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ORIGINAL ARTICLE

Prevalence of Vitamin D Deficiency in Patients with Autoimmune Thyroid Disorders at Tertiary Care Hospital, Karachi

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ABSTRACT

Objective: This study aimed to ascertain the magnitude of vitamin D deficiency in those with autoimmune thyroid disorders (AITDs).

Methodology: A cross-sectional study was conducted at the National Institute of Diabetes and Endocrinology, Dow University of Health Sciences, Ojha Campus, Karachi, Pakistan from February 2024 to June 2024. Patients who attended the outpatient department and were diagnosed with AITDs, such as autoimmune hypothyroidism and Grave's disease, based on positive anti-thyroid antibodies were included in the study. The 25-hydroxy vitamin D levels in these patients were then measured.

Results: The study had 60 participants, with a mean age of 35.23 ± 9.934 years. The majority of participants had low vitamin D levels (28.3% had insufficient and 48.3% had deficient levels). Additionally, it was discovered that vitamin D status and AITDs were related, where a majority of individuals had low vitamin D levels (P-value = 0.014). Further, it was revealed that anti-TPO antibodies followed by the presence of anti-TG antibodies were more indicative of low vitamin D levels.

Conclusion: The individuals with AITDs, specifically hypothyroidism had a noticeably higher prevalence of vitamin D deficiency followed by insufficiency.

Keywords: Prevalence, vitamin D deficiency, autoimmune, thyroid disorder, Karachi

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[1,2]Conception; Literature research; manuscript design and drafting; [3,4] Critical analysis and manuscript review; [4]Data analysis; Manuscript Editing.

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Introduction

Autoimmune thyroid diseases (AITDs), namely Grave's disease and Hashimoto's thyroiditis, appear to share a common genetic predisposition and are the most prevalent organ-specific autoimmune conditions. AITDs are multifactorial with the interplay of genetics and environmental triggering factors that are manifested by thyroid gland infiltration with lymphocytes and leading to the production of autoantibodies[1]. Anti-thyroglobulin (anti-TG) and anti-thyroid peroxidase (anti-TPO) antibodies cause B and T lymphocytes with type 1 T helper and CD4 cells to infiltrate the thyroid, resulting in atrophic autoimmune hypothyroidism, a condition mediated by T-cells. The lymphocyte infiltration in Grave's disease is minimal and contains CD4+ type 2 T helper cells, which bind to thyroid-stimulating hormone (TSH) receptors to

make antibodies. This activates the thyroid's follicular cells, which results in hyperthyroidism[1].

Therefore, environmental factors that disturb immunological-endocrine interactions in genetically predisposed individuals can change the stability of the Type 1 and 2 helper T cell immune response. This results in a hyperreactive Type 2 T-helper cells mediated humoral response against receptors of TSH with antibodies which are stimulatory causing hyperthyroidism in Grave's disease; however, in atrophic autoimmune hypothyroidism, this leads to a Type 1 T-helper mediated autoimmune response with destruction of thyrocytes leading to hypothyroidism[1, 2].

In addition to its immune-regulating capabilities, vitamin D has anti-inflammatory effects. It influences T regulatory cells, encourages the growth of Th2 helper cells, and inhibits dendritic cell differentiation to affect the adaptive immune system[3, 4]. Vitamin D can improve tolerogenic qualities and prevent T-cell activation that is dependent on dendritic cells, which encourages the induction of regulatory T cells rather than effector T cells[5].

This is further corroborated by the fact that these cells contain vitamin D receptors, demonstrating the localized action of vitamin D on the immune system. The relevance of vitamin D in autoimmune illnesses is highlighted by the correlation found between the pathophysiology of multiple autoimmune conditions and polymorphisms in the CYP27B1 gene or vitamin D receptor genes[6]. Lack of vitamin D has been connected to a number of autoimmune conditions. Evidence indicates that taking vitamin D supplements may delay the onset of certain autoimmune diseases[7, 8]. Vitamin D serves as an immune system regulator, and recent studies have indicated that its deficiency is linked to several autoimmune diseases[5]. Studies on the connection between autoimmune thyroid illnesses and vitamin D insufficiency have been conducted extensively in the past several years, with varying degrees of success. Low levels of vitamin D are linked to both Hashimoto's thyroiditis and Graves' disease, according to a meta-analysis of vitamin D deficiency in autoimmune thyroiditis[8]. However, because there are still a lot of unanswered problems, further research is required to properly understand the relationship between vitamin D and autoimmune thyroid illnesses. To ascertain the degree of vitamin D deficiency in people with autoimmune thyroid diseases, a tertiary care facility hosted this study.

Methodology

A cross-sectional study was conducted at the Department of National Institute of Diabetes & Endocrinology (NIDE), Dow University of Health Sciences, Ojha Campus in Karachi, from February 2024 to June 2024 through a non-probability consecutive sampling technique.

The sample size of the study was determined using Roasoft, an open-source calculator[9]. A 95% confidence interval, a margin of error of 5%, response rate of 50%, and population size were kept according to a previous study conducted in 2022[10], where 74.68% of thyroid dysfunction females had vitamin D deficiency. Therefore, 52 patients with AITDs were determined to be the sample size for the current study. The final adjusted sample size was 52/(1-0.10) = 52/0.9 = 58 after accounting for the 10% non-response rate in the case above. After receiving approval from the hospital's ethical review committee, patients who attended the outpatient department and were diagnosed with AITDs, such as atrophic autoimmune hypothyroidism and Grave's disease, based on positive anti-thyroid antibodies, such as anti-TPO, Anti-Tg, and TSH receptor antibodies (TRAB), were included in the study. However, patients with a history of thyroid malignancy and chronic renal disease, and patients on vitamin D supplements, corticosteroids, and anti-convulsant medications were excluded. Further, patients who did not visit the outpatient department of NIDE and those who did not consent to participate

in the study were also excluded. The 25-hydroxy vitamin D levels of these patients were measured, within 12 hours, using Chemiluminescence immunoassay. Based on the Endocrine Society Guidelines these were then categorized into three categories. A 25(OH)D blood levels ≥ 30 to 100/mL, ranging from 21 to 29 ng/mL, and values < 20 ng/mL were considered as sufficient, insufficient, and deficient, respectively[11].

Version 26.0 of Statistical Package of Social Sciences (SPSS) software was used to enter and analyze all the data. The patient's age was calculated using descriptive statistics to determine its mean and standard deviation. The frequency and proportion of all categorical variables, including TSH receptor antibodies, anti-TPO antibodies, anti-TG antibodies, and marital status and community type were displayed. Using a p-value of < 0.05, the Chi-Square test was applied to assess the statistical significance threshold. And 2*2 contingency table was made to assess the association of autoantibodies with the magnitude of vitamin D among the patients.

Results

A total of 60 participants were included in the study with a mean age of 35.23 ± 9.934 years (ranged 14 to 58 years). Most of the participants were females (n=43, 71.7%), housewives (n=30, 50%), married (n=44, 73.3%), middle class (n=56, 93.3%), lived in urban areas (n=39, 65%), and had deficient vitamin D levels (n=29, 48.3%). Further, AITDs were also found to be associated with vitamin D status where most participants had deficient vitamin D levels (P-value = 0.014) (Table II).

Further, assessment based on the presence of auto-antibodies revealed that the majority of the hypothyroid patients had deficient (n=20) and insufficient (n=7) vitamin D levels as compared to the individuals who were diagnosed with Grave's disease, in which the majority had sufficient (n=10) vitamin D levels followed by insufficient levels (n=9). The results revealed that anti-TPO antibodies followed by the presence of anti-TG antibodies were more indicative of low vitamin D levels (Table I).

Table I: Association of Autoimmune thyroid diseases and low vitamin D levels (n=60)

Autoimmune thyroid disorder		Vitamin D Status			Total
		Sufficiency (n=14)	Insufficiency (n=17)	Deficiency (n=29)	
Hypothyroidism (n=34)	anti-TG antibody	4	7	20	31
	anti-TPO antibody	5	7	22	34
Grave's Disease (n=26)	TRAB antibody	10	9	7	26

Discussion

This study adds to the mounting body of research suggesting that vitamin D insufficiency may be a contributing factor in AITDs, such as atrophic autoimmune hypothyroidism and Graves' disease. The study demonstrated the significant prevalence of vitamin D deficiency in AITD patients, which supported previous findings. The findings of this inquiry are consistent with other research on the relationship between vitamin D insufficiency and AITDs[12]. Numerous investigations have shown that vitamin D insufficiency was highly prevalent in patients with AITDs.

The results of the current investigation showed that the existence of anti-TG antibodies, followed by anti-TPO antibodies, was a stronger indicator of low vitamin D levels. A study by Anaraki PV et al. found that vitamin D insufficiency was more common in people with Hashimoto's thyroiditis than in controls[13]. Turashvili et al.'s investigation, which found similar results to the current study, found that females with AITDs—specifically, hypothyroidism—were more likely to have vitamin D deficiency[14].

Table II: Demographic Characteristics of the patients in association with vitamin D status (n=60)					
Demographic Variables	**Vitamin D Status**			**Total (n=63)**	**P-value**
	Sufficiency (n=14)	**Insufficiency (n=17)**	**Deficiency (n=29)**		
Age					
<35 years	7 (50%)	10 (58.82%)	16 (55.17%)	33 (55%)	0.886
>35 years	7 (50%)	7 (41.17%)	13 (44.82%)	27 (45%)	
Gender					
Male	4 (28.57%)	4 (23.52%)	9 (31.03%)	17 (28.3%)	0.862
Female	10 (71.42%)	13 (76.47%)	20 (68.95%)	43 (71.7%)	
Marital Status					
Unmarried	3 (21.42%)	7 (41.17%)	6 (20.68%)	16 (26.7%)	0.279
Married	11 (78.57%)	10 (58.82%)	23 (79.31%)	44 (73.3%)	
Educational Level					
Illiterate	1 (7.14%)	4 (23.52%)	1 (3.44%)	6 (10%)	0.181
High school	4 (28.57%)	5 (29.41%)	6 (20.68%)	15 (25%)	
College	9 (64.28%)	8 (47.05%)	22 (75.86%)	39 (65%)	
Occupation					
Student	0 (0%)	4 (23.52%)	3 (10.34%)	7 (11.7%)	
Housewife	9 (64.28%)	6 (35.29%)	15 (51.72%)	30 (50%)	0.480
Office Job	3 (21.42%)	3 (17.64%)	6 (20.68%)	12 (20%)	
Others	2 (14.28%)	4 (23.52%)	5 (17.24%)	11 (18.3%)	
Community					
Urban	10 (71.42%)	8 (47.05%)	21 (72.41%)	39 (65%)	0.186
Rural	4 (28.57%)	9 (52.94%)	8 (27.58%)	21 (35%)	
Economic Status					
Lower Class	1 (7.14%)	2 (11.76%)	1 (3.44%)	4 (6.7%)	0.549
Middle Class	13 (92.85%)	15 (88.23%)	28 (96.55%)	56 (93.3%)	
Comorbidity					
Absent	13 (92.85%)	14 (82.35%)	24 (82.75%)	51 (85%)	0.642
Present	1 (7.14%)	3 (17.64%)	5 (17.24%)	9 (15%)	
Diagnosis					
Hypothyroidism	5 (35.71%)	7 (41.17%)	22 (75.86%)	34 (56.7%)	0.014
Grave's Disease	9 (64.28%)	10 (58.82%)	7 (24.13%)	26 (43.3%)	

Furthermore, Koehler et al. found a slight negative correlation between anti-TPO antibodies and 25(OH)D levels in patients with autoimmune thyroiditis[15]. Thus, the present investigation proposed a potential relationship between vitamin D levels and thyroid autoantibodies. For instance, anti-TG antibodies and 25OHD deficiency were found to be positively correlated with a higher risk by Fang et al.[16]. Mangaraj et al. discovered a negative correlation between serum vitamin D levels and thyroid volume in patients with recently diagnosed Graves' sickness[17]. The natural course of Hashimoto's thyroiditis, which frequently evolves from subclinical to overt hypothyroidism over time, is consistent with the preponderance of hypothyroidism in the research population[18]. The results of Chao G et al., who noted reduced vitamin D levels in individuals with newly onset Graves' illness, provide evidence for the substantial correlation between TRAB antibody levels and vitamin D status[19].

However, routine monitoring for vitamin D levels should be part of the clinical management of patients with autoimmune thyroid disorders to identify and correct deficiencies early[20]. Further research is needed to determine how vitamin D supplementation affects the onset and management of autoimmune thyroid disorders. Controlled trials might offer insightful information about the best dosage and possible therapeutic advantages. Confirmation of these results and a deeper comprehension of the wider consequences of vitamin D deficiency in thyroid health await bigger sample sizes and more diverse populations in future research. Examining the molecular processes via which vitamin D affects thyroid autoimmunity might

lead to a better understanding and the identification of possible therapeutic targets. Moreover, public health programs that enhance vitamin D status utilizing dietary guidelines, fortification, and safe sun exposure practices might be advantageous to populations at risk for autoimmune thyroid disorders and vitamin D deficiency. The holistic management of patients necessitates collaboration among endocrinologists, dietitians, and primary care physicians to ensure that vitamin D status is taken into account in addition to other treatment options for thyroid diseases.

However, this study had some limitations. The study's relatively modest sample size of only 60 participants might have limited how broadly the results might be applied. More extensive research is required to validate these findings and offer more reliable information. Since non-probability consecutive sampling does not guarantee that the sample was representative of the larger population with autoimmune thyroid problems, it might introduce selection bias. The study's cross-sectional design merely offers a point in time and does not prove a link between autoimmune thyroid diseases and vitamin D deficiency. To ascertain the relationship's direction, longitudinal research is necessary. Because only one hospital in Karachi was used for the study, it is possible that the results would not be applied to other areas or populations with different demographics and environmental exposures.

Conclusion

Vitamin D deficiency and subsequent insufficiency were significantly more common in individuals with AITDs, particularly in those with hypothyroidism. Given that over 50% of the subjects had low levels of vitamin D, the findings implied that vitamin D could potentially play a function in the development and course of AITDs. This correlation brought to light the significance of tracking and controlling vitamin D levels in patients with AITDs in order to potentially enhance treatment results.

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