Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2020, 9(2): 57-62

Vitamin D Status Association with Thyroid Antibodies in Hypothyroidism Patients

Balqees Sadoon Jasim[1], Najat Saeed Hussein[2] and Maytham Salim AL-Nasrawii[1*]

[1] Community Health Department, Technical Institute of Karbala, AL-Furat Al-Awsat Technical University, Karbala, Iraq

[2] Specialized Center for Endocrinology and Diabetes, Baghdad, Iraq

**Corresponding e-mail: maytham83n@gmail.com*

ABSTRACT

Background: *Deficiency in Vitamin D is a global health issue, in the recent decade, there has been substantial proof that low levels of Vitamin D can lead to thyroid disorders. The present study aims to analyze the relationship between hypothyroidism and the level of Vitamin D, as well as to analyze the relationship between Vitamin D level with thyroid antibodies (TPO-Abs and TG-Abs).* ***Methods:*** *Forty patients diagnosed as hypothyroidism which compared with twenty healthy control groups with matching in sex and age between studied groups. The blood sample was collected from both groups to estimate the level of vitamin D, T3, T4, TSH hormones and the existence of thyroid autoantibodies.* ***Results:*** *Patients with hypothyroidism showed a significantly lower mean of Vitamin D level compared with the healthy control group (p=0.0001). Half (20/40) of the hypothyroid group tested positive for TPO-Ab, (15/40) were positive for TG-Ab, and (14/40) of hypothyroidism patients have positive results for Anti-Thyroid Peroxidase and Anti-Thyroglobulin antibodies with highly statistical significant between hypothyroid group according to the presences of autoantibodies. As for the interaction of vitamin D levels with autoantibodies in patients with hypothyroidism, we observed that levels of Vitamin D were correlated with neither TPO antibodies (p=0.292) nor TG antibodies (p=0.108).* ***Conclusion:*** *The levels of vitamin D were significantly lower in patients with hypothyroidism relative to healthy control. Vitamin D does not have a strong association with the titers of thyroid antibodies.*

Keywords: Hypothyroidism, Vitamin D deficiency, T3, T4, TSH, Thyroid peroxidase Antibodies, Thyroglobulin antibodies

INTRODUCTION

Vitamin "D" is a fat-soluble vitamin that normally presents in a very few diets and as well as being generally available as a dietary supplement. As UV rays activate their synthesis in the skin, our body will generate vitamin D. All of Vitamin D is not active, and in order to start working it needs to be processed by our liver and kidneys. We have an important Vitamin D structure at the end of this process called calcitriol [1]. Vitamin D maintains a balance of minerals such as calcium, iron, magnesium, phosphate, and zinc. Up until recently, it was thought Vitamin D works to preserve the health of bones. Nevertheless, current studies have shown that it can also play a role in many hormonal diseases, autoimmune diseases as well as cancer [2,3]. In addition to a function in physiological metabolism, in endocrinopathies such as type 1 and type 2 diabetes mellitus, adrenal and polycystic ovarian syndrome, Vitamin D has been recognized as both exogenous and endogenous [4,5].

Vitamin D mediates its role by binding to the Vitamin D receptor (VDR) and by activating VDR-responsive genes. VDR genes are consistent with polymorphism with autoimmune thyroid diseases (AITDs) was found. [3]. Calcitriol works in the body by connecting it to the receptor of Vitamin D. VDR is seen almost in all nucleated cells. Any genetic change in the VDR predisposes the person to autoimmune thyroid disorders including Hashimoto's thyroiditis and Graves' disease [6,7]. Evidence has shown that the lack of Vitamin D in people with an underactive thyroid can lead to problems of memory and concentration, which increases the risk of depression and lower everyday quality of life in people with Hashimoto's disease [8,9]. Other studies have shown that Graves' disease patients also have low

serum Vitamin D levels [10,11]. The findings of observational studies show that thyroid autoimmunity is linked to low vitamin D status [12].

In the immune system, Vitamin D receptors have been identified and many immune cells (macrophages, T and B lymphocytes, and dendritic cells) are capable of transforming 25-hydroxyvitamin D into calcitriol, supplying significant quantities of calcitriol for operational efficiency [13]. Calcitriol prevents the proliferation of Th1 cells and the synthesis of Th1 cell cytokines decreases the surface expression of the major class II antigens of histocompatibility and contributes to B cell apoptosis [14-16]. Hence, we performed a case-control analysis evaluating the level of vitamin D in hypothyroid patients and comparing it with healthy controls. This work also aims to detect thyroid autoantibodies and compared Vitamin D levels between positive and negative thyroid autoantibodies (TPO-Ab and TG-Ab) in the hypothyroid group.

SUBJECTS AND METHODS

Forty hypothyroid patients were conducted in this study, who attended the Specialized Center for Endocrinology and Diabetes/Baghdad, during the period from June 2019 to September 2019. The age and sex of patients balanced with 20 healthy individuals as a control group. Both study groups were included 14 males and 46 females with age groups ranging from 14 to 72 years. All patients in this study were diagnosed as hypothyroid patients by specialists' physicians in the Specialized Center for Endocrinology and Diabetes, Baghdad, according to the clinical manifestations and thyroid function test. Five ml of blood sample has been taken from all subjects enrolled in this study for laboratory investigations comprise:

Serum T3, T4 and TSH, with reference range (0.92-2.33 nmol/L for T3), (60-120 nmol/L for T4) and (0.25-5 μIU/mL for TSH). These analysts were assessed by VIDAS assay (Vitek Immunodiagnostic Assay System) which acts in principle quantitative Enzyme-Linked Fluorescent Immunoassay (ELFA) for the estimation of thyroid function hormones concentration in serum

Determining serum level 25 (OH)D using VIDAS (Vitek Immunodiagnostic Assay System). Deficiency vitamin D was defined as a serum level of 25 (OH) D of ≤ 20 ng/ml, insufficiency as a serum level between 20-30 ng/ml, and normal 30-100 ng/ml

Determination of serum Anti-TPO (normal range was less than 8.0 IU/ml) and Anti-TG (normal range was less than 18.0 IU/ml) levels by VIDAS (bioMérieux SA English). The VIDAS Anti-TPO and Anti-TG assay is an automated quantitative procedure based on the methodology of ELFA (Enzyme-Linked Fluorescent Assay)

Statistical Analysis

The data gathered were analyzed using SPSS (Statistical Package for Social Sciences) software version 25. To evaluate the significant difference between variables, t-test and Chi-square are applied. p-value<0.05 was considered statistically significant.

RESULTS

Table 1 represents the number and percentage of the distribution of gender and age in all studied groups. There was no statistical difference between age groups and sex (p>0.05). The present study has illustrated the comparison of laboratory parameters between hypothyroidism patients and healthy control groups by using t-test, mean serum of T3, T4 and TSH hormones of cases and control groups presented in Table 2. The levels of serum antiTPO and antiTG show a significant difference between the groups analyzed (p=0.02 and 0.04) as shown in Table 2. Mean ± SD of Vitamin D was recorded highly statistically significant (p=0.0001) in hypothyroid patients compared with healthy individuals. As can be observed in Table 3, the number of hypothyroidism patients with TPO-Ab positive was n=20, while 15 patients have positive TG-Ab. On the other hand, in the present study, 14 subjects have positive for both TPO-Ab and TG-Ab with the highly statistical difference in the prevalence of autoantibodies in hypothyroidism patients, Table 4. Lastly, no significant statistical correlation was present between Vitamin D levels and Thyroid Peroxidase and Thyroglobulin antibodies, observed in Table 5.

Table 1 Dermatological characteristic of the hypothyroidism patient and healthy control groups

Age groups	Case		Control		p-value
	No.	%	No.	%	
>20	7	17.5%	1	5%	0.1
20-40	15	37.5%	7	35%	
40-60	15	37.5%	9	45%	
<60	3	7.5%	3	15%	
Total	40	100%	20	100%	
Gender	**Case**		**Control**		**p-value**
	No.	**%**	**No.**	**%**	
Male	7	17.5%	7	35%	0.2
Female	33	82.5%	13	65%	
Total	40	100%	20	100%	

Table 2 Clinical characteristics of the hypothyroidism patient and healthy control groups

Independent Samples T-test				
Variable	**T**	**Mean**	**S.D**	**p-value**
T3	Case	1.9	0.52	0.002*
	Control	1.5	0.34	
T4	Case	89.88	15.04	0.3
	Control	85.65	8.95	
TSH	Case	6.8	18.25	0.4
	Control	2.97	0.697	
Anti-TPO	Case	153.43	276.99	0.02
	Control	5.23	2.51	
Anti-TG	Case	87.5	162.26	0.04
	Control	9.28	3.56	
Vitamin D	Case	19.17	24.03	0.0001*
	Control	41.98	17.27	

Table 3 Positivity of the TPO-Ab and TG-Ab in hypothyroidism patients

Variable, Total case (40)		No.	%
Anti-TPO	Negative	20	50%
	positive	20	50%
Anti-TG	Negative	25	62.5%
	positive	15	37.5%

Table 4 Prevalence of the autoantibodies in hypothyroidism patients

Variable, Total case (40)		Anti-TG		p-value
		Negative	positive	
Anti-TPO	Negative	19	1	0.001
	positive	6	14	

Table 5 Connection of vitamin D levels with autoantibodies in patients with hypothyroidism

Anti-TPO* Vit. D		Vit. D		Total	df	p-value
		Negative	Positive			
Anti-TPO	Negative	1	19	20	1	χ^2=1.111
	Positive	3	17	20		p=0.292
Total		4	36	40		NS

Anti-TG* Vit. D		Vit. D		Total	df	p-value
		Negative	Positive			
Anti-TG	Negative	1	24	25	1	χ^2=2.667
	Positive	3	12	15		p=0.108
Total		4	36	40		NS

DISCUSSION

The importance of Vitamin D in non-skeletal activity has been studied over the past few decades, including the role of Vitamin D in autoimmune diseases, metabolic syndromes, cardiovascular disease, cancers, and all-cause mortality [17]. Approximately 82.5% of the hypothyroid patients were women in this research, also the majority of hypothyroid patients fall in the age group 20 to 60 years. This result has been supported by previous findings that indicate a significantly greater incidence of hypothyroidism in women compared to men [18,19]. In the current study, patients of hypothyroidism and healthy controls observed extremely statistically significant levels of Vitamin D, we further studied the possible correlation of Vitamin D deficiency with thyroid autoantibodies in patients with hypothyroidism. In many studies, VDD has been widely reported and is consistent with the general occurrence of VDD in our study [20,21]. Two factors that can clarify low levels of Vitamin D in patients with hypothyroidism are: (1) this may be due to inadequate absorption of Vitamin D in the bowel and (2) the body might not appropriately activate Vitamin D [6].

Another result from our study is that 20 out of 40 patients tested TPOAb positively while 15/40 patients tested TGAb positively and 14/40 patients tested all autoantibodies positively. Thyroid autoimmunity, especially anti-TPO and anti-TG, is characterized by thyroid autoantibodies [22], and about 10% of autoimmune thyroid (AITD) patients may not have detectable serum antibodies [23]. A meta-analysis of 20 case-control studies recently concluded that lower mean vitamin D levels relative to controls in patients with AITD were consistent with our findings [24].

However, we are documented a statistically negative association between Vitamin D levels and thyroid antibodies, this result comes in agreement with Hosny, et al. [25], who found a negative relation between serum 25(OH) Vitamin D and antiTPO and antiTG. As well as, Khare, et al. [26], noted that the amount of serum 25(OH)D did not differ significantly between positive TPO-Ab and negative TPO-Ab subjects, which is in accordance with our results. Also, Yasmeh, et al. [27], have found no association with anti-TPO positivity and a poor inverse correlation between the levels of Vitamin D and anti-TPO has been found, which is contradictory to our findings. In other studies, several researchers found that the incidence of 25(OH)D_3 deficiency among TPO-Ab positive was significantly higher than in TPO-Ab negative hypothyroid patients [28,29]. The contradictory and different results of the study are partly due to inter-assay and inter-laboratory variability in 25(OH) levels of Vitamin D, seasonal differences in 25(OH) blood samples.

CONCLUSION

In summary, based on the findings in our study, hypothyroid patients suffer from the deficiency of Vitamin D relative to healthy control. Vitamin D deficiency may be correlated with the existence of thyroid autoantibodies and impaired thyroid functions. Depending on this finding, the screening test is recommended for a lack of vitamin D in all patients with hypothyroid. More studies are needed to establish if vitamin D deficiency is the hypothyroidism and AITD causative factor.

DECLARATIONS

Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Del Valle, Heather B., et al., eds. “Dietary reference intakes for calcium and vitamin D.” National Academies Press, 2011.

[2] Schwalfenberg, Gerry K., and Stephen J. Genuis. "Vitamin D, essential minerals, and toxic elements: Exploring interactions between nutrients and toxicants in clinical medicine." *The Scientific World Journal,* 2015, pp. 1-8.

[3] Tamer, Gonca, et al. "Relative vitamin D insufficiency in Hashimoto's thyroiditis." *Thyroid,* Vol. 21, No. 8, 2011, pp. 891-96.

[4] Agmon-Levin, Nancy, et al. "Vitamin D in systemic and organ-specific autoimmune diseases." *Clinical Reviews in Allergy and Immunology,* Vol. 45, No. 2, 2013, pp. 256-66.

[5] Muscogiuri, Giovanna, et al. "Vitamin D as a potential contributor in endocrine health and disease." *European Journal of Endocrinology,* Vol. 171, No. 3, 2014, pp. R101-10.

[6] Mackawy, Amal Mohammed Husein, Bushra Mohammed Al-Ayed, and Bashayer Mater Al-Rashidi. "Vitamin D deficiency and its association with thyroid disease." *International Journal of Health Sciences,* Vol. 7, No. 3, 2013, p. 267.

[7] Meng, Shuai, et al. "Genetic susceptibility to autoimmune thyroid diseases in a Chinese Han population: role of vitamin D receptor gene polymorphisms." *Annales d'endocrinologie,* Vol. 76, No. 6, pp. 684-9.

[8] LeMoult, Joelle, and Ian H. Gotlib. "Depression: A cognitive perspective." *Clinical Psychology Review,* Vol. 69, 2019, pp. 51-66.

[9] Scanlan, James M., et al. "Cognitive impairment, chronic disease burden, and functional disability: A population study of older Italians." *The American Journal of Geriatric Psychiatry,* Vol. 15, No. 8, 2007, pp. 716-24.

[10] Yasuda, Tetsuyuki, et al. "Serum vitamin D levels are decreased and associated with thyroid volume in female patients with newly onset Graves' disease." *Endocrine,* Vol. 42, No. 3, 2012, pp. 739-41.

[11] Li, X., et al. "Serum 25-hydroxyvitamin D predict prognosis in radioiodine therapy of Graves' disease." *Journal of Endocrinological Investigation,* Vol. 38, No. 7, 2015, pp. 753-59.

[12] Mansournia, Nasrin, et al. "The association between serum 25OHD levels and hypothyroid Hashimoto's thyroiditis." *Journal of Endocrinological Investigation,* Vol. 37, No. 5, 2014, pp. 473-76.

[13] Lucas, R. M., et al. "Vitamin D and immunity." *F1000prime Reports,* Vol. 6, p. 118.

[14] Guillot, Xavier, et al. "Vitamin D and inflammation." *Joint Bone Spine,* Vol. 77, No. 6, 2010, pp. 552-57.

[15] Vanoirbeek, Els, et al. "The anti-cancer and anti-inflammatory actions of 1, 25$(OH)_2D_3$." *Best Practice and Research Clinical Endocrinology and Metabolism,* Vol. 25, No. 4, 2011, pp. 593-604.

[16] Muscogiuri, G., et al. "Vitamin D and thyroid disease: to D or not to D?" *European Journal of Clinical Nutrition,* Vol. 69, No. 3, 2015, pp. 291-96.

[17] Kim, Dohee. "The role of vitamin D in thyroid diseases." *International Journal of Molecular Sciences,* Vol. 18, No. 9, 2017, p. 1949.

[18] Sinha, R., Bhushan, I. "The study of serum calcium and 25-OH Vitamin D levels in newly diagnosed hypothyroid patients." *The Journal of Dental and Medical Sciences,* Vol. 18, No. 6, 2019, pp. 18-21.

[19] Idiculla, Jyothi, et al. "Vitamin D and primary hypothyroidism: Is there an association?" *Thyroid Research and Practice,* Vol. 15, No. 1, 2018, p. 34.

[20] ElRawi, Hoda A., et al. "Study of Vitamin D level and Vitamin D receptor polymorphism in hypothyroid Egyptian patients." *Journal of Thyroid Research,* 2019, pp. 1-10.

[21] Macdonald, Isabel K., Celine B. Parsy-Kowalska, and Caroline J. Chapman. "Autoantibodies: Opportunities for early cancer detection." *Trends in Cancer,* Vol. 3, No. 3, 2017, pp. 198-213.

[22] Prasad, I., R. Kumari, and A. Saran. "Vitamin D evaluation in autoimmune thyroid diseases." *International Journal of Contemporary Medical Research,* Vol. 3, No. 12, 2016, pp. 2393-15.

[23] Almandoz, Jaime P., and Hossein Gharib. "Hypothyroidism: Etiology, diagnosis, and management." *Medical Clinics,* Vol. 96, No. 2, 2012, pp. 203-21.

[24] Wang, Jiying, et al. "Meta-analysis of the association between vitamin D and autoimmune thyroid disease." *Nutrients,* Vol. 7, No. 4, 2015, pp. 2485-98.

[25] Hosny, Salwa S., et al. "The relationship between vitamin D level and thyroid antibodies in primary hypothyroidism." *The Egyptian Journal of Internal Medicine,* Vol. 31, No. 2, 2019, p. 164.

[26] Khare, Jaideep, et al. "Vitamin D deficiency and its association with thyroid peroxidase antibodies positive hypothyroidism-Experience in a tertiary center in South India." *Medical Journal of Dr. DY Patil University,* Vol. 10, No. 4, 2017, p. 355.

[27] Yasmeh, J., et al. "Hashimoto thyroiditis not associated with vitamin D deficiency." Endocrine *Practice,* Vol. 22, No. 7, 2016, pp. 809-13.

[28] Shin, Dong Yeob, et al. "Low serum vitamin D is associated with anti-thyroid peroxidase antibody in autoimmune thyroiditis." *Yonsei Medical Journal,* Vol. 55, No. 2, 2014, pp. 476-81.

[29] Kivity, Shaye, et al. "Vitamin D and autoimmune thyroid diseases." *Cellular and Molecular Immunology,* Vol. 8, No. 3, 2011, pp. 243-47.