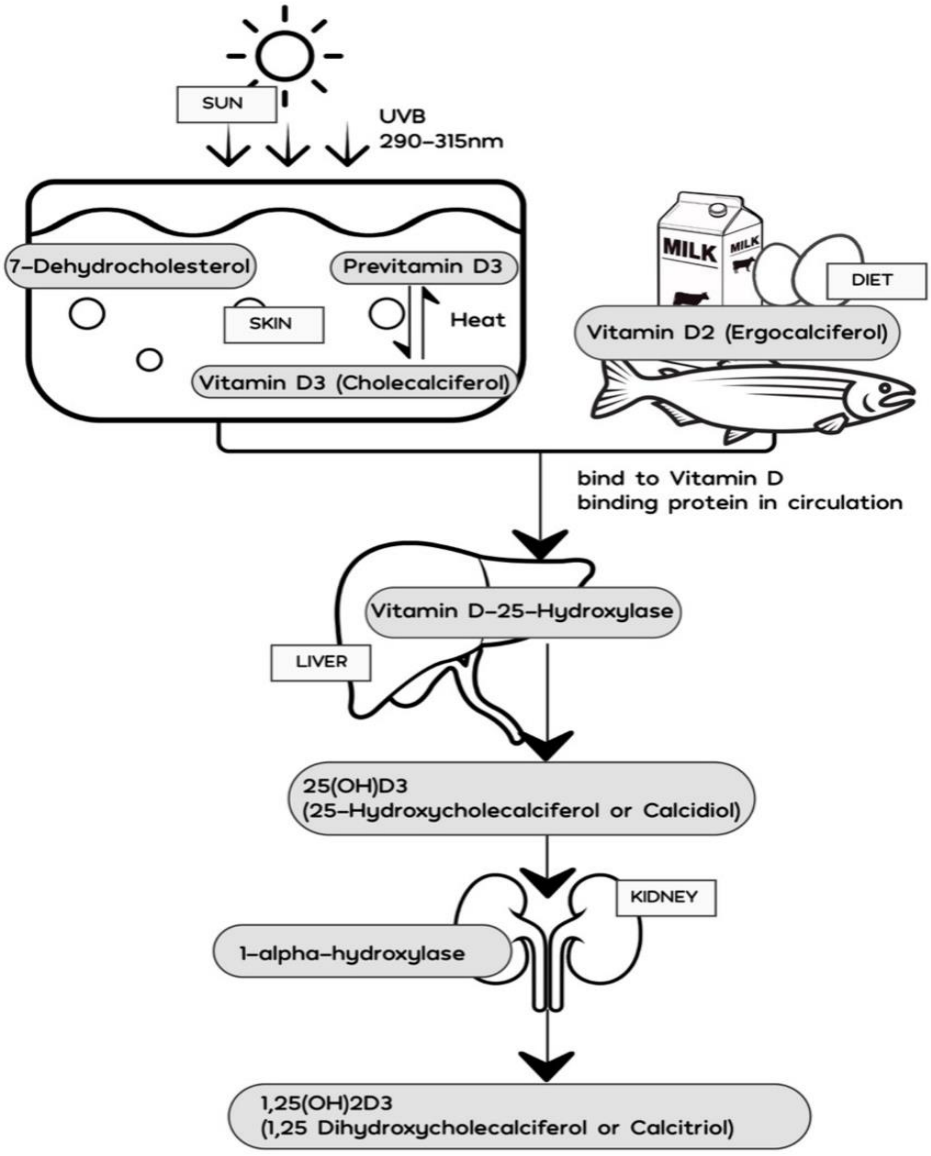

Fig. 1 Metabolism of Vitamin D [4]

The nuclear-VDR binds to the active 1,25(OH)2D form, which then works on the target genes' vitamin D response elements (VDRE) to exercise its effects. Around 200 genes, including those in charge of controlling cellular proliferation, differentiation, apoptosis, and angiogenesis, are directly and indirectly regulated by 1,25(OH)2D. Immune cells, the prostate, the breast, the colon, and the brain are among the organs that express VDR and react to 1,25(OH)2D. In addition to being a powerful immunomodulator, 1,25(OH)2D reduces the cellular proliferation of both healthy and cancer cells and causes their terminal differentiation. A membrane-bound VDR may mediate the more rapid, non-genomic effects of 1,25(OH)2D. [2, 5]

Role of Vitamin D in Thyroid Autoimmune Diseases and Effects of Supplementation

Role of Vitamin D in hypothyroidism

Although there is growing evidence that the interplay of environmental risk factors and genetic predisposition leads to hyperthyroidism, the precise process is still understood. Several clinical investigations have connected this condition to the development of papillary thyroid cancer, and despite normal thyroid function, one research also found neuroinflammation that led to emotional changes. It is regrettably largely asymptomatic, and its occurrence has recently been rising. Patients can only eventually appear with malignant tumors, aberrant thyroid function, and other connected diseases, which can be distressing psychologically and financially. For the sake of overall public health, it is crucial to comprehend how hyperthyroidism manifests in healthy persons and how it relates to the right indicators. [6, 7]

An autoimmune thyroid condition known as HD manifests histologically as chronic lymphocytic thyroiditis. Although its etiology is uncertain, recent research has demonstrated that the Th1/Th2 imbalance and elevated Th1 cell activity are the most significant pathogenic variables. Vitamin D's function as an immunosuppressive drug may decrease the immunological response in HD. When active vitamin D interacts with receptors, various significant signalling molecules are activated, which has biological impacts. Protein-dependent transport is made possible by the heterodimeric molecule formed when 1,25(OH)2-vitamin D3 binds to the VDR on target cells. [8] The first link between vitamin D deficiency and HT was first studied on 2009 among more than 600 patients; the result of the study supported the significant inverse association between vitamin D level and the presence of circulating TPOAb [9]; This correlation was supported in the following studies. [10-13] Moreover, a recent study represented TPOAb and TgAb levels were significantly decreased by the vitamin D replacement therapy. [14, 15]

It has been established that vitamin D is crucial for the maturation of macrophages. It was also shown to enhance the anti-tumor actions of mononuclear macrophages, accelerate monocyte differentiation in macrophages, and raise phagocytosis and chemotaxis (Figure 1) Toll-like receptors TLR2 and TLR4 on monocyte surface expression can be inhibited by vitamin D, which prevents these receptors from recognizing pathogen-associated molecular patterns and, as a result, reduces immune responsiveness, the production of inflammatory cytokines, and the development of an excessive immune response. Inflammation is decreased as a whole.[16]

Role of Vitamin D in hyperthyroidism

Another somewhat common autoimmune thyroid ailment called GD results in the development of TRAb, which results in hyperthyroidism. Numerous genetic and environmental factors influence its pathogenesis. In female participants with newly diagnosed GD, blood concentrations of vitamin D have been linked to thyroid volume and have recently been demonstrated to play a role. Several variants in the vitamin D gene, such as VDR and vitamin D-binding protein, have been connected to GD based on data from the literature. [17] The first correlation between vitamin D levels and women with and without GD remission was done on result in the prevalence of hypovitaminosis D was twice as high as in healthy controls. [17]

It has been demonstrated in BALB/c mice that a vitamin D shortage affects hyperthyroidism in GD via immunizing the thyrotropin receptor. Moreover, it prevents the production of CXCL10, a Th1 chemokine that has been linked to the pathophysiology of GD in human thyroid cells. Moreover, vitamin D reduces the inflammatory reactions responsible for developing GD and the metabolic syndrome. When compared to GD participants who were in remission, the serum levels of vitamin D in the non-remission group was considerably lower. In the group without remission, the durations of hyperthyroidism from the onset of GD were considerably longer than in the other group.[18] a recent study in South Korea among 210 patents with GD and vitamin D deficiency suggested that Vitamin D supplementation might have a protective effect against graves' disease recurrence and have significant recurrence rate reduction. [19]

Vitamin D Supplementation in Thyroid Diseases

The use of vitamin D supplements to treat thyroid disorders has shown promising results. In a study, vitamin D-deficient patients with Hashimoto thyroiditis received 1,200–4,000 IU of vitamin D per day for four months; after that, their anti-thyroid antibody levels were noticeably reduced. Another study found increased thyroid-stimulating hormone levels in hypothyroid patients who took additional vitamin D tablets for 12 weeks. However, the extra vitamin D did not affect levels of the actual thyroid hormones T3 and T4. [4, 20]

The current recommendation for the treatment of hypovitaminosis D situations involves vitamin D supplementation. The US Endocrine Society guidelines define vitamin D deficiency as having a 25(OH)D3 level of less than 20 ng/ml (50 nmol/l), vitamin D insufficiency as having a level between 21 and 29 ng/ml, and the upper cut-off to reduce the risk of side effects as having a level of 25(OH)D3 equal to 100 ng/ml (250 nmol/l). The US Institute of Medicine study recommends different 25(OH)D3 levels as "cut-offs," with a 25(OH)D3 concentration more than 20 2 (50 nmol/l) covering the needs of the vast majority (97.5%) of the population and 50 ng/ml (125 nmol/l) serving as the upper safety margin for hypercalcemia. [21, 22]

The most reliable marker for assessing vitamin D levels is 25(OH)D3. With a half-life of two to three weeks, this is the main form of circulating vitamin D. As 1,25(OH)2D3 has a half-life of only 4 hours, peripheral levels are 1000 times lower than those of 25(OH)D3, and PTH, calcium, and phosphate closely regulate it, it does not indicate the status of vitamin D. 57 The US Endocrine Society guidelines encourage screening for vitamin D deficiency in people with particular diseases who are at risk for this deficiency. The list of these conditions excludes any probable thyroid problems.[21]

The US Endocrine Society recommends that all individuals consume 600–800 IU of vitamin D daily through food sources. Supplementation is required in cases of deficiency or insufficiency, and vitamin D2 or vitamin D3 can be administered. To increase the blood level of 25 (OH)D above 30 ng/ml in adults who are vitamin D deficient, it is recommended that they get the equivalent of 6000 IU of vitamin D2 or vitamin D3 daily or 50 000 IU of vitamin D2 or vitamin D3 once per week for eight weeks. A maintenance dose of 1500–2000 IU per day should be used as a supplement.[21]

Although it has been demonstrated that vitamin D may be helpful in the management of a number of autoimmune disorders, the issue of whether vitamin D supplementation in autoimmune disease is still up for dispute. In terms of autoimmune thyroid illness, the evidence is much less certain.[23]

Studies on vitamin D supplementation for autoimmune thyroid disease are seriously lacking in the literature. Only experimental animal research have shown that vitamin D administration positively impacts the management or prevention of autoimmune thyroid disease. In the first investigation, mice with experimental autoimmune thyroiditis responded to daily therapy with cyclosporin or 1,25(OH)2D3 by reducing the severity of histological lesions by up to 26%. When mice were given low doses of both 1,25(OH)2D3 and cyclosporin at the same time, there was no change in the levels of thyroid autoantibodies. Still, there was a significant reduction in the severity of the clinical disease compared to the control group and a lower incidence of thyroid autoimmune pathology. [24, 25]

CONCLUSION:

Although several findings support the role of vitamin D in the pathogenesis of thyroid diseases and the strong association in the treatment plan, there is a lack of evidence, and a dearth of intervention studies and clinical trials suggest that vitamin D insufficiency or deficiency may be associated with increased risk of thyroid disease. Therefore, no guidelines or recommendations are currently available for or against recommending vitamin D by the Endocrine Society.

List of Abbreviation:

1,25(OH)2D3: 1,25-Dihydroxyvitamin D

25(OH)D3: 25-Hydroxyvitamin D

AITD: Autoimmune Thyroid Disorders

CXCL10: Motif Chemokine Ligand 10

GD: Graves' Disease

HT: Hashimoto's Thyroiditis

IU: International Units

Ng/Ml : Nanograms Per Milliliter

Nmol/L: Nanomoles Per Litre

T3: Triiodothyronine

T4: Thyroxine

Tgab: Anti-Thyroglobulin Antibodies

Th1 Chemokine : T Cell Chemokine Receptor

Tpoab: Anti-Thyroid Peroxidase

Trab: TSH Receptor Antibodies

VDR: Vitamin D Receptor

Vitamin D2:Ergocalciferol

Vitamin D3: Cholecalciferol

REFERENCES:

1. Adams, J.S. and M. Hewison, *Unexpected actions of vitamin D: new perspectives on the regulation of innate and adaptive immunity.* Nat Clin Pract Endocrinol Metab, 2008. **4**(2): p. 80-90.
2. Menconi, F., C. Marcocci, and M. Marinò, *Diagnosis and classification of Graves' disease.* Autoimmun Rev, 2014. **13**(4-5): p. 398-402.
3. Bikle, D., *Nonclassic actions of vitamin D.* J Clin Endocrinol Metab, 2009. **94**(1): p. 26-34.
4. Mazokopakis, E.E., et al., *Is vitamin D related to pathogenesis and treatment of Hashimoto's thyroiditis?* Hell J Nucl Med, 2015. **18**(3): p. 222-7.
5. Wacker, M. and M.F. Holick, *Vitamin D - effects on skeletal and extraskeletal health and the need for supplementation.* Nutrients, 2013. **5**(1): p. 111-48.
6. Moon, S., et al., *Associations between Hashimoto Thyroiditis and Clinical Outcomes of Papillary Thyroid Cancer: A Meta-Analysis of Observational Studies.* Endocrinol Metab (Seoul), 2018. **33**(4): p. 473-484.
7. Kust, D. and N. Matesa, *The impact of familial predisposition on the development of Hashimoto's thyroiditis.* Acta Clin Belg, 2020. **75**(2): p. 104-108.
8. Krysiak, R., W. Szkróbka, and B. Okopień, *The Effect of Vitamin D on Thyroid Autoimmunity in Levothyroxine-Treated Women with Hashimoto's Thyroiditis and Normal Vitamin D Status.* Exp Clin Endocrinol Diabetes, 2017. **125**(4): p. 229-233.
9. Goswami, R., et al., *Prevalence of vitamin D deficiency and its relationship with thyroid autoimmunity in Asian Indians: a community-based survey.* British Journal of Nutrition, 2009. **102**(3): p. 382-386.
10. Unal, A.D., et al., *Clinical immunologyVitamin D deficiency is related to thyroid antibodies in autoimmune thyroiditis.* Central European Journal of Immunology, 2014. **39**(4): p. 493-497.
11. Wang, X., et al., *Low Serum Vitamin D Is Associated with Anti-Thyroid-Globulin Antibody in Female Individuals.* Int J Endocrinol, 2015. **2015**: p. 285290.
12. ElRawi, H.A., et al., *Study of Vitamin D Level and Vitamin D Receptor Polymorphism in Hypothyroid Egyptian Patients.* J Thyroid Res, 2019. **2019**: p. 3583250.
13. Shin, D.Y., et al., *Low serum vitamin D is associated with anti-thyroid peroxidase antibody in autoimmune thyroiditis.* Yonsei Med J, 2014. **55**(2): p. 476-81.
14. Simsek, Y., et al., *Effects of Vitamin D treatment on thyroid autoimmunity.* J Res Med Sci, 2016. **21**: p. 85.
15. Krysiak, R., K. Kowalcze, and B. Okopień, *Selenomethionine potentiates the impact of vitamin D on thyroid autoimmunity in euthyroid women with Hashimoto's thyroiditis and low vitamin D status.* Pharmacological Reports, 2019. **71**(2): p. 367-373.
16. Sadeghi, K., et al., *Vitamin D3 down-regulates monocyte TLR expression and triggers hyporesponsiveness to pathogen-associated molecular patterns.* Eur J Immunol, 2006. **36**(2): p. 361-70.
17. Yasuda, T., et al., *Serum vitamin D levels are decreased in patients without remission of Graves' disease.* Endocrine, 2013. **43**(1): p. 230-232.
18. Sheriba, N.A., et al., *Effect of vitamin D3 in treating hyperthyroidism in patients with graves' disease.* The Egyptian Journal of Internal Medicine, 2017. **29**(2): p. 64-70.
19. Cho, Y.Y. and Y.J. Chung, *Vitamin D supplementation does not prevent the recurrence of Graves' disease.* Scientific Reports, 2020. **10**(1).
20. Talaei, A., F. Ghorbani, and Z. Asemi, *The Effects of Vitamin D Supplementation on Thyroid Function in Hypothyroid Patients: A Randomized, Double-blind, Placebo-controlled Trial.* Indian J Endocrinol Metab, 2018. **22**(5): p. 584-588.
21. Holick, M.F., et al., *Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline.* J Clin Endocrinol Metab, 2011. **96**(7): p. 1911-30.
22. Ashok, T., et al., *Relationship Between Vitamin D and Thyroid: An Enigma.* Cureus, 2022. **14**(1): p. e21069.
23. Agmon-Levin, N., et al., *Vitamin D in systemic and organ-specific autoimmune diseases.* Clin Rev Allergy Immunol, 2013. **45**(2): p. 256-66.
24. Fournier, C., et al., *In vivo beneficial effects of cyclosporin A and 1,25-dihydroxyvitamin D3 on*

the induction of experimental autoimmune thyroiditis. Clin Immunol Immunopathol, 1990. **54**(1): p. 53-63.
25. Chen, W., H. Lin, and M. Wang, *Immune intervention effects on the induction of experimental autoimmune thyroiditis.* J Huazhong Univ Sci Technolog Med Sci, 2002. **22**(4): p. 343-5, 354.