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Association between vitamin D levels and thyroid status; diagnostic insights into hyperthyroidism and hypothyroidism – A cross-sectional diagnostic study

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Abstract

Introduction: The correlation of vitamin D and thyroid function has been a growing area of interest in endocrinology, particularly regarding its potential diagnostic and therapeutic implications for hyperthyroidism and hypothyroidism.

Objectives: This cross-sectional diagnostic study explores the correlation of vitamin D with thyroid health, offering insights into these interactions' mechanisms and clinical relevance.

Patients and Methods: This prospective cross-sectional diagnostic study was conducted on 98 patients at Al-Sader teaching hospital in Misan, Iraq, between October 2018 and March 2019. Demographic and clinical data were collected through interviews and hospital records, while serum samples were obtained for analysis of thyroid hormones (TSH, FreeT4 and FreeT3) and vitamin D levels. Patients were categorized as euthyroid, hypothyroid, or hyperthyroid based on TSH levels and the correlation between them with vitamin D levels was assessed using statistical tests.

Results: The analysis revealed differing associations between vitamin D levels and thyroid status. For hyperthyroidism, a modest inverse correlation was observed, with an unadjusted odds ratio (OR) of 0.89 indicating an 11% reduced likelihood of hyperthyroidism per nanogram per milliliter (ng/mL) increase in vitamin D levels, though this was not statistically significant after adjustment (adjusted OR: 0.90). In contrast, a significant inverse relationship was found for hypothyroidism, with unadjusted and adjusted ORs of 0.68 and 0.62, respectively, showing that higher vitamin D levels reduced the likelihood of hypothyroidism by 32% and 38%, even after controlling for confounders. Diagnostic analysis using the area under curve (AUC) values showed moderate discriminatory ability for identifying non-hyperthyroidism (AUC: 0.715) with a sensitivity of 80% and specificity of 39% at a cutoff of 22.50 ng/mL. However, the diagnostic performance for non-hypothyroidism was excellent (AUC: 0.925), with a sensitivity of 85% and specificity of 97% at a cutoff of 20.00 ng/mL.

Conclusion: The analysis suggests that vitamin D levels are significantly associated with a reduced likelihood of hypothyroidism; however, showed a modest significant association with hyperthyroidism only in the unadjusted analysis. Diagnostic performance was excellent for identifying non-hypothyroidism but moderate for non-hyperthyroidism, indicating a stronger role for vitamin D in hypothyroidism. These findings suggest that vitamin D may play a more substantial role in hypothyroidism than hyperthyroidism.

Keywords: Vitamin D, Thyroid dysfunction, Hypothyroidism, Hyperthyroidism, Thyroid-stimulating hormone, Thyroxin, Triiodothyronine

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Introduction

Thyroid dysfunction encompasses a range of disorders affecting the thyroid gland, including hypothyroidism, hyperthyroidism, and subclinical variations. These conditions can significantly impact various physiological systems. Subclinical thyroid dysfunction, characterized by abnormal thyroid-stimulating hormone (TSH) levels with normal free T4 (FT4) and free T3 (FT3) levels, is increasingly diagnosed and linked to cardiovascular risks, bone health issues, and other systemic effects, though its treatment remains controversial due to inconsistent clinical guidelines (1). Thyroid dysfunction is also

associated with comorbidities such as diabetes, gastric autoimmune disorders, and disrupted lipid profiles (2).

Vitamin D is essential in calcium and phosphate homeostasis, which is crucial for adequate bone mineralization and overall health (3). Beyond its classic effects on bone, vitamin D modulates innate and adaptive immune responses, with deficiencies linked to increased risks of autoimmune diseases and infections (4, 5). The active form of vitamin D, 1,25-dihydroxyvitamin D3, influences the expression of over 1000 genes across various human tissues, highlighting its importance in gene regulation and health maintenance (3). Optimal serum

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■ Implication for health policy/practice/research/medical education

The significant inverse association between vitamin D levels and hypothyroidism suggests that maintaining adequate vitamin D levels could be a potential strategy for reducing the risk of hypothyroidism, warranting consideration in public health initiatives and clinical guidelines. The excellent diagnostic performance of vitamin D levels for identifying non-hypothyroidism highlights its potential as a biomarker in thyroid disorder screening and management. For hyperthyroidism, the modest correlation in the unadjusted analysis calls for further research to clarify the role of vitamin D. These insights should be integrated into the clinical setting to enhance understanding of the interplay between micronutrients and thyroid health, encouraging a more comprehensive approach to endocrine care.

levels of 25-hydroxyvitamin D are recommended to be above 30 ng/mL (75 nmol/L) to ensure health benefits, with higher levels potentially offering additional protection against various diseases (6,7). Regular supplementation may be necessary for individuals with low vitamin D status, particularly during winter months when sunlight exposure is limited (7).

The concentrations of vitamin D have been demonstrated to exhibit a significant correlation with thyroid functionality, especially in the context of autoimmune thyroid disorders including Hashimoto's thyroiditis and Graves' disease. Studies indicate that vitamin D deficiency is more prevalent in hypothyroidism individuals, and is associated with increased levels of thyroid antibodies, such as anti-thyroid peroxidase (anti-TPO) antibodies (8,9). For example, a particular investigation revealed that individuals exhibiting deficient vitamin D concentrations encountered a 1.6- to 1.7-fold elevated likelihood of manifesting hypothyroidism in contrast to those possessing optimal levels (9). Additionally, vitamin D insufficiency negatively correlates with serum TSH levels, suggesting a potential role in regulating thyroid function (10). Vitamin D consumption was found to be effective in reducing thyroid antibody titers, particularly in patients treated for Hashimoto's thyroiditis, indicating its potential therapeutic benefit in reducing thyroid autoimmunity (11). This study aimed to evaluate the potential role of vitamin D levels in the occurrence of thyroid dysfunction, focusing specifically on hyperthyroidism and hypothyroidism.

Objectives

This study aimed to investigate the associations between vitamin D levels and thyroid status, specifically hyperthyroidism and hypothyroidism, and to evaluate the diagnostic utility of vitamin D levels in identifying these thyroid conditions within a cross-sectional framework.

Patients and Methods

Study design

This prospective cross-sectional diagnostic study was conducted on 98 patients referred to the surgery

department at Al-Sader teaching hospital in Misan, Iraq, between October 2018 and March 2019. The primary aim was to assess the correlation of vitamin D levels with thyroid function while also evaluating the diagnostic utility of vitamin D in predicting hyperthyroidism and hypothyroidism.

Inclusion and exclusion criteria

The inclusion criteria for this study encompass patients aged 18 years or older who were referred to Al-Sader teaching hospital in Misan, Iraq. Eligible participants were required to have no underlying conditions that could interfere with the assessment of the relationship between vitamin D levels and thyroid dysfunction. Patients with chronic liver or kidney diseases, along with those diagnosed with endocrinological conditions necessitating vitamin D supplementation, were excluded from the study to minimize confounding factors. Additionally, individuals taking medications known to influence vitamin D metabolism such as anticonvulsants, calcium channel blockers, antacids, thiazide diuretics, and isoniazid, were also excluded.

Data collection

Demographic characteristics, such as gender, smoking status, age, diabetes, rheumatoid arthritis, and family history of thyroid dysfunction, were collected through patient interviews or by reviewing clinical documents from the hospital archive using a standardized checklist. To assess vitamin D and thyroid hormone levels, 5cc of venous blood was drawn aseptically from the antecubital fossa of each patient. The samples were centrifuged and stored at -70°C until analysis. In the hospital laboratory, serum TSH, FT4, and FT3 levels were measured using a FT4-CTX radioimmunoassay (RIA) kit (Diasorin, Saluggia, Italy) and an RIA-gnost® hTSH kit (Cisbio Bioassays, Codolet, France). Patients were classified as euthyroid if their TSH levels ranged between 0.25–5 µIU/mL, hypothyroid if levels exceeded 5 µIU/mL, and hyperthyroid if levels were below 0.25 µIU/mL (12). Serum vitamin D levels were quantified using spectrophotometry at a wavelength of 500 nanometers and recorded as continuous quantitative data (13).

Outcomes

The primary outcome is assessing the correlation between serum vitamin D and the presence of hyperthyroidism or hypothyroidism, while secondary outcomes include assessing the diagnostic utility of vitamin D levels (sensitivity and specificity) in identifying these thyroid conditions.

Statistical analysis

Data analysis was conducted using IBM Corp's Statistical Package for the Social Sciences (SPSS) version 27. Data normality was assessed with the Kolmogorov-Smirnov

test, while data frequency distributions between groups were evaluated using chi-square and independent t-tests. Binary logistic regression analyses were performed to investigate the relationship between vitamin D levels and thyroid status. The optimal cut-off values for vitamin D were determined via receiver operating characteristic (ROC) curve analysis, with the area under the curve (AUC) used to assess its predictive effectiveness for thyroid dysfunction. Additionally, key diagnostic metrics, including sensitivity and specificity, were computed for vitamin D, since a *P* value of less than 0.05 was considered statistically significant.

Results

The study results revealed the distribution of thyroid function status among the 98 participants included in the analysis. Of these, the majority (71 individuals) were classified as euthyroid, indicating normal thyroid function. In contrast, 13 participants were identified as hyperthyroid, reflecting an overactive thyroid gland, while 14 were diagnosed as hypothyroid, signifying an underactive thyroid gland. The evaluation of demographic factors and vitamin D levels between euthyroid and hyperthyroid groups revealed no statistically significant differences in the frequency distributions of age, gender, smoking status, diabetes, rheumatoid arthritis, or family history of thyroid dysfunction. However, vitamin D levels demonstrated a notable distinction between euthyroid and hyperthyroid individuals, and in the hyperthyroid patients were significantly lower than normal thyroid individuals (Table 1).

Demographic factors analysis between euthyroid and hypothyroid groups revealed no significant differences in the frequency distribution of gender, smoking status, family history of thyroid dysfunction, presence of diabetes, rheumatoid arthritis, or age. However, a significant difference was found in vitamin D levels between the two groups, suggesting a potential association between

vitamin D deficiency and hypothyroidism (Table 2).

The association between vitamin D and thyroid disorders revealed notable findings. For hyperthyroidism, the unadjusted odds ratio (OR) of 0.89 indicated a modest inverse relationship, with each nanogram per milliliter (ng/mL) increase in vitamin D levels reducing the likelihood of hyperthyroidism by 11%. However, this association was not statistically significant after adjustment, with an adjusted OR of 0.90. In contrast, a stronger inverse relationship was observed for hypothyroidism. The unadjusted OR of 0.68 and the adjusted OR of 0.62 demonstrated that higher vitamin D levels were significantly associated with a reduced likelihood of hypothyroidism, even after controlling for confounders, including age, gender, smoking, diabetes, rheumatoid arthritis, and family history of thyroid dysfunction. Specifically, each ng/mL increase in vitamin D levels is across with a decreased the likelihood of hypothyroidism by 32% in the unadjusted model and by 38% in the adjusted model (Table 3).

The diagnostic value of vitamin D levels in predicting thyroid status was assessed using AUC analysis. For identifying non-hyperthyroidism, the AUC was 0.715, indicating moderate discriminatory ability. At a vitamin D cutoff level of 22.50 ng/mL, the sensitivity was 80%, meaning that, the test correctly identified 80% of individuals who were not hyperthyroid. The specificity was 39%, indicating that the test correctly identified 39% of individuals who did not have hyperthyroidism. In contrast, the diagnostic performance for identifying non-hypothyroidism was notably higher, with an AUC of 0.925, demonstrating excellent discriminatory ability. Using a cutoff of 20.00 ng/mL, the sensitivity was 85%, correctly identifying 85% of individuals who were not hypothyroid, and the specificity was 97%, correctly identifying 97% of individuals who did not have hypothyroidism. These results suggest a strong diagnostic value of vitamin D levels, particularly in ruling out hypothyroidism (Table 4 and Figure 1).

Table 1. Frequency distribution of demographic factors and vitamin D status in euthyroid and hyperthyroid groups

Variable	Thyroid status				P value	
	Euthyroid (n = 71)		Hyperthyroid (n = 13)			
	No.	%	No.	%		
Gender	Female (n = 76)	63	82.9	13	17.1	0.203*
	Male (n = 8)	8	100	0	0	
Smoking	No (n = 81)	68	84	13	16	0.450*
	Yes (n = 3)	3	100	0	0	
Family history of thyroid dysfunction	No (n = 61)	83	86.9	8	13.1	0.330*
	Yes (n = 23)	18	78.3	5	21.7	
Diabetes	No (n = 75)	65	86.7	10	13.3	0.117*
	Yes (n = 9)	6	66.7	3	33.3	
Rheumatoid arthritis	No (n = 73)	60	82.2	13	17.8	0.128*
	Yes (n = 11)	11	0	0	0	
Variable	Mean	SD	Mean	SD	P value	
Age (year)	44.80	15.39	42.54	15.14	0.328**	
Vitamin D level (ng/mL)	27.37	7.15	23.15	3.00	>0.001**	

SD: Standard deviation. * Chi-square, ** Independent T-test.

Table 2. Comparative of the frequency distribution of demographic data and Vitamin D levels in euthyroid and hypothyroid subjects

Variable		Thyroid status				P value
		Euthyroid (n = 71)		Hypothyroid (n = 14)		
		No.	%	No.	%	
Gender	Female (n = 76)	63	84	12	16	0.749*
	Male (n = 10)	8	80	2	20	
Smoking	No (n = 82)	68	82.9	14	17.1	0.434*
	Yes (n = 3)	3	100	0	0	
Family history of thyroid dysfunction	No (n = 61)	53	86.9	8	13.1	0.184*
	Yes (n = 24)	18	75	6	25	
Diabetes	No (n = 78)	65	83.3	13	46.7	0.871*
	Yes (n = 7)	6	85.7	1	14.3	
Rheumatoid arthritis	No (n = 72)	60	83.3	12	16.7	0.909*
	Yes (n = 13)	11	84.6	2	15.4	
Variable		Mean	SD	Mean	SD	P value
Age (year)		44.80	15.39	43.00	14.04	0.686**
Vitamin D level (ng/mL)		27.37	7.15	16.07	3.88	<0.001**

SD: Standard deviation. * Chi-square, ** Independent T-test.

Table 3. The correlation between vitamin D levels and thyroid status using Binary logistic regression

Variable		P Value	OR	95% CI	
				Lower	Upper
Hyperthyroid					
Vitamin D (ng/mL)	Unadjusted	0.045	0.89	0.79	0.99
	Adjusted	0.098	0.90	0.80	1.01
Hypothyroid					
Vitamin D (ng/mL)	Unadjusted	<0.001	0.68	0.56	0.82
	Adjusted	<0.001	0.62	0.48	0.81

OR, Odds ratio; CI, Confidence interval.

Table 4. Diagnostic value of vitamin D levels in predicting thyroid status

Thyroid status	Vitamin D diagnostic value						
	AUC (0-1)	P value	95% CI		Cut off (ng/mL)	Sensitivity (%)	Specificity (%)
			Lower	Upper			
Non-hyperthyroid	0.715	0.014	0.592	0.837	22.50	80	39
Non-hypothyroid	0.925	<0.001	0.861	0.989	20.00	85	97

AUC, Area under curve; CI, Confidence Interval.

Discussion

The results revealed differing associations between vitamin D levels and thyroid conditions. For hyperthyroidism, a modest inverse relationship was observed, but this association was not statistically significant after adjustment. In contrast, a significant inverse relationship was found for hypothyroidism, indicating that higher vitamin D levels were associated with a reduced likelihood of the condition, even after accounting for other factors. Diagnostic analysis showed that vitamin D levels had moderate accuracy in identifying individuals without hyperthyroidism, while their accuracy in identifying individuals without hypothyroidism was excellent.

The finding that vitamin D has an inverse relationship with hypothyroidism with a significant diagnostic value in the diagnosis of this disorder aligns with existing evidence on the role of vitamin D in thyroid disorders. Prior studies have consistently demonstrated that vitamin D deficiency is significantly associated with hypothyroidism, particularly

autoimmune conditions like Hashimoto's thyroiditis, where lower serum vitamin D levels correlate with disease severity and antibody levels. The study by Appunni et al indicated a potential association between vitamin D levels and hypothyroidism, particularly in autoimmune-related cases (9). Aktaş et al conducted a study involving 130 individuals diagnosed with autoimmune hypothyroidism, revealing a significant correlation between vitamin D deficiency and the condition. Their findings contribute to the growing body of evidence suggesting that low levels of vitamin D may play a critical role in the pathogenesis of autoimmune thyroid diseases, particularly hypothyroidism. The study highlights that patients with autoimmune hypothyroidism often exhibit lower serum vitamin D levels, which may exacerbate their condition (8). Mackawy et al in a case-control study comparing 30 hypothyroid patients with 30 healthy individuals, revealed a significant correlation between vitamin D deficiency and hypothyroidism; their findings indicated

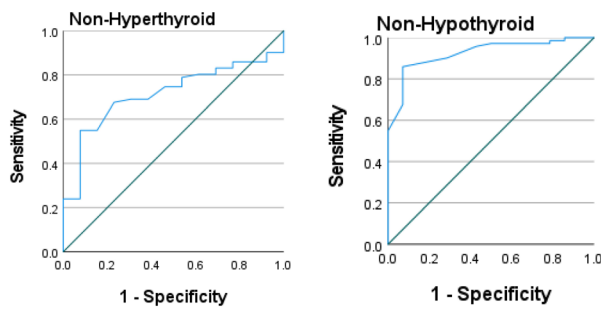


Figure 1. Diagnostic value of vitamin D levels in differentiating non-hypothyroid and non-hyperthyroid states; an analysis using ROC curve

that patients with hypothyroidism often experience lower serum vitamin D levels compared to controls (14). On the other hand, in contrast to our findings, a clinical trial conducted by Waterhouse et al in Australia revealed that vitamin D supplementation did not significantly reduce the incidence of hypothyroidism. This study, which involved a substantial cohort of 17 851 participants from the D-Health Trial, found no overall benefit from vitamin D supplementation in preventing hypothyroidism (15). Overall, the observed inverse relationship between vitamin D levels and hypothyroidism, along with its significant diagnostic value, aligns with a growing body of literature that underscores the role of vitamin D in thyroid health. Numerous studies have consistently demonstrated that individuals with hypothyroidism often exhibit lower serum vitamin D levels, suggesting that vitamin D deficiency may contribute to the pathogenesis of this disorder. This correlation not only reinforces the need for routine screening of vitamin D levels in hypothyroid patients but also highlights the potential benefits of vitamin D supplementation as a therapeutic strategy. Given the complexity of thyroid hormone metabolism and the multifactorial nature of autoimmune thyroid diseases, further research is warranted to elucidate the mechanisms underlying this relationship and to establish causative links. Ultimately, addressing vitamin D deficiency could enhance patient management strategies and improve clinical outcomes for those affected by hypothyroidism.

In this study, lower vitamin D also demonstrated a significant correlation with hyperthyroidism occurrence, supporting findings from previous research. In a study conducted by Pan et al, it was found that pregnant women with hyperthyroidism exhibited significantly lower levels of vitamin D compared to healthy individuals. This research highlights the potential implications of vitamin D deficiency on thyroid function during pregnancy, suggesting that inadequate vitamin D status may adversely affect maternal health and thyroid hormone regulation (16). Additionally, the study by Alhuzaim and Aljohani indicated that vitamin D deficiency exacerbates Graves' disease and is associated with increased thyroid volume and autoantibody levels in humans, suggesting a role in disease severity and progression (17). A systematic review

study by Saad-Omer et al found that prolonged vitamin D supplementation may regulate thyroid hormone levels in autoimmune conditions with hyperthyroid (18). Overall, this alignment with earlier studies suggests that vitamin D may play a crucial role in the regulation of thyroid function and the development of hyperthyroid conditions. The consistency of these results across multiple investigations highlights the importance of further exploring the relationship between vitamin D levels and thyroid health, as it could have implications for both prevention and treatment strategies for individuals affected by hyperthyroidism.

Conclusion

In conclusion, this study reveals a compelling relationship between vitamin D levels and thyroid status, yielding important diagnostic insights. While the observed inverse association between vitamin D levels and hyperthyroidism did not retain statistical significance after adjusting for confounders, a strong inverse association emerged for hypothyroidism. Higher vitamin D levels were significantly associated with a decreased likelihood of hypothyroidism, even after controlling for key confounders. These results suggest a potentially more pronounced role for vitamin D in the pathophysiology and risk modulation of hypothyroidism compared to hyperthyroidism. Furthermore, diagnostic analysis emphasizes the clinical utility of vitamin D levels in thyroid assessment. Although the discriminatory ability for identifying non-hyperthyroidism was moderate, the diagnostic performance for ruling out non-hypothyroidism was excellent. The high sensitivity and specificity observed at cutoff values of 20.00 ng/mL for non-hypothyroidism and 22.5 for non-hyperthyroidism, which approaches the level considered vitamin D sufficient, suggests its reliability as a marker for excluding hypothyroidism and hyperthyroidism in clinical settings. These findings underscore the potential benefit of integrating vitamin D assessment into the diagnostic workup for thyroid disorders, particularly hypothyroidism; while highlighting the need for continued research to clarify underlying causal mechanisms and optimize clinical applications.

Limitations of the study

First, it cannot establish causality between vitamin D levels and thyroid status, as data were collected at a single point in time, making it unclear whether changes in vitamin D levels influenced thyroid dysfunction or vice versa. Additionally, the relatively small sample size of 98 patients may limit the generalizability of the findings to broader populations. Potential biases, such as selection bias and recall bias, could also affect the reliability of the results, particularly since demographic data were partly obtained through interviews. Furthermore, the study did not account for confounding factors that might influence vitamin D levels, such as seasonal variation, sun exposure,

dietary habits, obesity, or vitamin D supplementation history. Finally, the absence of measurements for thyroid autoantibodies and other markers of autoimmune thyroid disease restricts a more comprehensive understanding of the relationship between vitamin D and thyroid dysfunction.

Authors' contribution

Conceptualization: Ihsan S. Sahi and Ishraq J. Hasan.

Data curation: Ihsan S. Sahi and Ishraq J. Hasan.

Formal analysis: Ali Laibi Zamil.

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Methodology: Ishraq J. Hasan and Ali Laibi Zamil.

Project Management: Ishraq J. Hasan.

Resources: All authors.

Supervision: Ihsan S. Sahi.

Validation: Ihsan S. Sahi.

Writing—original draft: All authors.

Writing—reviewing and editing: All authors.

Conflicts of interest

The authors declare no conflict of interest.

Ethical issues

The research was conducted in accordance with the principles outlined in the Declaration of Helsinki. This study resulted from a research project approved by the College of Medicine, University of Misan, Misan, Iraq. Accordingly, written informed consent taken from all participants before any intervention. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

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