

## THE EFFECT OF VITAMIN D IN KIDNEY FUNCTION AND THYROID GLAND

A. J. R. Al-Sa'ady

Lecturer

Dept. Biot. Coll. Sci. University of Baghdad.

[ali.jabbar15@yahoo.com](mailto:ali.jabbar15@yahoo.com)

M. H. Hilal

Assist. lecturer

### ABSTRACT

This study was aimed to determine the role of vitamin D on renal function and thyroid gland. Eighty blood samples were collected (20 patients and 20 healthy) of different sex with different ages (28-88) years from Baghdad's hospitals to study the renal function, as well as samples from (20 patients and 20 healthy) of different sex with various ages (12-62) years were collected to study the thyroid gland function. The blood samples of kidney were tested for urea, creatinine and vitamin D, whereas other samples tested for Thyroid stimulating hormone (TSH), Thyroxine (T4), and Tri-iodothyronine (T3), and vitamin D. The results were shown that 70.4% from renal patients have vitamin D deficiency, whereas 29.6% of a healthy individual also suffering from vitamin D difficult. Furthermore, the relative risk (RR) was 9.15 of cohort renal patient. On the other hand, there were weak correlation between gender and age with vitamin D level. Also, the results reveal that 84.6 % of patient with thyroid were suffering from vitamin D deficient and 15.4 % of healthy individual also suffering from vitamin D deficient, therefor the relative risk (RR) was 2.54 of cohort thyroid patient. And there were no significant relationship between gender, age with vitamin D level in patient with thyroid.

**Keywords:** chronic kidney diseases (CKD), thyroid stimulating hormone (TSH), thyroxine (T4), and tri-iodothyronine (T3).

الساعدي وهلال

مجلة العلوم الزراعية العراقية -2020: 51(3): 924-929

تأثير فيتامين د على وظائف الكلى والغدة الدرقية

ماجد حميد هلال

مدرس مساعد

علي جبار رشك الساعدي

مدرس

قسم التقنيات الاحيائية/ كلية العلوم/ جامعة بغداد

المستخلص

هدفت الدراسة الحالية الى تحديد دور فيتامين د في وظائف الكلى والغدة الدرقية، حيث تم جمع 80 عينة دم مختلفة (20 مريض و 20 سليم) لرجال ونساء تتراوح اعمارهم بين (28-88) عام من مستشفيات بغداد لدراسة وظائف الكلى. كما تم جمع عينات (20 مريض و 20 سليم) لرجال ونساء تتراوح اعمارهم بين (12-62) عام لدراسة وظائف الغدة الدرقية. اختبرت عينات الكلى لقيمة اليوريا والكرياتينين و فيتامين د في حين اختبرت عينات الغدة الدرقية هرمون محفز الغدة الدرقية (TSH)، هرمون الغدة الدرقية (T4)، وثلاثي يودوثيرونين (T3)، وفيتامين د. أظهرت النتائج أن 70,4 % من مرضى الكلى يعانون من نقص فيتامين د، بينما لوحظ ان 29,6 % من الأفراد الأصحاء عانوا هذا النقص أيضاً، لذا كان الخطر النسبي (RR) مساوي الى 9,15 من مجموع مرضى الفشل الكلوي من ناحية اخرى بينت النتائج ان نقص فيتامين د المرتبط بمرضى الفشل الكلوي غير مرتبط بالجنس او العمر. كما اوضحت النتائج ان 84,6 % من مرضى الغدة الدرقية يعانون من نقص في فيتامين د وان 15,4 % من الاشخاص الاصحاء يعانون هذا النقص أيضاً لذا فان الخطر النسبي (RR) يساوي 2,54 من مجموع المرضى. كما لا توجد اي علاقة بين مستويات فيتامين د مع العمر والجنس.

الكلمات المفتاحية: أمراض الكلى المزمنة (CKD)، الهرمون المحفز للغدة الدرقية (TSH)، هرمون الغدة الدرقية (T4)، وثلاثي يودو ثيرونين (T3).

## INTRODUCTION

Vitamin D is a steroid molecule, fundamentally produced in the skin, which regulate by several genes in expression it. The vitamin D receptor (VDR) is found in most tissues and cells in the body. The main role of vitamin D is regulating bone metabolism, calcium, and phosphorus homeostasis. Recent evidence suggests that vitamin D deficiency, which is common worldwide, could also have non-skeletal actions, including an important role in autoimmune diseases, cancers, metabolic syndromes, cardiovascular disease, chronic kidney disease (CKD), thyroid diseases, and infection, as well as all-cause mortality (10, 17). In CKD patients, the non-classical role of vitamin D to comprise organizing of the renin-angiotensin system (RAS) and the nuclear factor (NF)- $\kappa$ B pathway, two pathways utilized in a broad extent of the pathological processes. These emerging results instituted a new model in approaching treatment to rubric both non-classical and the classical effects of vitamin D in patients affected by vitamin D deficiency, particularly those with CKD (23, 22). One specific pathway that manifests to controlled via the autocrine function of vitamin D in the CKD patient is the renin-angiotensin system (RAS). This cascade features a sequential activation of angiotensin II, which, in patients with CKD, is likely to have deleterious effects on blood pressure and the vasculature, and may contribute to renal parenchymal damage. Furthermore, when the animal models are administered of the activated vitamin D analogs, that are mimic various stages of CKD, a repressed activation of the RAS system was proved along with tubule-interstitial destruction, concurrent attenuation of glomerular and improvement in blood pressure, underlining the importance of this cascade in renal harms (6). Low levels of vitamin D have also been associated with autoimmune thyroid diseases (AITD) such as Hashimoto's thyroiditis (HT) and Graves' disease (GD) (2). Impaired vitamin D signaling has been reported to encourage thyroid tumorigenesis (12). The thyroid gland is an endocrine gland that presents in the human neck. It makes two types of hormones that are excreted into the human blood including triiodothyronine (T3) and thyroxine (T4). Thyroid hormones are needful for all the cells

in the human body to work normally. Thyroid deficiency is very common and resorts to fundamentally to occur in women, as well an anybody can be affected like children, men, teenagers, and babies, too. The T3, or rather the T3 derived from it, and the T4 excreted directly from the thyroid gland, are the effect on the metabolism of body cells. Whereas, it regulates the velocity work of body cells (4, 19). If the thyroid hormones are secreted too much, the body cells work speedier than normal, and it forms hyperthyroidism (7, 20). If turn hyperthyroid duo to of too much excretion of the hormones by the thyroid gland, the excessed activity of body cells or body organs may lead to a speeding of heart rate or excessed activity of the intestine, therefore, it has frequent intestines movement or even diarrhea. On the other hand, if the production of thyroid hormones was lower (known as hypothyroidism), the cells and organs of body slow works down, these lead to that the intestines will work slowly, so become constipated (26, 14). This study was aimed to determined the relationship between the level of vitamin D with renal and thyroid diseases.

## MATERIALS AND METHODS

**Collection of samples:** A total of 80 blood samples were collected from Baghdad hospitals, whereas 20 samples for patients suffering from renal disease with 20 samples as healthy individuals (control group), as well as 20 blood samples were collected from patients suffering from thyroid disease with 20 samples as healthy individuals (control group). These samples selected randomly with different sex and various ages (28-88) years of kidney disease and (12-62) years of thyroid diseases. The samples with renal disease were tested for urea, creatinine and vitamin D value, while the samples with thyroid disease were tested for TSH, T3, T4, and vitamin D value. A details of each case was investigation by filled up with their socioeconomic status, clinical signs, age, and gender.

### Renal function tests

Urea and creatinine were diagnostic with auto-analyser device and reagents of specific kits (Biology Co. China), by adding 100 ml of serum for each test in glass tube then in auto-analyzer.

### Vitamin D value test

Fifty  $\mu\text{l}$  of serum were added to 50  $\mu\text{l}$  of releasing buffer solution, then mixed for 5 minutes at 25  $^{\circ}\text{C}$ , then after add 100  $\mu\text{l}$  of detection solution to the mixed solution, mixed for 10 times for 15 minutes at 25  $^{\circ}\text{C}$ . then take 75  $\mu\text{l}$  of latest solution (detection, releasing and serum) and put on I-chroma cassette incubate at 35  $^{\circ}\text{C}$  for 12 minutes.

#### Thyroid hormones

Thyroid-stimulating hormone (TSH), Triiodothyronine (T3), Thyroxin (T4) and Vitamin D, were detected by using I-Chroma II kits (Boditech Co. Korea) according to manufactures instructions. For TSH test added 150  $\mu\text{l}$  of serum to a 75  $\mu\text{l}$  of reagent buffer solution and mixed for 10 times, then take 75  $\mu\text{l}$  of the mixture and added on cassette, and incubate at 25  $^{\circ}\text{C}$  for 12 minutes. Also, for T4 and T3 test, take 75  $\mu\text{l}$  of serum and mixed with 75  $\mu\text{l}$  of the reagent buffer of each test for 10 times, and incubate at 25  $^{\circ}\text{C}$  for 8 min., then take 75  $\mu\text{l}$  of the mixture and added on cassette then incubated at 25  $^{\circ}\text{C}$  for 10 minutes

#### Statistical analysis

**Table 1. Distribution of renal patients and healthy individual according to Vitamin D levels**

Vitamin D	Deficiency	Count	Patient 19	Healthy 8	Total 27
		% within Vitamin D	70.4%	29.6%	100.0%
	Non-deficiency	Count	1	12	13
		% within Vitamin D	7.7%	92.3%	100.0%
Total		Count	20	20	40
		% within Vitamin D	50.0%	50.0%	100.0%

Furthermore, the relative risk (RR) was 9.15 of cohort renal patient. Thus, a rising occurrence and infection of renal failure along with in-

The data were analyzed by using SPSS, IBM version 25 IBM. The proportion and their frequencies were checked by applying the chi-square and cross tab. One sample test used to calculate the significant, mean and standard error of patient ages. The odds ratio test was done to determine the relative risk between vitamin D deficiency and disease appearance. Also, the regression for vitamin D value was calculated for renal and thyroid patients. The P-values  $\leq 0.05$  considered statistically significant.

## RESULTS AND DISCUSSIONS

### Renal function tests and vitamin D detection

The results indicated that the values range of vitamin D deficiency were (5-15.2 ng/ml) for kidney failure patients. The results in the table (1) shows that 70.4 % of renal patients have vitamin D deficiency, while 29.6% of healthy individual observed that deficiency. Thus, there are statistical differences between study groups ( $\chi^2=13.79$ ,  $P<0.01$ ).

creasing vitamin D deficiency than non-deficient individuals (odds ratio value 28.5) as observed in the table (2).

**Table 2. Correlation the vitamin D relative risk of renal patients with healthy individuals**

	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for Vitamin D (Deficiency / Non-deficiency)	28.500	3.155	257.444
For cohort Renal Failure = Patient	9.148	1.370	61.097
For cohort Renal Failure = Healthy	0.321	0.176	0.586
N of Valid Cases	40		

On the other hand, the weak correlation between gender and age with vitamin D levels is 0.22 and -0.34, respectively. Thus, the age was not associated with vitamin D deficiency. Also, the percentage contrast, among factor study and renal disease is 43.15%. Moreover, there was regression significant between vitamin value and renal disease. The nutrition and sunlight exposure are not the only ones affecting on vitamin D insufficiency, but several factors can be affecting include sex, race, age, obesity,

poor vitamin D synthesis and metabolism (4). Proofs the researches from clinical studies and related data from examination survey of the third national health and nutrition were showed that an inverse connection between the degree of albuminuria and level of vitamin D. These results suggest that vitamin D may possess anti-proteinuric effects, likely through a RAS-angiotensin II-mediated mechanism (18). As well as to its important role in the evolution of proteinuria and renal disease, the

locally synthesized intrarenal (autocrine) angiotensin II has an effect on the cardiovascular system by its effect on vascular smooth muscle cells, blood pressure, and cardiac myocytes. Due to the cardiovascular disease is the main cause of death in CKD patients, the potentially important role of vitamin D to positively regulate of a system may be significant in affecting premature mortality related with CKD (11). Another pathway important in CKD, that may be regulated by the actions of non-classical autocrine to vitamin D are the NF- $\kappa$ B pathway. The nuclear factor (NF)- $\kappa$ B pathway is a point to a set of transcription factors that modify of genes involved in the immune response, in the process of inflammation and fibrosis, that underlie the pathogenesis of CKD (9). In patients with CKD, it appears that NF- $\kappa$ B may play important a role in both diabetic nephropathy and the progression of renal disease. the Activation of the NF- $\kappa$ B pathway excites cascade of events yielding chemokine's, cytokines and other inflammatory factors, which aggravate tissue injury in the renal disease process. at diabetic nephropathy, angiotensin II shows to activate of NF- $\kappa$ B, that in turn activates the expression of angiotensinogen in re-

nal cells when the hyperglycemia is existence (1). This cycle is likely partially accountable for the local accumulation of angiotensin II in diabetic nephropathy. In numerous studies about vitamin D demonstrated that it inhibited the activation of NF- $\kappa$ B and other studies have appeared a reverse relation between serum vitamin D levels and the grade of tissue inflammation existence in different types of kidney disease (13,21). The results were agree with results that obtain by Singh (24). Gois, *et.al.* (8) also found that vitamin D deficiency have an important role in chronic kidney disease, whereas vitamin D deficiency lead to causes and development of more renal function disease and hypothyroidism.

#### Thyroid hormones and vitamin D detection

The results showed that 84.6% of thyroid patients have vitamin D deficiency, while 15.4% of healthy individual observed deficiency. Thus, there were statistical differences between study groups ( $\chi^2=9.23$ ,  $P>0.01$ ) (Table 3). Whereas The results indicated that the values range of vitamin D deficiency were (6-15.3 ng/ml) for 11 patient with thyroid diseases.

**Table 3. Distribution of thyroid patients and health individual according to vitamin D levels**

Vitamin D	Deficiency	Count	Thyroid		Total
			Patient	Healthy	
		% within Vitamin D	84.6%	15.4%	100.0%
	Non-deficiency	Count	9	18	27
		% within Vitamin D	33.3%	66.7%	100.0%
<b>Total</b>		Count	20	20	40
		% within Vitamin D	50.0%	50.0%	100.0%

Furthermore, the relative risk (RR) was 2.54 of cohort thyroid patient. Thus, a rising occurrence and infection of thyroid disease along

with increasing vitamin D deficiency than non-deficient individuals (odds ratio value 11) as observed in the table (4).

**Table 4. Correlation the vitamin D relative risk of thyroid patients and healthy individuals**

	Value	95% Confidence Interval	
		Lower	Upper
<b>Odds Ratio for Vitamin D (Deficiency / Non-deficiency)</b>	<b>11.000</b>	<b>1.998</b>	<b>60.572</b>
<b>For cohort Thyroid = Patient</b>	<b>2.538</b>	<b>1.419</b>	<b>4.541</b>
<b>For cohort Thyroid = Healthy</b>	<b>0.231</b>	<b>0.063</b>	<b>0.849</b>
<b>N of Valid Cases</b>	<b>40</b>		

On the other hand, the weak correlation between age and gender with vitamin D levels is 0.1 and -0.34, respectively. Thus, the age increasing was not associated with vitamin D deficiency. Also, the percentage contrast,

among factor study and thyroid disease is approximately 40%. Moreover, there was regression significant between vitamin value and thyroid disease. Many researches mention significantly low levels of vitamin D in many pa-

tients with autoimmune thyroid diseases (AITD) and were associated with the existence of anti-thyroid antibodies and disordered thyroid function. Vitamin D insufficiency is generally observed in chronic kidney disease (CKD) and the clinically meaningful endpoints are still needed to estimate the advantage of various vitamin D compounds for CKD and dialysis patients (5). The results show that hypothyroidism patients experience from vitamin D insufficiency that is significantly connected with the severity and degree of the hypothyroidism (15). That support the advisability of vitamin D supplementation and recommends the screening for serum calcium levels and vitamin D insufficiency for all patients with hypothyroid (3). Nevertheless, current guidelines only admonish vitamin D treatment in CKD patients due to vitamin D insufficiency and secondary hyperparathyroidism. there are different problems must be resolved, including checking the various vitamin D analogs, estimating whether nutritional vitamin D justly excesses survival, and defining whether clinical results alter according to disease-specific vitamin D metabolism. Subsequently, further investigations are needed to reply to these questions and thereby discover the possibility of vitamin D treatment for patients with CKD. The results were agree with results of Talaei, *et.al.* (25). Mackawy, *et.al.* (16), found that vitamin D deficiency in patients lead to cause of hypothyroidism, and also they suffered with hypocalcemia, and it is significantly related with the severity and degree of hypothyroidism.

## REFERENCES

1. Al-Attab, A.K.T. and M. Q. D. Al-Lami, 2019. Role of calcium-regulating hormones, adipocytokines and renal function test in the progress of type 2 diabetes mellitus in a sample of Iraqi patients. *Iraqi Journal of Agricultural Sciences*. 50(1):343-352.
2. Baeke, F. , T. Takiishi , H. Korf , C. Gysemans , and C. Mathieu, 2010. Vitamin D: Modulator of the immune system. *Curr. Opin. Pharmacol.* 10: 482–496
3. Beski, S.M., 2019. Physiological and immunological responses of Japanese quails to oleobiotic. *Iraqi Journal of Agricultural Sciences*. 49(1). Retrieved from

<http://jcoagri.uobaghdad.edu.iq/index.php/intro/article/view/221>

4. D'Aurizio, F. , D. Villalta , P. Metus , P. Doretto , and R. Tozzoli , 2015. Is vitamin D a player or not in the pathophysiology of autoimmune thyroid diseases? *Autoimmun. Rev.* 14: 363–369.
5. Dilas, L.T. , T. Icin , J.N. Paro , and I. Bajkin, 2011. Autoimmune thyroid disease and other non-endocrine autoimmune diseases. *Med Pregl.* 64: 7-183
6. Eknayan, G. , A. Levin , and N.W. Levin, 2003. Bone metabolism and disease in chronic kidney disease. *Am. J. Kidney Dis.* 42: 1–201
7. Fountoulakis, S. and A. Tsatsoulis, 2004. On the pathogenesis of autoimmune thyroid disease: A unifying hypothesis. *Clin. Endocrinol.* 60: 397–409
8. Gois, P.H.F. , M. Wolley , D.Ranganathan , and A.C. Seguro, 2018. Vitamin D deficiency in chronic kidney disease: recent evidence and controversies. *Int. J. Environ. Res. Public Health* 15:1-16
9. Henry, H.L. , R. Bouillon , A.W. Norman , J.C. Gallagher , P. Lips , R.P. Heaney , R. Vieth , J.M. Pettifor , B. Dawson-Hughes , C.J. Lamberg-Allardt , *et al.* 2010. 14th Vitamin D Workshop consensus on vitamin D nutritional guidelines. *J. Steroid Biochem. Mol. Biol.* 121: 4–6.
10. Hewison, M. 2012. An update on vitamin D and human immunity. *Clin. Endocrinol.* 76: 315–325
11. Holick, M.F. , N.C. Binkley , H.A. Bischoff-Ferrari , C.M. Gordon , D.A. Hanley , R.P. Heaney , M.H. Murad , and C.M. Weaver, 2011. Evaluation, treatment, and prevention of vitamin D deficiency: An Endocrine Society clinical practice guideline. *J. Clin. Endocrinol. Metab.* 96: 1911–1930.
12. Holick, M.F. 2007. Vitamin D deficiency. *N. Engl. J. Med.* 357: 266–281
13. Jean, G. , J.C. Souberbielle , and C. Chazot, 2017. Vitamin D in Chronic Kidney Disease and Dialysis Patients. *Nutrients.* 9:1-15
14. Klecha, A.J. , M.L. Barreiro , L. Arcos, L. Frick, A.M. Genaro, and G. Cremaschi, 2008. Immune-endocrine interactions in autoimmune thyroid diseases. *Neuroimmunomodulation.* 15: 68–75.

15. Kumar, J. , P. Muntner , F.J. Kaskel , S.M. Hailpern , and M.L. Melamed, 2009. Prevalence and associations of 25-hydroxy vitamin D deficiency in US children: NHANES 2001–2004. *Pediatrics*. 124: 362–370
16. Mackawy, A.M.H. , B.M. Al-ayed , and B.M. Al-rashidi, 2013. Vitamin D deficiency and its association with thyroid disease. *International Journal of Health Sciences*. 7(3): 267–275
17. Makariou, S. , E.N. Liberopoulos , M. Elisaf , and A. Challa, 2011. Novel roles of vitamin D in disease: What is new in 2011. *Eur. J. Intern. Med*. 22: 355–362
18. Manson, J.E. , P.M. Brannon , C.J. Rosen , and C.L. Taylor, 2016. Vitamin D Deficiency Is There Really a Pandemic? *N. Engl. J. Med*. 375: 1817–1820.
19. Mathieu, C. and L. Adorini, 2002. The coming of age of 1,25-dihydroxyvitamin D3 analogs as immunomodulatory agents. *Trends Mol. Med*. 8: 174–179.
20. Mazokopakis, E.E. and A.K. Kotsiris, 2014. Hashimoto's autoimmune thyroiditis and vitamin D deficiency. *Current aspects. Hellenic Journal of Nuclear Medicine*. 37-40
21. Nguyen-Yamamoto, L. , A.C. Karaplis , R. St-Arnaud , and D. Goltzman, 2017. Fibroblast growth factor 23 regulation by systemic and local osteoblast-synthesized 1,25-dihydroxyvitamin D. *J. Am. Soc. Nephrol*. 28: 586–597.
22. Plum, L.A. and H.F. DeLuca, 2010. Vitamin D, disease and therapeutic opportunities. *Nat. Rev. Drug Discov*. 9: 941–955
23. Robien, K. , S.J. Oppeneer , J.A. Kelly , and J.M. Hamilton-Reeves 2013. Drug-vitamin D interactions: a systematic review of the literature. *Nutr Clin Pract*. 28: 194-208
24. Singh, A.K., 2009. Role of vitamin D in chronic kidney disease. *NIH Public Access*. 29(2): 113–121
25. Talaei, A. , F. Ghorbani , and Z. Asemi, 2018. The effects of vitamin D supplementation on thyroid function in hypothyroid patients: a randomized, double-blind, placebo-controlled trial. *Indian J. Endocrinol Metab*. 22(5): 584–588
26. Vondra, K. , L. Starka , and R. Hampl, 2015. Vitamin D and thyroid diseases. *Physiol. Res*. 64: 95–100.