

Relationship between Vitamin D Deficiency and Hypothyroidism-A Review

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ABSTRACT

Vitamin D has a crucial role in maintaining thyroid and immune function. In hypothyroidism, the gland is underactive and Vitamin D impacts this condition. Vitamin D regulates gene expression in thyroid hormone synthesis and influences the immune system, affecting overall thyroid health. From the literatures, it is evident that hypothyroidism is correlated with hypovitaminosis D. The immune-mediated properties of Vitamin D reduce the symptoms of hypothyroidism caused by autoimmune conditions. Understanding the correlation of Vitamin D with hypothyroidism is crucial as it holds potential therapeutic implications. Maintaining adequate Vitamin D improves gland function and prevents disease-related complications.

Keywords: Vitamin D, Hypothyroidism, Thyroid function, Vitamin D deficiency.

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INTRODUCTION

Vitamin D plays a vital role in the body by regulating calcium and potassium levels and contributing significantly to bone metabolism. Insufficient thyroid hormones can lead to hypothyroidism, if left untreated, may lead to serious health issues.¹ Hypothyroidism is typically defined based on biochemical criteria, as the condition presents with a variety of clinical manifestations and often lacks specific symptoms.²

Hypothyroidism is a common health issue in the adult Indian population. Among them, females are more vulnerable to the disease condition. Autoimmune mechanisms appear to be at the root of the disease in a large proportion of patients.²

In developed countries, hypothyroidism affects around 4-5% of its population and subclinical is prevalent in a range from about 4%-15%.³ In the United States, the disease prevalence ranges from 0.3% to 3.7%, while in Europe it is from 0.2% to 5.3%.⁴⁻⁶ In European countries, an estimated 5% of hypothyroidism is underdiagnosed, both mild and overt.⁴ Research indicates a higher incidence of the disease among women in comparison to men.⁷ The primary cause of the disease worldwide is commonly attributed to iodine deficiency. In places where there's enough iodine, hypothyroidism can be caused by factors like autoimmune

issues (such as Hashimoto's thyroiditis) or iatrogenic reasons.⁷ Research suggests that hypovitaminosis D in patients with hypothyroidism and Graves' disease may play an important role in musculoskeletal complications.⁸

The decrease in serum Vitamin D among hypothyroid patients can be described by two potential explanations. Firstly, it may result from insufficient absorption in the intestine. Furthermore, these patients might have difficulties in properly activating Vitamin D within their bodies. Vitamin D performs its biological functions by binding to the Vitamin D Receptor (VDR). Consequently, the activation of genes, found in specific target tissues, responsive to VDR is initiated.⁸

Vitamin D performs its biological functions by attaching to the VDR and triggering the activation of genes in specific target tissues that are responsive to the VDR. Vitamin D is produced in the body in two main ways, skin exposed to sunlight and consuming certain foods. Dietary origins of the Vitamin. D3 involve fish, including fatty cod, fresh salmon, sardines and dairy products.⁹

The standard serum range for Vitamin D typically spans from 30 to 80 ng/mL, with concentrations below 30 ng/mL generally regarded by most experts as indicative of insufficient Vitamin D. Recent research highlights the connection between a lack of Vitamin D and autoimmune issues related to the thyroid. This link seems to be present consistently across different age groups and it has been observed that supplements containing cholecalciferol effectively reduce levels of Thyroid Peroxidase



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Antibody (TPO-Ab) in individuals with Hashimoto's Thyroiditis (HT) who have a Vitamin D deficiency.⁹

Vitamin D plays a vital role in supporting immune function, bone growth and muscle development. Insufficient levels of Vitamin D, referred to as hypovitaminosis D, have been associated with the onset of autoimmune disorders. Studies have suggested that taking Vitamin D supplements can aid in preventing the onset or progression of these autoimmune diseases.¹⁰

Patients with HT often exhibit a lack of Vitamin D and taking Vitamin D supplements have the potential to slow down the advancement of the disease and prevent cardiovascular complications.¹¹ The main goal of this review is to analyze the effect of Vitamin D on hypothyroidism.

MATERIALS AND METHODS

Search Strategy

Data needed for the review were collected through a comprehensive search strategy involving multiple databases, including Pubmed, Scopus and Google Scholar, covering articles published between 1998-2023. The keywords used in the search included "hypothyroidism," "metabolism of Vitamin D," "thyroid disorders," and "role of Vitamin D in thyroid disorders."

Data Sources

The sources for data extraction consisted of both research articles and review articles. These articles were selected based on their relevance to the specified keywords and their potential to contribute valuable insights to the review.

Data Extraction

The data extraction process involved identifying relevant articles from the search results, followed by a thorough examination of these articles to extract the key study findings.

Data Assessment

The data assessment phase involved evaluating the quality of the extracted data. This included assessing the study design, sample size, methodologies used and the validity of the conclusions drawn in the articles. High-quality studies were included in the final review to ensure the credibility and accuracy of the findings.

DISCUSSION

Thyroid gland and Thyroid hormones

The thyroid gland is situated in the lower front part of the neck. Its primary role is to ensure the optimal presence of iodine within the body. This gland is also responsible for synthesizing and secreting thyroid hormones. The main functions of thyroid hormones include maintaining the basal metabolic rate, skeletal muscle maturation, regulation of internal body temperature, enhancement of skin and improvement in hair and nail growth.¹²

Sources of Vitamin D

For most of the population, sunlight is the main source of Vitamin D, acquired through the skin's synthesis. Since vit. D rich foods are not commonly included in daily diets, their contribution to Vitamin D intake is usually minimal.¹³ Throughout history, cod liver oil has been esteemed as a valuable source of Vitamin D.¹⁴ Natural sources encompass fatty fish like salmon, mackerel, tuna, sardines and egg yolks.^{15,16} The thyroid gland in the anterior section of the neck synthesizes thyroid hormones and regulates iodine. Individuals with hypovitaminosis D, either due to reduced Vitamin D synthesis in the skin or insufficient sunlight exposure, are often advised to take Vitamin D supplements.^{17,18} Ensuring sufficient Vitamin D levels can be achieved by enhancing both dietary and supplemental intake, along with moderate sun exposure. This typically involves spending 5-10 min in the sun on the arms, legs, hands and face at least two or three times per week.¹⁴ Various foods provide differing amounts of Vitamin D per serving, cooked salmon (3 ounces) contains 14.2 mcg (570 IU), while canned sardines in oil (2 sardines) offer 1.2 mcg (46 IU). Tuna fish canned in water (3 ounces) includes 1.0 mcg (40 IU) and a large scrambled egg contains 1.1 mcg (44 IU) of Vitamin D, predominantly in the yolk.¹⁹

Cod liver oil is notably high in Vitamin D, with 34.0 mcg (1360 IU) per tablespoon. Cheddar cheese (1 ounce) provides 0.3 mcg (12 IU) and fortified 2% milk (1 cup) offers 2.9 mcg (120 IU). Raw mushrooms exposed to UV light (½ cup) contain 9.2 mcg (366 IU), while diced raw portabella mushrooms (½ cup) contain only 0.1 mcg (4 IU). Similarly, roasted chicken breast (3 ounces) contains 0.1 mcg (4 IU). Fortified soy, almond and oat milks (various brands, 1 cup) provide between 2.5 and 3.6 mcg (100-144 IU) of Vitamin D.¹⁹

Causes of Vitamin D deficiency

The main factor leading to Vitamin D deficiency is insufficient uptake of the Vitamin from dietary sources or inadequate exposure to sunlight, combined with impaired absorption of Vitamin D within the body.²⁰⁻²² The other causes are certain medical conditions, certain medications (laxatives, steroids: prednisone, rifampin) and weight loss surgeries.^{23,24} Vitamin D per individual.

The recommended daily amount of Vitamin D varies by age and life stage. Infants up to 12 months old should receive 10 mcg (400 IU). Individuals aged between 1 and 70 years require 15 mcg (600 IU), which is the same amount recommended for pregnant and breastfeeding women. Adults aged 71 years and older need a higher intake of 20 mcg (800 IU) to maintain optimal health.¹⁹

Symptoms of hypovitaminosis D

The insufficiency of Vitamin D, referred to as hypovitaminosis D, can lead to various symptoms. These include muscle weakness,

bone pain, deformities in joints, fatigue and alterations in mood (Figure 1).

Metabolism of Vitamin D

The Vitamin D compound is composed of two variants, specifically Vitamin D2 (ergocalciferol) and Vitamin D3 (cholecalciferol). The predominant source of Vitamin D is through the synthesis occurring in the skin, where exposure to sunlight initiates the conversion of 7-dehydrocholesterol into cholecalciferol (Vitamin D3). Yeast acts as the primary supplier of Vitamin D2 (ergocalciferol). Both Vitamin D2 and D3 are initially biologically inactive. In the liver, Vitamin D undergoes metabolism facilitated by Vitamin D-binding proteins, leading to the formation of 25-hydroxyvitamin D (calcifediol) and 1,2,5-dihydroxyvitamin D (calcitriol). The primary role of Vitamin D is to regulate the blood levels of calcium and phosphorus by promoting the absorption of these essential nutrients from the small intestine.^{18,40}

Importance of Vitamin D in thyroid diseases

In the context of a community-based survey conducted among individuals aged 16-60, encompassing students, teachers and staff in India significant findings were observed. The results showed a significant relation with calcitriol to the decreased level in the anti-Thyroid Peroxidase antibody (TPO), especially when age was taken into account during the analysis.²⁵ In a parallel study, Chailurkit *et al.* in Thailand identified that young adults with elevated Vitamin D levels displayed reduced circulation of Thyroid-Stimulating Hormone (TSH).²⁶ According to Tamer *et al.*'s study, a deficiency in calcitriol (<30 ng/mL) was more prevalent among individuals with hypothyroidism compared to the control group.²⁷

Individuals who have been diagnosed with hypothyroidism or the early stages of hypothyroidism show a higher likelihood of having low levels of Vitamin D compared to those with normal thyroid function. A study by Racataianu *et al.* found that Vitamin D has a two-way connection with inflammation throughout the body in people who are obese, which could potentially affect how severe and how often hypothyroidism occurs.²⁸ Based on the research available, it seems that Vitamin D might have a role in affecting the development or worsening of hypothyroidism.²⁹

Vitamin D and Hypothyroidism

Vitamin D plays a vital role in keeping our bones and minerals balanced. Recent studies have revealed a link between low levels of Vitamin D and several health conditions, including heart disease, diabetes, cancer, obesity and osteoporosis. Multiple studies have established a significant link between Vitamin D and hypothyroidism. In a recent study, researchers found that women had lower levels of Vitamin D in their blood compared to both men in the control group and male patients. Additionally, they discovered a negative relationship between Vitamin D levels and both calcium and Thyroid-Stimulating Hormone (TSH) levels, highlighting its significance in maintaining overall health.^{10,30}

Vitamin D serves various purposes, such as controlling the immune system and addressing health issues linked to its shortage.³¹ Consequently, this autoimmune response may contribute to the development of hypothyroidism. The majority of hypothyroidism cases are linked to HT.³² The pituitary gland releases Thyroid-Stimulating Hormone (TSH) with the help of thyroglobulins and thyroperoxidase. This can be considered as the marker for HT. Decreased Vitamin D levels are observed in hypothyroidism, HT and other hormonal disorders.³³ The

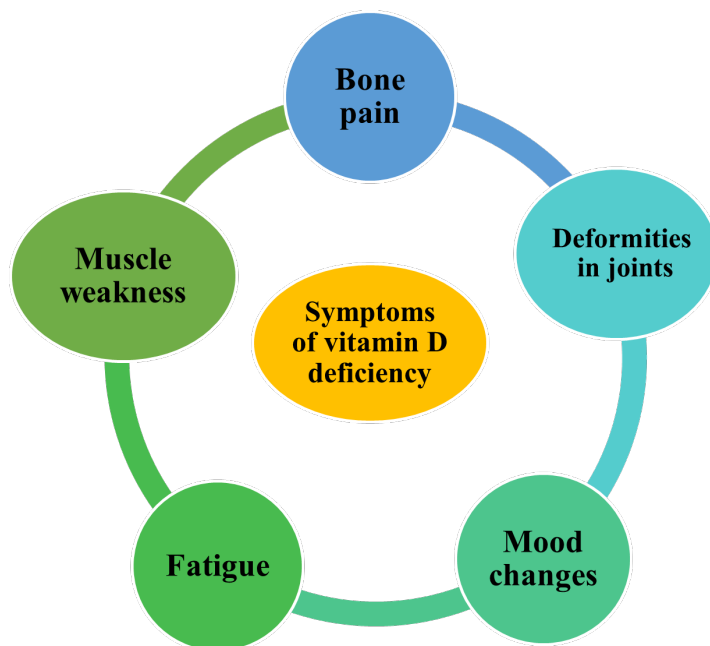


Figure 1: Symptoms of Vitamin D deficiency.

anti-inflammatory property of Vitamin D enhances thyroid function by reducing inflammation. So, maintaining sufficient Vitamin D levels is important for overall thyroid health.³⁴ (Figure 2).

Role of Vitamin D Supplementation

A clinical intervention study was conducted among individuals of Greek Caucasian descent diagnosed with hypothyroidism and hypovitaminosis D, aimed to evaluate the effectiveness of Vitamin D3 therapy in their treatment. Following a four-month period of cholecalciferol supplementation, a noteworthy reduction in serum levels of anti-Thyroid Peroxidase (anti-TPO) was observed.³⁵

In a study comparing 34 women with Hashimoto's Thyroiditis (HT) and normal Vitamin D levels, all on levothyroxine treatment for at least six months, they were split into two groups based on their preferences. Over six months, 18 participants took daily Vitamin D supplements with 2000 IU, while 16 did not receive such supplements. The results showed a significant decrease in antibody levels, particularly anti-TPO, only in those with subclinical hypothyroidism.^{36,37}

Another study by Talaei *et al.* focused on Vitamin D supplementation in hypothyroid patients. They found a noticeable decrease in serum Thyroid-Stimulating Hormone (TSH) levels

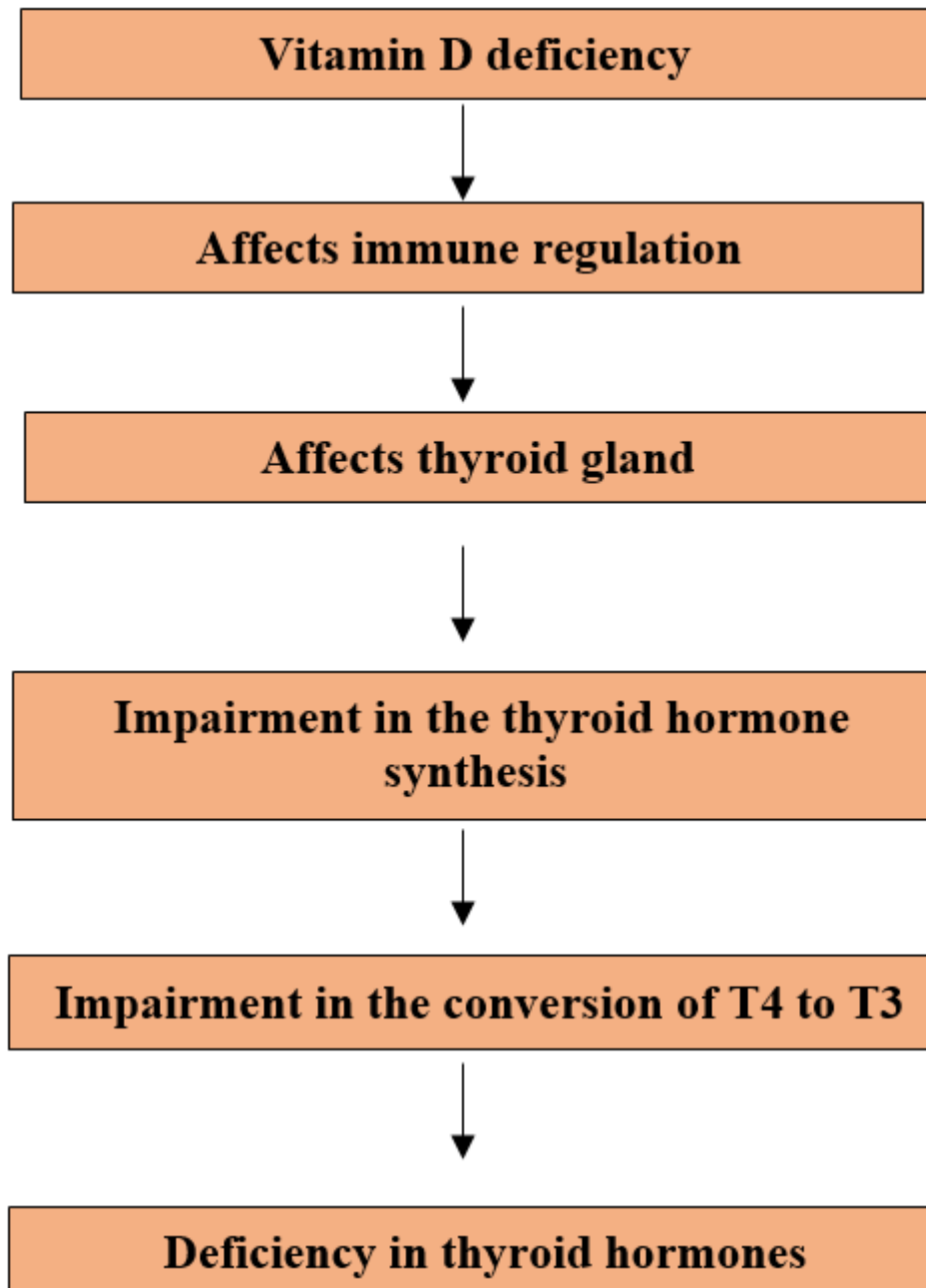


Figure 2: Vitamin D deficiency and Hypothyroidism.

after 12 weeks of Vitamin D supplementation. Further research is needed to fully understand the specific benefits of Vitamin D supplementation in thyroid diseases.⁸

Practical significance

Researchers have discovered an intriguing connection regarding the frequency of low Vitamin D levels and low calcium levels in people with hypothyroidism. These conditions are frequently observed in hypothyroid patients and display a substantial correlation with the severity of the disease, particularly in females. Recent research strongly suggests that taking Vitamin D supplements can reduce Thyroid-Stimulating Hormone (TSH) levels. When comparing Vitamin D supplementation to a placebo in hypothyroidism patients over a 12-week period, there was an enhancement in serum TSH and calcium concentrations, while no impact on T3 and T4 concentrations was observed.⁸ Screening for Vitamin D levels can be considered in hypothyroidism patients, especially in overt hypothyroidism, if symptoms persist or if high TSH levels persist despite levothyroxine therapy.³⁸ Vitamin D supplementation, possibly in conjunction with levothyroxine, may be considered for hypothyroidism patients with hypovitaminosis D, but further research studies are needed in this area to establish the safety and efficacy.^{39,40}

Clinical implications

Maintaining sufficient levels of Vitamin D is crucial for the overall health of individuals diagnosed with hypothyroidism. Vitamin D plays a key role in supporting bone health, strengthening the immune system and alleviating symptoms associated with hypothyroidism. It is crucial to make sure that individuals with hypothyroidism take in enough Vitamin D. This can be done through exposure to sunlight, consuming Vitamin D rich foods, or by using supplements.

CONCLUSION

Vitamin D exerts an impact on thyroid function and holds a pivotal role in the regulation of the immune system. Hypovitaminosis D and hypocalcemia are prevalent among hypothyroid patients. This can worsen the disease condition and reduce the overall quality of life. Screening for hypovitaminosis D can be considered in hypothyroid patients if symptoms persist or therapeutic goals are not achieved despite levothyroxine therapy. For individuals with both hypothyroidism and low Vitamin D levels, Vitamin D supplements may be recommended. Nevertheless, further research is needed to assess the safety and effectiveness of this supplementation.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

VDR: Vitamin D Receptor; **HT:** Hashimoto's Thyroiditis; **TSH:** Thyroid Stimulating Hormone; **T4:** Thyroxine; **T3:** Triiodothyronine; **TPO:** Thyroid Peroxidase; **Vit. D:** Vitamin D.

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