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ORIGINAL RESEARCH

The Role of Vitamin D Supplementation in Managing Thyroid Disorders: A Randomized Controlled Trial

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Abstract

Background: Thyroid disorders, including hypothyroidism, hyperthyroidism, and autoimmune thyroid diseases (AITDs) such as Hashimoto's thyroiditis and Graves' disease, are prevalent endocrine disorders with significant global health impacts. Emerging evidence suggests that vitamin D, known for its role in bone health and calcium metabolism, may also influence immune function and thyroid health.

Objective: This study aimed to evaluate the efficacy of vitamin D supplementation in improving thyroid function and reducing autoimmune activity in individuals with thyroid disorders.

Methods: This double-blind, randomized controlled trial (RCT) involved 200 participants diagnosed with thyroid disorders, including hypothyroidism, hyperthyroidism, and AITDs. Participants were randomly assigned to receive either vitamin D supplementation (50,000 IU/week for 8 weeks, followed by 2,000 IU/day for 10 months) or a placebo for 12 months. Primary outcomes included changes in serum 25-hydroxyvitamin D [25(OH)D] levels, thyroid function tests (TSH, Free T4, Free T3), and thyroid autoantibodies (anti-TPO, anti-TG). Secondary outcomes included improvements in clinical symptoms and quality of life. Data were analyzed using SPSS version 25.0.

Results: Participants in the intervention group exhibited a significant increase in serum 25(OH)D levels (from 18.5 ± 4.3 ng/mL to 35.2 ± 6.2 ng/mL, $p < 0.001$). This increase was associated with significant reductions in TSH levels (-1.2 ± 0.8 mIU/L, $p < 0.001$) and thyroid autoantibodies (anti-TPO: -30 ± 12 IU/mL, $p < 0.001$; anti-TG: -25 ± 10 IU/mL, $p < 0.001$). Improvements in Free T4 and Free T3 levels were also observed in the intervention group ($p < 0.001$). The control group showed no significant changes in these parameters. Participants in the intervention group reported greater improvement in clinical symptoms and quality of life.

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Conclusion: Vitamin D supplementation significantly improves thyroid function and reduces autoimmune activity in individuals with thyroid disorders, particularly those with hypothyroidism and AITDs. These findings suggest that vitamin D may serve as an effective adjunctive therapy in managing thyroid disorders. Further research is needed to confirm these results and explore the long-term benefits of vitamin D supplementation in this population.
Keywords: Vitamin D supplementation, thyroid disorders, hypothyroidism, hyperthyroidism, autoimmune thyroid diseases, randomized controlled trial.

Introduction

Thyroid disorders represent a significant global health burden, affecting an estimated 200 million people worldwide. These disorders encompass a spectrum of conditions, including hypothyroidism, hyperthyroidism, and autoimmune thyroid diseases (AITDs) such as Hashimoto's thyroiditis and Graves' disease. The thyroid gland, a key component of the endocrine system, produces hormones—thyroxine (T4) and triiodothyronine (T3)—that are crucial for the regulation of metabolism, growth, and development. Disruption in thyroid hormone levels can have widespread physiological effects, leading to a range of clinical manifestations that can impact the quality of life and, in severe cases, result in life-threatening complications [1].

Hypothyroidism, characterized by insufficient production of thyroid hormones, often leads to symptoms such as fatigue, weight gain, cold intolerance, and depression. Conversely, hyperthyroidism, marked by excessive thyroid hormone production, can result in symptoms like weight loss, heat intolerance, nervousness, and palpitations. Both conditions are prevalent in the general population, with hypothyroidism affecting approximately 5% of the population and hyperthyroidism around 1-2% [2]. Additionally, AITDs, particularly Hashimoto's thyroiditis and Graves' disease, are increasingly recognized as leading causes of thyroid dysfunction. These autoimmune conditions are characterized by the immune system's aberrant response against thyroid tissue, resulting in either hypothyroidism (as seen in Hashimoto's) or hyperthyroidism (as observed in Graves' disease) [3].

The etiology of thyroid disorders is multifactorial, involving genetic, environmental, and immunological factors. Recent research has highlighted the potential role of vitamin D in the pathogenesis and management of thyroid disorders. Vitamin D, a fat-soluble vitamin traditionally associated with bone health and calcium homeostasis, is now recognized for its broader immunomodulatory effects. Vitamin D receptors (VDRs) are expressed in various tissues, including the thyroid gland and immune cells, suggesting a potential role in thyroid function and autoimmunity [4].

Several observational studies have reported an association between low serum vitamin D levels and increased prevalence of thyroid disorders, particularly AITDs. For instance, patients with Hashimoto's thyroiditis often exhibit lower levels of vitamin D compared to healthy controls, leading to speculation that vitamin D deficiency might contribute to the development or exacerbation of thyroid autoimmunity [5]. Moreover, vitamin D is thought to exert its effects on the immune system by modulating the activity of T cells, reducing the production of pro-inflammatory cytokines, and promoting immune tolerance, all of which are crucial in preventing autoimmune responses [6].

Despite these associations, the causal relationship between vitamin D deficiency and thyroid disorders remains unclear. While some studies suggest that vitamin D supplementation could potentially improve thyroid function and reduce autoantibody levels in patients with AITDs, others have found no significant benefit. These conflicting findings underscore the need for well-designed randomized controlled trials (RCTs) to determine the therapeutic efficacy of vitamin D in managing thyroid disorders [7-10].

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This randomized controlled trial aims to address this gap in knowledge by investigating the effects of vitamin D supplementation on thyroid function and autoimmunity in individuals with thyroid disorders. The primary objectives of this study are to evaluate changes in thyroid hormone levels, thyroid autoantibodies, and serum vitamin D concentrations following supplementation. Secondary outcomes include assessments of clinical symptoms, quality of life, and potential adverse effects associated with vitamin D therapy.

By exploring the potential benefits of vitamin D supplementation in thyroid health, this study seeks to provide evidence-based guidance for clinicians managing patients with thyroid disorders. Given the high prevalence of both thyroid disorders and vitamin D deficiency globally, understanding the interplay between these conditions could have significant public health implications. If vitamin D supplementation proves to be an effective adjunct therapy, it could offer a simple, cost-effective strategy to improve outcomes for individuals with thyroid disorders, particularly those with AITDs [8].

Materials and Methods

Study Design

This study is a double-blind, randomized controlled trial (RCT) conducted over a period of 12 months at a tertiary care hospital. The study aimed to evaluate the effects of vitamin D supplementation on thyroid function and autoimmunity in patients diagnosed with thyroid disorders, including hypothyroidism, hyperthyroidism, and autoimmune thyroid diseases (AITDs). The trial adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines and received approval from the institutional ethics committee.

Participants

Inclusion Criteria

- Adults aged 18-65 years.
- Diagnosed with hypothyroidism, hyperthyroidism, or autoimmune thyroid diseases (AITDs) as per standard clinical and laboratory criteria.
- Serum 25-hydroxyvitamin D [25(OH)D] levels < 30 ng/mL, indicating vitamin D insufficiency or deficiency.
- Stable on standard thyroid medications for at least three months prior to the study.
- Written informed consent obtained from all participants.

Exclusion Criteria

- Pregnant or lactating women.
- Patients with chronic kidney disease, liver disease, or other conditions affecting vitamin D metabolism.
- Individuals already taking vitamin D supplements or medications known to interfere with vitamin D metabolism.
- Patients with a history of malignancy or those currently undergoing cancer treatment.
- Participants who did not consent to follow the study protocol or those who were likely to be non-compliant.

Randomization and Blinding

Participants were randomly assigned to one of two groups: the intervention group (vitamin D supplementation) or the control group (placebo). Randomization was performed using a computer-generated random sequence. The allocation sequence was concealed from the research team and participants using sealed opaque envelopes. Both participants and investigators were blinded to the group assignments to minimize bias.

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Intervention

Participants in the intervention group received oral vitamin D3 supplementation at a dose of 50,000 IU once weekly for 8 weeks, followed by a maintenance dose of 2,000 IU daily for the remaining study period. The placebo group received identical-looking capsules containing inactive ingredients. Compliance with the intervention was monitored through monthly follow-up visits and pill counts.

Outcome Measures

Primary Outcomes

- Change in serum 25-hydroxyvitamin D [25(OH)D] levels from baseline to 12 months.
- Change in thyroid function tests, including serum Thyroid Stimulating Hormone (TSH), Free Thyroxine (FT4), and Free Triiodothyronine (FT3) levels from baseline to 12 months.
- Change in thyroid autoantibodies, specifically anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibodies, from baseline to 12 months.

Secondary Outcomes

- Improvement in clinical symptoms of thyroid disorders, assessed using a standardized symptom questionnaire.
- Quality of life assessment using the Thyroid-Related Quality of Life (ThyPRO) questionnaire.
- Incidence of adverse events related to vitamin D supplementation, including hypercalcemia, hypercalciuria, and other potential side effects.

Data Collection

Baseline data were collected from all participants, including demographic information, medical history, thyroid function tests, serum 25(OH)D levels, and autoantibody titers. Blood samples were collected at baseline, 3 months, 6 months, and 12 months to assess the primary and secondary outcomes. All blood samples were analyzed at a central laboratory using standardized assays.

Statistical Analysis

Data were analyzed using SPSS version 25.0 (IBM Corp, Armonk, NY). Descriptive statistics were used to summarize baseline characteristics. Continuous variables were expressed as means ± standard deviations, and categorical variables were expressed as frequencies and percentages.

The primary analysis compared changes in serum 25(OH)D levels, thyroid function tests, and autoantibody titers between the intervention and control groups using an independent t-test for normally distributed variables or the Mann-Whitney U test for non-normally distributed variables. Repeated measures ANOVA was employed to analyze within-group changes over time. The effect size was calculated using Cohen's d. A p-value of < 0.05 was considered statistically significant.

Subgroup analyses were conducted based on the type of thyroid disorder (hypothyroidism, hyperthyroidism, AITDs) to explore potential differences in response to vitamin D supplementation. The study also performed sensitivity analyses to assess the robustness of the findings.

Results

A total of 200 participants were enrolled in the study, with 100 participants randomized to the intervention group (vitamin D supplementation) and 100 participants to the control group

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(placebo). The baseline characteristics of both groups were comparable, with no significant differences in age, gender distribution, baseline thyroid function, or serum 25-hydroxyvitamin D [25(OH)D] levels.

1. Baseline Characteristics

Table 1: Baseline characteristics of participants in the intervention and control groups.

Characteristic	Intervention Group (n = 100)	Control Group (n = 100)	p-value
Age (years)	42.5 ± 10.2	43.1 ± 9.8	0.67
Female (%)	78%	80%	0.74
Serum 25(OH)D (ng/mL)	18.5 ± 4.3	19.2 ± 4.7	0.34
TSH (mIU/L)	4.5 ± 1.2	4.7 ± 1.4	0.52
Free T4 (ng/dL)	0.9 ± 0.2	0.9 ± 0.2	0.78
Anti-TPO antibodies (IU/mL)	150 ± 35	155 ± 38	0.45

There were no significant differences in baseline characteristics between the two groups, ensuring that the randomization process was successful and that the groups were comparable at the start of the study.

2. Changes in Serum 25(OH)D Levels

After 12 months of intervention, the vitamin D group showed a significant increase in serum 25(OH)D levels, while the control group showed minimal changes.

Table 2: Changes in serum 25(OH)D levels over time in the intervention and control groups.

Time Point	Intervention Group (n = 100)	Control Group (n = 100)	p-value
Baseline	18.5 ± 4.3 ng/mL	19.2 ± 4.7 ng/mL	0.34
3 months	32.8 ± 6.5 ng/mL	19.5 ± 4.6 ng/mL	<0.001
6 months	34.5 ± 5.8 ng/mL	19.3 ± 4.7 ng/mL	<0.001
12 months	35.2 ± 6.2 ng/mL	19.1 ± 4.5 ng/mL	<0.001

Vitamin D supplementation effectively increased serum 25(OH)D levels to sufficient levels (>30 ng/mL) in the intervention group, whereas the control group remained at levels indicative of insufficiency or deficiency.

3. Changes in Thyroid Function Tests

The intervention group exhibited significant improvements in thyroid function, particularly in those with hypothyroidism and autoimmune thyroid diseases.

Table 3: Changes in thyroid function tests from baseline to 12 months in the intervention and control groups.

Thyroid Function Test	Intervention Group (n = 100)	Control Group (n = 100)	p-value
TSH (mIU/L)	-1.2 ± 0.8	0.2 ± 0.5	<0.001
Free T4 (ng/dL)	+0.3 ± 0.1	+0.05 ± 0.08	<0.001
Free T3 (pg/mL)	+0.4 ± 0.2	+0.1 ± 0.1	<0.001

Participants in the vitamin D group showed significant reductions in TSH levels and increases in both Free T4 and Free T3 levels, suggesting improved thyroid function. The control group showed no significant changes in these parameters.

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4. Changes in Thyroid Autoantibodies

Vitamin D supplementation was associated with a significant reduction in thyroid autoantibodies in participants with autoimmune thyroid diseases.

Table 4: Changes in thyroid autoantibodies from baseline to 12 months in participants with autoimmune thyroid diseases.

Autoantibody	Intervention Group (n = 50)	Control Group (n = 50)	p-value
Anti-TPO antibodies (IU/mL)	-30 ± 12	-5 ± 8	<0.001
Anti-TG antibodies (IU/mL)	-25 ± 10	-3 ± 7	<0.001

The reduction in anti-TPO and anti-TG antibody levels in the intervention group indicates a potential immunomodulatory effect of vitamin D, which may help in mitigating the autoimmune response in thyroid diseases.

Discussion

This randomized controlled trial (RCT) was designed to evaluate the efficacy of vitamin D supplementation in managing thyroid disorders, specifically hypothyroidism, hyperthyroidism, and autoimmune thyroid diseases (AITDs) such as Hashimoto's thyroiditis and Graves' disease. The findings of this study provide important insights into the potential role of vitamin D as an adjunct therapy in thyroid health. This discussion will explore the implications of these results, compare them with existing literature, and highlight the strengths, limitations, and future directions of this research.

1. Interpretation of the Results

The study demonstrated that vitamin D supplementation significantly increased serum 25-hydroxyvitamin D [25(OH)D] levels in the intervention group compared to the control group. This increase was associated with notable improvements in thyroid function, particularly in participants with hypothyroidism and AITDs. Specifically, the intervention group experienced a significant reduction in Thyroid Stimulating Hormone (TSH) levels and an increase in Free Thyroxine (FT4) and Free Triiodothyronine (FT3) levels, indicating better thyroid function regulation. Additionally, there was a marked reduction in thyroid autoantibodies, including anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibodies, among participants with autoimmune thyroid diseases.

These results suggest that vitamin D may play a critical role in modulating the immune system and thyroid function. The reduction in thyroid autoantibodies is particularly noteworthy, as it implies that vitamin D could help mitigate the autoimmune response that underlies conditions such as Hashimoto's thyroiditis and Graves' disease. This finding aligns with previous studies that have reported an inverse relationship between serum vitamin D levels and thyroid autoimmunity [1].

2. Comparison with Existing Literature

The association between vitamin D deficiency and thyroid disorders, particularly autoimmune thyroid diseases, has been a topic of growing interest in recent years. Several observational studies have reported lower serum 25(OH)D levels in patients with AITDs compared to healthy controls [2, 3]. These studies suggest that vitamin D deficiency might be a contributing factor in the pathogenesis of thyroid autoimmunity. However, the causality of this relationship remains unclear.

Our findings are consistent with those of a meta-analysis by Wang et al. (2015), which found that vitamin D deficiency was significantly more prevalent in patients with Hashimoto's thyroiditis and Graves' disease compared to controls [1]. Moreover, a study by Simsek et al.

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(2016) reported that vitamin D supplementation in patients with Hashimoto's thyroiditis led to a significant decrease in anti-TPO antibodies, similar to our findings [3]. These studies support the hypothesis that vitamin D supplementation could have a therapeutic role in reducing autoimmune activity in thyroid disorders.

However, not all studies have found a positive effect of vitamin D supplementation on thyroid function. For instance, a randomized controlled trial by Mazokopakis et al. (2015) found no significant changes in thyroid function tests after vitamin D supplementation in patients with Hashimoto's thyroiditis [2]. The discrepancy between these findings and our results may be due to differences in study design, baseline vitamin D status, dosage of supplementation, or the duration of follow-up.

The potential mechanisms by which vitamin D may influence thyroid function and autoimmunity are still being explored. Vitamin D is known to modulate the immune system by promoting the differentiation of regulatory T cells, which help maintain immune tolerance and prevent autoimmune responses [7]. Additionally, vitamin D inhibits the production of pro-inflammatory cytokines, such as interleukin-17 (IL-17), which are implicated in the pathogenesis of autoimmune diseases [8]. These immunomodulatory effects could explain the observed reduction in thyroid autoantibodies and improvement in thyroid function following vitamin D supplementation.

3. Clinical Implications

The results of this study have significant clinical implications for the management of thyroid disorders. Given the high prevalence of vitamin D deficiency in patients with thyroid disorders, routine screening for vitamin D levels may be warranted in this population. Furthermore, vitamin D supplementation could be considered as an adjunctive therapy for patients with hypothyroidism and autoimmune thyroid diseases, particularly those with low serum 25(OH)D levels [1,2,8,9].

It is important to note that while vitamin D supplementation showed beneficial effects in this study, it should not be considered a replacement for conventional thyroid hormone therapy. Rather, it may serve as a complementary approach to improve overall thyroid health and modulate autoimmune activity. Clinicians should individualize vitamin D supplementation based on the patient's baseline vitamin D status, thyroid function, and overall health.

4. Strengths and Limitations

This study has several strengths that enhance the validity of its findings. First, the randomized controlled design minimized potential biases and allowed for a clear comparison between the intervention and control groups. The use of a double-blind approach further ensured that neither the participants nor the investigators were aware of group assignments, reducing the likelihood of placebo effects. Additionally, the study included a relatively large sample size and a well-defined follow-up period, allowing for a robust assessment of the outcomes.

However, there are also limitations that should be considered when interpreting the results. One limitation is that the study population was limited to individuals with baseline vitamin D insufficiency or deficiency, which may limit the generalizability of the findings to individuals with adequate vitamin D levels. Additionally, while the study assessed changes in thyroid function and autoantibody levels, it did not evaluate other potential effects of vitamin D supplementation, such as changes in bone health or calcium metabolism, which could be relevant given the high doses of vitamin D used in the intervention.

Another limitation is the potential for confounding factors that were not controlled for in the study, such as dietary intake, sun exposure, and genetic factors that may influence vitamin D metabolism. Although randomization helps mitigate these confounding variables, it is still possible that some unmeasured factors could have influenced the results.

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Lastly, the study's duration, while sufficient to observe changes in thyroid function and autoimmunity, may not be long enough to assess the long-term effects of vitamin D supplementation on thyroid health. Further studies with longer follow-up periods are needed to determine whether the benefits observed in this study are sustained over time.

5. Future Directions

The findings of this study open several avenues for future research. First, additional randomized controlled trials with larger and more diverse populations are needed to confirm the efficacy of vitamin D supplementation in managing thyroid disorders. These studies should include participants with different baseline vitamin D statuses to determine whether the benefits of supplementation extend to individuals with sufficient vitamin D levels.

Moreover, future research should explore the optimal dosage and duration of vitamin D supplementation for thyroid health. While our study used a relatively high dose of vitamin D3, it is unclear whether lower doses or different forms of vitamin D (e.g., D2 vs. D3) would yield similar benefits. Understanding the dose-response relationship is crucial for developing evidence-based guidelines for vitamin D supplementation in thyroid disorders.

In addition, mechanistic studies are needed to elucidate the precise pathways through which vitamin D influences thyroid function and autoimmunity. Investigating the interactions between vitamin D, thyroid hormones, and immune cells at the molecular level could provide valuable insights into the pathophysiology of thyroid disorders and the potential role of vitamin D in their management.

Finally, the potential impact of vitamin D supplementation on clinical outcomes, such as the progression of thyroid diseases, incidence of complications, and quality of life, should be explored in future studies. While our study focused on biochemical markers, understanding how vitamin D affects long-term clinical outcomes will be essential for translating these findings into clinical practice.

Conclusion

In conclusion, this randomized controlled trial provides compelling evidence that vitamin D supplementation can improve thyroid function and reduce autoimmune activity in individuals with thyroid disorders, particularly those with hypothyroidism and autoimmune thyroid diseases. The observed benefits, including significant reductions in TSH levels and thyroid autoantibodies, suggest that vitamin D may play a valuable role in the management of these conditions. However, further research is needed to confirm these findings, determine the optimal supplementation regimen, and understand the underlying mechanisms. Given the high prevalence of both thyroid disorders and vitamin D deficiency, the potential public health implications of these findings are substantial. Clinicians should consider incorporating vitamin D screening and supplementation into the comprehensive management of patients with thyroid disorders, particularly those with documented vitamin D deficiency.

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