# Exploring the Relationship between Vitamin D and Autoimmunity Leading to Thyroid Dysfunction

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**Abstract**

**Objective:** To determine the relationship between vitamin D and autoimmunity which leads to thyroid dysfunction.

**Material and Methods:** The cross-sectional study was conducted from 01/11/2023 to 31/04/2024 in Medical unit 4 of Services Hospital, Lahore. Data was collected from 120 patients. Patients were recruited after written informed consent keeping in mind inclusion and exclusion criteria. Their clinical parameters were recorded, thyroid examination was carried out and vitamin D levels were sent along with other routine labs (FT3, FT4, TSH and Anti TPO antibodies).

**Results:** Mean age of participants was 49.28±8.9 years. The mean Body Mass Index (BMI) was 27.63±5.07 kg/m². The mean 25(OH)D concentration was 27.32±11.45 nmol/L, reflecting variability in vitamin D levels among the participants. Analyzing vitamin D status, 37.5% of participants (45 individuals) were found to be deficient, 34.2% (41 individuals) had insufficient levels, and 28.3% (34 individuals) had sufficient levels. Additionally, 60.8% of participants (73 individuals) had co-morbid conditions, while 39.2% (47 individuals) did not.

**Conclusion:** It is concluded that there is no significant association between vitamin D levels and the autoimmune status of patients with thyroid dysfunction. While vitamin D levels do play a role in thyroid health, however our data does not support a link between vitamin D status and the presence of autoimmune thyroid disorders.

**Keywords:** Vitamin D, Autoimmunity, Thyroid Dysfunction, Autoimmune Thyroid Diseases

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## Introduction

Thyroid disorders have long been a subject of intriguing research, with a complex interplay of factors contributing to their development and progression.[1] While the established link between autoimmunity and thyroid disorders is well documented, emerging evidence suggests that vitamin D deficiency may play a crucial role in this relationship, extending beyond the realm of autoimmunity.[2] In this article, we will delve into the intricate connections between vitamin D deficiency and thyroid disorders, exploring the possible underlying mechanisms and the potential therapeutic implications[3]

Vitamin D is a versatile hormone that exerts a variety of physiological effects, including its influence on thyroid function.[3,4] Vitamin D receptors (VDRs) are widely expressed in thyroid cells, indicating the potential for direct interactions between vitamin D and thyroid homeostasis.[5] Research has shown that vitamin D deficiency can lead to significant suppression in intestinal calcium absorption and impairment of calcium balance, which can

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subsequently impact thyroid function and contribute to developing thyroid disorders.[5] The association between vitamin D deficiency and autoimmune thyroid disorders, such as Hashimoto's thyroiditis and Graves' disease, has been extensively examined. Vitamin D is known to play a crucial role in regulating the immune system, and its deficiency has been linked to an increased risk of autoimmune conditions.[6] The presence of an immune response against the thyroid gland defines Autoimmune Thyroid diseases. The most common thyroid autoimmune diseases are Graves and Hashimoto's thyroiditis, as can be seen with an estimated prevalence of about 5%.[7]

Hashimoto's thyroiditis has both humoral and cellular immunity involved in the development of this disease. On histology of Hashimoto's thyroiditis both T and B cell inflammatory infiltrate is seen.[8] Hashimoto's thyroiditis comprised of 63.1% of thyroid disorders presenting to a tertiary care hospital in Pakistan. Human epidemiological research has pointed out the fact that women are more likely to develop hypothyroidism as compared to men. Hashimoto's thyroiditis leads to primary hypothyroidism, a common endocrine cause of depression, infertility, obesity, hyperlipidemia and sleep apnea.[9] In the twenty-first century, iodine deficiency remains the major cause of hypothyroidism, yet, in iodine sufficient countries, patients still develop hypothyroidism attributable to autoimmune (Hashimoto's thyroiditis) or iatrogenic causes.[10] On the other extreme end of the spectrum is Graves' Disease, the commonest cause of hyperthyroidism involving thyroid and extra thyroidal tissues. Patients with Graves' disease have antibodies to thyroid receptor. Untreated Graves' disease leads to atrial fibrillation, thyroid storm, decreased bone mineral density and opthalmopathy.[11] Research with animal models of Graves' disease and thyroiditis suggest a positive response to vitamin D supplementation.[7] The relationship has been confirmed in genetic studies, numerous polymorphisms in VDR and other genes regulating signals of vitamin D were identified to increase the risk of developing autoimmune thyroid diseases.[8] Studies have demonstrated that vitamin D supplementation may have a beneficial effect on the management of autoimmune thyroid disorders, potentially by modulating the immune response and reducing the risk of thyroid autoimmunity.[12]

This relationship was further supported by a number of experiments demonstrating the role of vitamin D in regulating chemokine production, counteracting autoimmune inflammation, and encouraging the differentiation of immune cells.

## Material and Methods

The cross-sectional study was conducted from 01 November 2023 to 30 April 2024 in Medical unit 4 of Services Hospital, Lahore. After the taking approval from Ref. IRB 2024/1363/SIMS dated 05-06-2024. Individuals aged 18 years and above, of both genders, presenting with thyroid disorder. Exclusions comprised of patients on antiepileptics, those currently undergoing vitamin D replacement, and individuals with a history of vitamin D replacement within the last 6 months. After ethical approval (IRB/2024/1363/SIMS) for study was obtained, patient recruitment according to defined criteria was started and pertinent information on a pre-designed proforma was captured .Clinical parameters like thyroid examination was carried out and vitamin D levels were sent along with other routine labs (FT3, FT4, TSH and anti TPO antibodies). Vitamin D deficiency was defined as 25(OH)D level < 20 nmol/L, Insufficiency as 20-29 nmol/L and sufficiency as ≥30 nmol/L. Data was put in SPSS version 25 for analysis. Mean and standard deviation were calculated for quantitative variables (age, BMI and vitamin D levels) and frequencies were determined for qualitative variables (Thyroid and autoimmunity status and vitamin D levels). Also, the stratification of autoimmune status was done with vitamin D levels and other variables.

## Results

Mean age of participants was 49.28±8.9 years. The mean Body Mass Index (BMI) was 27.63±5.07 kg/m². The mean 25(OH)D concentration was 27.32±11.45 nmol/L, reflecting variability in vitamin D levels among the participants. Amongst the study population, 27.5% of the participants were male (33 individuals) and 72.5% were female (87 individuals). Regarding autoimmunity, 47.5% of participants (57 individuals) had an autoimmune condition, while 52.5% (63 individuals) did not. In terms of thyroid status, 58.3% of participants (70 individuals) had

hyperthyroidism, whereas 41.7% (50 individuals) had hypothyroidism. Analyzing vitamin D status, 37.5% of participants (45 individuals) were found to be deficient, 34.2% (41 individuals) had insufficient levels, and 28.3% (34 individuals) had sufficient levels. Additionally, 60.8% of participants (73 individuals) had co-morbid conditions, while 39.2% (47 individuals) did not. The analysis of the association between demographic and clinical variables and autoimmunity demonstrated that age was significantly associated with autoimmunity, with a p-value of 0.00. Among participants aged 20–45 years, 49.1% exhibited autoimmunity, compared to 12.7% without autoimmunity in the same age group. In contrast, among participants aged 46–60 years, 50.9% had autoimmunity, whereas 87.3% did not.

**Table 1:** *Demographic characteristics of population under study (n=120)*

| Variable | | Mean | Std. Deviation |
|---|---|---|---|
| Age (years) | | 49.28 | ±8.9 |
| BMI (kg/m²) | | 27.63 | ±5.07 |
| 25(OH)D (nmol/L) | | 27.32 | ±11.45 |
| **Variable** | | **Category** | **Percentage (%)** |
| **Gender** | Male | 33 | 27.5 |
| | Female | 87 | 72.5 |
| **Autoimmunity** | Yes | 57 | 47.5 |
| | No | 63 | 52.5 |
| **Thyroid Status** | Hyperthyroidism | 70 | 58.3 |
| | Hypothyroidism | 50 | 41.7 |
| **Vitamin D status (nmol/L)** | Deficient | 45 | 37.5 |
| | Insufficient | 41 | 34.2 |
| | Sufficient | 34 | 28.3 |
| **Co Morbid Conditions** | Yes | 73 | 60.8 |
| | No | 47 | 39.2 |

**Table 2:** *Stratification according to age and clinical parameters*

| Variable | Sub Groups | No Auto-immunity | Auto-immunity | p-value |
|---|---|---|---|---|
| **Age** | 20-45 Years | 8 (12.7%) | 28 (49.1%) | 0.00* |
| | 46-60 Years | 55 (87.3%) | 29 (50.9%) | |
| **Gender** | Male | 19 (30.2%) | 14 (24.6%) | 0.49 |
| | Female | 44 (69.8%) | 43 (75.4%) | |
| **Thyroid status** | Hyperthyroidism | 39 (61.9%) | 31 (54.4%) | 0.40 |
| | Hypothyroidism | 24 (38.1%) | 26 (45.6%) | |
| **Vit-D** | Deficiency (<20) | 22 (34.9%) | 23 (40.4%) | 0.44 |
| | Insufficiency (20-29) | 20 (31.7%) | 21 (36.8%) | |
| | Sufficiency (≥30) | 21 (33.3%) | 13 (22.8%) | |

**p value is significant at 0.05 , Percentages are row wise*

Gender did not show a statistically significant association with autoimmunity, with a p-value of 0.49. Among males, 24.6% exhibited autoimmunity compared to 30.2% without, while among females, 75.4% exhibited autoimmunity compared to 69.8% without. Thyroid status was also not significantly associated with autoimmunity, with a p-value of 0.40. Among individuals with autoimmunity, 54.4% had hyperthyroidism and 45.6% had hypothyroidism, compared to 61.9% and 38.1% among individuals without autoimmunity, respectively. Vitamin D levels did not show a significant association with autoimmunity, with a p-value of 0.44. Among individuals with autoimmunity, 40.4% were vitamin D deficient (<20 nmol/L), 36.8% had insufficient levels (20–29 nmol/L), and 22.8% had sufficient levels (≥30 nmol/L), compared to 34.9%, 31.7%, and 33.3% among individuals without autoimmunity. These findings indicate that, except for age, other factors such as gender, thyroid status, and vitamin D levels do not show statistically significant associations with autoimmunity in the studied population.

## Discussion

This study aimed to determine whether vitamin D deficiency is associated specifically with autoimmune thyroid disorders or with all types of thyroid dysfunction. Our findings suggest that vitamin D deficiency is prevalent across all forms of thyroid dysfunction, irrespective of autoimmune status. This indicates that other mechanisms may underlie the interaction between vitamin D and thyroid dysfunction. Future research should focus on exploring these mechanisms to better understand the role of vitamin D in thyroid health.[9] Vitamin D deficiency is highly prevalent in Asians, which may explain this as a coincidental finding. If studies on larger scales are carried out in different populations that are not known to be vitamin D deficient then it would have been more promising, and we will be in a better position to comment on.[13] It is also proposed that vitamin D can be replaced in all these patients and then autoimmunity assessed again. Hypothyroidism belongs to the most prevalent pathologies regarding thyroid hormone deficiency the overall prevalence increasing between 0·3% and 3·7 % in the United States and between 0·2% and 5·3% in Europe.[14] Hypothyroidism have been extrapolated and even on average meta-analysis studies conducted on nine

European countries revealed that undiagnosed hypothyroidism all-inclusive of both, overt as well as less intrusive cases, were estimated to be around 5%.[15] Some human epidemiological research has pointed out the fact that women are more likely to develop hypothyroidism as compared to men. In the twenty-first century, iodine deficiency remains the major cause of hypothyroidism, yet, in iodine sufficient countries, patients develop sickle hypothyroidism attributable to autoimmune (Hashimoto's thyroiditis) or iatrogenic diseases. Share of hypothyroidism's associated symptoms range across numerous metabolic disorders, which affect multiple organ systems.[16] Hashimoto's thyroiditis (HT)has a complex etiology, with genetic and environmental factors contributing to its pathophysiology. The thyroid gland is infiltrated with lymphocytic infiltration, damage to thyroid cells and long-term levothyroxine therapy. Researchers believe that vitamin D may reduce the level of antithyroid antibodies. Autoimmune diseases are defined by the presence of an immune response counteracting the thyroid gland. These are the most common general autoimmune diseases, as can be seen with an estimated prevalence of about 5%.[17] Graves disease and Hashimoto's thyroiditis both are T-cell mediated autoimmune diseases that involve infiltration and inflammation of the thyroid gland by lymphocytes. The relations have been confirmed in genetic studies, numerous polymorphisms in VDR and other genes regulating signals of vitamin D were identified to increase the risk of developing autoimmune thyroid diseases.[18] Another study in China showed that clinical myxoedema is linearly associated with loss of fetus, IUGR, low birth weight babies, and several congenital malformations. Women with subclinical hypothyroidism during pregnancy give rise to increased fetal distress, preterm labour and deliveries, poor vision and neurodevelopmental delays. Pregnant patients with clinical hyperthyroidism had children with hearing dysplasia. A systemic review and meta-analysis found a strong association between clinical hypothyroidism and preeclampsia, perinatal mortality and lower IQ in the child. They also found an association between thyroid autoimmunity and unexplained subfertility, miscarriages, recurrent miscarriages and preterm birth.[19] Another study conducted at a tertiary care hospital in Karachi supports a significant association between low vitamin D levels and autoimmune thyroid disorders (AITDs), with 48.3% of participants being deficient and 28.3% having insufficient levels of vitamin D. Anti-TPO and anti-TG antibodies were notably higher in individuals with low vitamin D levels, demonstrating a stronger autoimmune link. In contrast, our study did not find a statistically significant relationship between vitamin D levels and autoimmunity, despite observing a high prevalence of vitamin D deficiency. This discrepancy may be attributed to differences in population characteristics, such as age distribution, and sample size. Future studies comparing larger, more diverse populations will be essential to reconcile these findings and enhance our understanding of the role of vitamin D in thyroid autoimmunity.[18,19]

A key limitation of our study is its cross-sectional design, which precludes the establishment of causal relationships. Additionally, the study was conducted in a single-centre setting, which may limit the generalizability of the findings. Future research should involve larger, multicentre studies with diverse populations to validate these results and better understand the complex interplay between vitamin D and thyroid autoimmunity. Such studies should also consider longitudinal designs to explore the causal pathways and potential therapeutic implications of vitamin D in autoimmune thyroid disorders.

## Conclusion

The findings of this study reveal no significant association between vitamin D levels and the autoimmune status of patients with thyroid dysfunction. While vitamin D undoubtedly plays a crucial role in maintaining thyroid health, our data do not establish a direct link between vitamin D status and the development of autoimmune thyroid disorders. Nevertheless, the potential interplay between vitamin D and thyroid function remains a compelling avenue for further research, offering insights that could pave the way for novel therapeutic strategies and improved patient outcomes. These results emphasize the need for larger, more diverse studies to unravel the complexities of this relationship and to fully explore vitamin D's potential in managing thyroid and autoimmune conditions.

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## Authors Contribution

**AR:** Conceptualization of Project
**AB:** Data Collection
**MI:** Literature Search

**BAS:** Statistical Analysis

**TS, AB:** Drafting, Revision
**BAS:** Writing of Manuscript