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Original Article

# Vitamin D Levels in Patients with Benign Recent Onset Thyroid Lesions

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## Abstract

**Objectives:** Many studies suggested a link between hypovitaminosis D and benign and malignant thyroid lesions. However, some authors suggested that hypovitaminosis D may be a result and not a risk factor for thyroid lesions. So, the present study aimed to assess vitamin D levels in patients presented with recent onset of thyroid lesions with normal daily life activities. **Methods:** The study included 100 patients with benign thyroid lesions and 50 age and sex matched healthy controls. All participants were subjected to careful history taking and thorough clinical examination. The demographic characteristics including education, residence and occupation were also reported. The performed laboratory investigations included CBC, thyroid function tests and vitamin D assessment for all subjects. The studied groups were investigated using the Activities of Daily Living Questionnaire (ADL). Rates of sun exposure were also assessed using the Sun Exposure Questionnaire. **Results:** Patients had significantly lower sun exposure score when compared with controls (9.1 ± 2.5 versus 10.3 ± 3.3, p=0.025). However, patients and controls had comparable ADL scores (92.4 ± 4.7 versus 93.2 ± 3.9, p=0.29). Vitamin D levels in patients and controls were 19.3 ± 9.5 ng/ml and 33.3 ± 12.4 respectively (p<0.001). Patients group comprised significantly higher frequency of cases with vitamin D deficiency (58.0 % versus 6.0 %, p<0.001). **Conclusions:** Vitamin D deficiency may be a risk factor for development of thyroid lesions even in patients with normal level of daily life activities.

**Keywords:** Thyroid nodules, Thyroid hormones, Vitamin D.

## Introduction

The recent decades have witnessed a dramatic change in our understanding of the pathophysiological roles of vitamin D. Beyond the orthodox view of the vitamin as a hormone regulating bone and mineral health, studying its functions in almost all body systems continue to dominate the published clinical and experimental research literature **(1-4).**

At the molecular level, vitamin D mediates its actions through the active form, 1α,25-dihydroxyvitamin D3 which has a direct effect on the expression of hundreds of genes via its nuclear vitamin D receptor (VDR) **(5).**

Focusing on thyroid diseases, conclusions from observational studies indicate that vitamin D deficiency may be considered as a significant risk factor for thyroid autoimmunity and cancer **(6).** Subsequent meta-analyses confirmed these relations **(7, 8).** Moreover, the meta-analysis of **Wang et al (9)** suggested that vitamin D supplementation could provide short term benefit to patients with autoimmune thyroiditis.

However, the critical review of **Kim (10)** raised many concerns about the conclusions of these studies. Their main argument was that vitamin D deficiency in thyroid patients may be a sequence of limited outdoor activity in those patients rather that being a risk factor for disease development. The present study sought to address the methodological flaws related to this issue. We aimed to study vitamin D levels in patients presented with recent onset of benign thyroid nodules.

## Subjects and Methods

This case control study was conducted at Mansoura University Hospital, Egypt in the period from January to December, 2021. The study was performed in harmony with the Declaration of Helsinki on clinical research involving human subjects. All participants gave informed consent before enrollment in the study.

The present study included 100 patients with recent onset of thyroid nodules or enlargement within the previous three months. We chose this thyroid symptom because it is the most common presenting symptom of benign and malignant thyroid conditions and we restricted patients' selection to those with recent onset disease to minimize the bias related to the limiting effects of more prolonged disease on outdoor activities. In addition to the studied

patients, there were 50 age and sex matched healthy controls. Exclusion criteria include patients with chronic or activity limiting diseases, history of vitamin D supplementation in the previous year or malignant thyroid disease.

All participants were subjected to careful history taking and thorough clinical examination. The demographic characteristics including education, residence and occupation were also reported. The performed laboratory investigations included CBC, thyroid function tests and vitamin D assessment for all subjects. Thyroid patients were further subjected to ultrasonographic and pathological investigations until the final diagnosed was established. All investigations were conducted within the three months of Winter 2019/2020.

To avoid bias related to variable levels of outdoor activity, the studied groups were investigated using the Activities of Daily Living Questionnaire (ADL) **(11).** Rates of sun exposure were also assessed using the Sun Exposure Questionnaire (SEQ) developed and validated by **Hanwell et al (12).**

In adults, vitamin D deficiency is defined as a serum 25-hydroxy-vitamin D level of less than 20 ng/mL (50 nmol/L). Vitamin D insufficiency is defined as a serum 25-hydroxy-vitamin D level of 20 to 30 ng/mL (50 to 75 nmol/L) **(13).**

Data obtained from the present study was expressed as mean and standard deviation or number and percent. Categorical data were compared using chi-square test while numerical data were compared using t test. Correlations were achieved using Pearson's correlation coefficient. Logistic regression analysis was used to identify predictors of low vitamin D levels. All statistical calculations were processed by SPSS 26 (IBM, USA). P values less than 0.05 was considered statistically significant.

## Results

The present study included 100 patients with recent onset thyroid nodules in addition to 50 age and sex matched controls. Patients had significantly lower sun exposure score when compared with controls (9.1 ± 2.5 versus 10.3 ± 3.3, p=0.025). However, patients and controls had comparable ADL scores (92.4 ± 4.7 versus 93.2 ± 3.9, p=0.29). It was also found that patients had significantly lower Hb levels in comparison to controls (11.4 ± 2.4 versus 13.6 ± 1.2 gm/dl, p<0.001). As expected, patients had significantly higher TSH levels when compared to controls (10.2 ± 8.9 versus 3.5

± 1.7 µIU/ml, p<0.001). Vitamin D levels in patients and controls were 19.3 ± 9.5 ng/ml and 33.3 ± 12.4 respectively (p<0.001). Patients' group comprised significantly higher frequency of cases with vitamin D deficiency (58.0 % versus 6.0 %, p<0.001) (Table-1). Final diagnosis in the studied patients revealed hypothyroidism in 82 % of patients, thyroiditis in 11.0 % of patients and multinodular goiter in 7.0 % of patients **(Table-1).**

In the studied patients, vitamin D levels showed significant direct correlation with sun exposure score (r=0.2, p=0.013) and significant inverse correlation with TSH levels **(Table-2).** It was also shown that female patients had significantly lower vitamin D levels when compared with male patients (17.5 ± 9.1 versus 23.9 ± 9.3 ng/ml, p=0.002) **(Fig.1).** Comparison between patients with different clinical diagnoses regarding vitamin D levels revealed no statistically significant differences **(Fig.2).** Logistic regression analysis identified low sun exposure as an independent predictor of low **vitamin** D levels [OR (95% CI): 0.73 (0.58-0.91), p=0.005] **(Table-3).**

**Table-1:** Clinical and laboratory data in the studied groups

| | **Patients** N=100 | **Controls** N=50 | **P value** |
|---|---|---|---|
| **Age** (years) mean ± SD | 44.0 ± 14.9 | 41.2 ± 15.1 | 0.76 |
| **Male/female** n | 29/71 | 13/37 | 0.7 |
| **BMI** (Kg/m^2) | 31.3 ± 6.9 | 33.2 ± 8.7 | 0.56 |
| **ADL scale** mean ± SD | 92.4 ± 4.7 | 93.2 ± 3.9 | 0.29 |
| **Sun exposure score** mean ± SD | 9.1 ± 2.5 | 10.3 ± 3.3 | 0.025 |
| **WBCs** (×10^3/ml) mean ± SD | 8.0 ± 2.9 | 7.9 ± 2.0 | 0.94 |
| **Hb** (gm/dl) mean ± SD | 11.4 ± 2.4 | 13.6 ± 1.2 | <0.001 |
| **Platelets** (×10^3/ml) mean ± SD | 297.7 ± 83.6 | 292.9 ± 70.3 | 0.7 |
| **Uric acid** (mg/dl) mean ± SD | 4.9 ± 0.9 | 4.8 ± 0.4 | 0.31 |
| **TSH** (µIU/ml) mean ± SD | 10.2 ± 8.9 | 3.5 ± 1.7 | <0.001 |
| **FT3** (ng/dl) mean ± SD | 3.4 ± 2.5 | 3.3 ± 2.1 | 0.74 |
| **FT4** (ng/dl) mean ± SD | 11.6 ± 2.6 | 12.1 ± 2.4 | 0.25 |
| **Vitamin D** (ng/ml) mean ± SD | 19.3 ± 9.5 | 33.3 ± 12.4 | <0.001 |
| **Vitamin D status** n (%) | | | |
| Normal | 19 (19.0 %) | 31 (62.0 %) | |
| Insufficiency | 23 (23.0 %) | 16 (32.0 %) | <0.001 |
| Deficiency | 58 (58.0 %) | 3 (6.0 %) | |
| **Final diagnosis** n (%) | | | |
| Hypothyroidism | 82 (82.0 %) | - | |
| Thyroiditis | 11 (11.0 %) | - | - |
| Multinodular goiter | 7 (7.0 %) | - | |

ADL: Activities of daily living, BMI: Body mass index, TSH: Thyroid stimulating hormone, WBCs: White blood cells.

**Table-2:** Correlation between vitamin D levels and the clinical and laboratory data in the studied patients

| | Vitamin D Levels | |
|---|---|---|
| | **r** | **p** |
| **Age** | -0.009 | 0.92 |
| **BMI** | 0.1 | 0.22 |
| **ADL scale** | 0.15 | 0.11 |
| **Sun exposure score** | 0.39 | <0.001 |
| **WBCs** | 0.02 | 0.78 |
| **Hb** | 0.38 | <0.001 |
| **Platelets** | 0.03 | 0.73 |
| **Uric acid** | -0.15 | 0.07 |
| **TSH** | -0.3 | <0.001 |
| **FT3** | -0.15 | 0.07 |
| **FT4** | 0.14 | 0.1 |

**Table-3:** Predictors of vitamin D deficiency in the studied patients

| | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | **OR** | **95% CI** | **P** | **OR** | **95% CI** | **P** |
| **Age** | 1.0 | 0.97-1.04 | 0.79 | - | - | - |
| **Sex** | 0.36 | 0.13-1.02 | 0.055 | 0.47 | 0.16-1.39 | 0.17 |
| **ADL scale** | 1.0 | 0.89-1.11 | 0.92 | - | - | - |
| **Sun exposure score** | 0.71 | 0.57-0.88 | 0.002 | 0.73 | 0.58-0.91 | 0.005 |
| **TSH** | 1.05 | 0.98-1.12 | 0.14 | - | - | - |

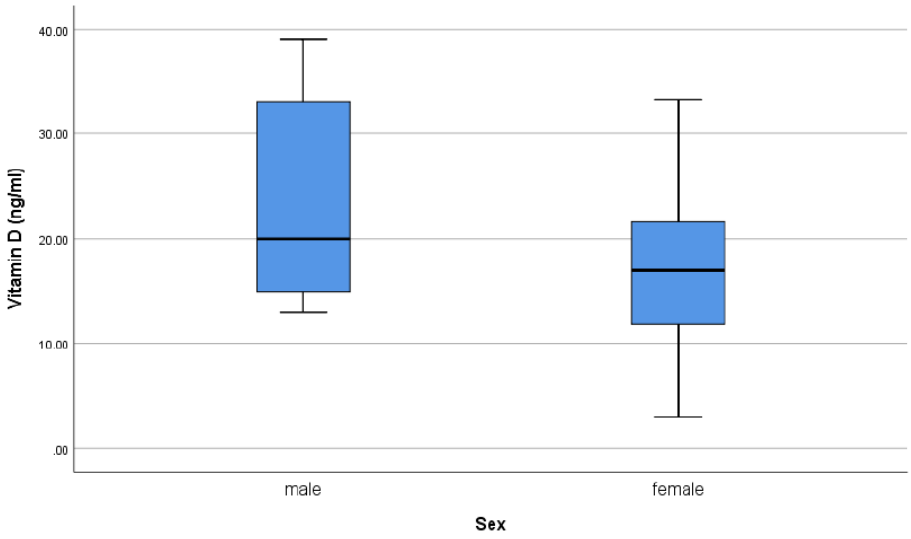


**Fig. (1)** Vitamin D levels in males and females

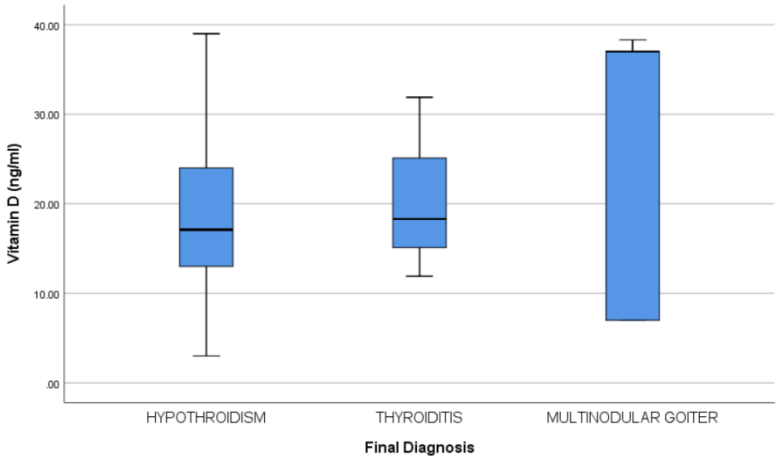


**Fig. (2)** Vitamin D levels in different clinical diagnoses

## Discussion

The present study identified vitamin D deficiency as a possible risk factor of recent onset thyroid lesions. This finding is supported by previous studies. In the study of **Laney et al (14),** the prevalence of vitamin D deficiency was comparable in patients with benign thyroid nodules and thyroid cancer and was higher than the general population. In another study, it was suggested that diabetic patients with thyroid nodules expressed significantly lower vitamin D levels when compared with patients without **Bener et al (15).** Likewise, low vitamin D levels and vitamin D deficiency were recognized as a risk factor of thyroid nodules in severely obese patients **(16).** Moreover, the study of **Du et al (17)** noted the protective role of high vitamin D levels against development of thyroid nodules.

In spite of these reports, **Kim (10)** raised some skepticism about the findings of these studies. They claimed that low vitamin D deficiency in patients with different thyroid disorders can be explained by the limited activity of the affected patients. From this viewpoint, hypovitaminosis D is a result but not a risk factor for thyroid disease.

The present study was designed to reduce the bias related to these reasonable considerations. The study was conducted only on patients with recent onset thyroid lesions and the level of daily life activities of the affected patients was comparable to healthy controls. Moreover, we assessed the sun exposure level of the affected patients to

find out a probable cause of vitamin D deficiency in those patients.

Interestingly, the sun exposure score was significantly lower in the affected patients in spite of the fact that their level of daily activities was matched with controls. In logistic regression, low sun exposure was found to be an independent predictor of low vitamin D levels in the studied patients. This suggests that lower sun exposure rate in the affected patients is probably attributed to other factors than the limited activity which may include life style factors.

In support of this suggestion, the current study noted significant lower vitamin D levels in female patients as compared to male counterparts. The high prevalence of hypovitaminosis D in Middle Eastern women is frequently reported in the literature **(18-20).**

Finally, in the current study, vitamin D levels showed significant inverse correlation with TSH levels which is consistent with the conclusions of a population-based Chinese study **(21).**

## Conclusion:

The present study found that vitamin D deficiency may be a risk factor for development of thyroid lesions even in patients with normal level of daily life activities. Low sun exposure may be related to low vitamin D levels in those patients.

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