

Estimation of the Serum Concentration Levels of Ferritin and Vitamin D for Hypothyroid Patients

Amera Kamal Mohammed¹, Thanaa Abdulmahdi², Zainab Nasser Nabat²

¹College of Pharmacy, Kirkuk University, 52001, Kirkuk, Iraq. ORCID ID: 0000-0002-8984-6824,

²Babylon Technical Institute, Al-Furat Al-Awsat Technical University, 51015, Babylon, Iraq.

Abstract

The paper investigates the serum concentration levels and the association between the levels of ferritin or vitamin D with thyroid dysfunction in Hypothyroid Patients. 90 participants were involved in this study; 47 healthy people (controls) (18 males and 29 females) and 43 hypothyroid patients (16 males and 27 females). Both groups have a mean age (age \pm standard error) and body mass index (BMI) (BMI \pm standard error) of 34.36 ± 1.19 years and 27.55 ± 0.52 kg/m², respectively. The obtained results indicated that the age of participants played an ignorable role in this investigation ($P > 0.05$), while significant differences were noticed between the patients and controls ($P < 0.05$) in terms of BMI, 25(OH) vit D, ferritin, TSH, T3 and T4. There was also a significant difference ($P < 0.05$) between male and female patients in terms of ferritin, TSH, T3 and T4 in comparison with the controls.

Keywords: Hypothyroid; vitamin D; ferritin; TSH; BMI.

Introduction

Thyroid hormones are very essential and have various actions, for instance, they maintain normal growth and regulate metabolism. Therefore, hypothyroid patients usually suffer from fatigue and cold, and easily gain weight due to their altered metabolism ¹. There are two thyroid hormones in the human body, Thyroxin (T4) and triiodothyroxine (T3); these hormones are produced in the thyroid gland ². The latter converts the iodine in food, in a series of reactions, into thyroid hormones. Although a disorder of the thyroid hormones, which is also known as hypothyroidism, can be easily diagnosed and treated, late diagnosis and consequently late treatment could cause adverse effects, such as slowed metabolism, and changes in the levels of serum ferritin and vitamin D ³. Previous studies have confirmed that hypothyroidism is directly related to the concentration of iodine, as the ability of the thyroid gland to produce the required amount of T3 and T4 is limited by the

concentration of iodine in the body, where excess or lack of this element could result in disorder of thyroid hormones ⁴. Hypothyroidism is mainly diagnosed by investigating the inverse relationship between TSH and T4 and T3, where it is expected that a normal person will have a low level of T4 or T3 and a high level of TSH ⁵. It is estimated that hypothyroidism occurs in from 3.8% to 4.6% of the world's population ⁶. However, some studies have indicated that the occurrence of hypothyroidism varies according to the area of the study and ages of the studied people, where it could reach 8.4% ⁷. Moreover, the clinical indicators of hypothyroidism are highly influenced by different factors, such as the duration and the deficiency level of the thyroid hormones. Generally, hypothyroidism gives a set of associated symptoms such as tiredness, cold, weight increase and dryness of skin, which could be used to diagnose this disease ⁸. Thyroperoxidase enzyme, which is a thyroid hormone, plays an important role in the synthetisation of thyroid hormones ⁹. Recent studies have demonstrated that the synthetisation process of the thyroperoxidase enzyme requires a certain amount of iron, which explains the association between the disorder of thyroid hormones and the ferritin level ¹⁰. For example, both Takamatsu, Majima ¹¹ and Sachdeva, Singh ¹⁰ have demonstrated that the thyroid profile is highly influenced by the ferritin

Corresponding Author:

Amera Kamal Mohammed

Environmental Research and Studies Center, Babylon University, Hilla, Iraq

Email: amira_babylon@yahoo.com.

levels. It is noteworthy to mention that ferritin is an iron storage protein, with a diameter ca 10–12 nm; it is essential for physiologic and pathologic activities (12-14).

Materials and Method

The current study involved 90 participants; these participants were divided into two groups: healthy (controls) and hypothyroid patient groups. The hypothyroid patient group consists of 16 Males (37.21%) and 27 Females (62.79%), while the healthy people group consists of 18 Males (38.30%) and 29 Females (61.70%). The members of the control group were not suffering from any chronic diseases, and had no history of thyroid disease, nor were they on any medication that may interfere with the obtained results. They were living in Babylon Governorate, Iraq. They were examined at the laboratories of Marajan hospital and at Ibn al-Nafis specialist laboratory during the period of study (September 2017 to January 2018). The mean of their ages was 34.36 ± 1.19 years (mean \pm S.E), and the mean of their body mass index (BMI) was 27.55 ± 0.52 kg/m² (mean \pm S.E). The BMI was calculated using the formula $BMI = \text{weight (kg)} / \text{height}^2 \text{ (m)}^2$. Vitamin D (25-hydroxyvitamin D), ferritin, T3, T4 and TSH levels were measured using the ELFA (Enzyme Linked Fluorescent Assay, Model: bioMérieux). It is noteworthy to highlight that the normal limit for vitamin D is ranging between 30 and 100 ng/ml. while the limits of ferritin are: male: 20-434 ng/ml, cyclic

women: 20-159 ng/ml, menopausal women: 20-278 ng/ml. Finally, limits for serum T3, T4 and TSH thyroid dysfunction patients (hypothyroid) are: T3 between 0.9 to 2.33nmol/l, hyperthyroid <0.15, hypothyroid T4 between 60-and120 nmol/l, TSH thyroid 0.25->7.0. It is noteworthy to highlight that the results were analysed using SPSS package (version 18).

Results and Discussion

The obtained results showed that there was no relationship between the age of participants and the thyroid disorder, while the rest of the studied parameters showed a significant relationships ($P < 0.05$). For example, it has been found that the values of BMI, 25(OH) vit D, ferritin, TSH, T3 and T4 in the patients were 23.93 ± 0.39 , 32.01 ± 2.76 , 33.16 ± 3.02 , 2.26 ± 0.18 , 3.60 ± 0.12 and 19.04 ± 0.66 , respectively. In contrast, the values of these parameters in the healthy people (controls) were 31.48 ± 0.56 , 18.29 ± 1.54 , 24.46 ± 1.90 , 11.82 ± 0.56 , 1.18 ± 0.07 and 9.20 ± 0.18 , respectively, as shown in Table 1. These differences indicate a significant association between these parameters and the thyroid disorder. Table 2 shows that the sex of the participants did not cause any a significant differences in the Age (years), BMI (kg/M²) and in the levels 25(OH) vit D (ng/ml) . However, a significant variation was observed in the levels of ferritin(ng/ml), TSH(μ u/ml), T3 (nmol/L)and T4(nmol/L) in male and female patients in comparison with the controls.

Table 1: Comparison between hypothyroid patients and control subjects for both sex.

Parameters	Controls (Mean ±S.E)		Patients (Mean ±S.E)		p- value
	Male (n=18)	Female (n=29)	Male (n= 16)	Female (n=27)	
Age (years)	2.88±32.16 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	1.69±31.58 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	2.93±32.93 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	2.17±39.62 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	0.93 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction
BMI (Kg/M2)	0.79±24.21 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	0.41±23.77 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	1.03±29.18 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	0.49±32.85 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	0.30 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction
25(OH) vit D (ng/ml)	1.81±53.96	1.32±18.38	2.52±28.05	0.71±12.50	0.31

Ferritin (ng/ml)	4.85±51.44 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	1.87±21.82 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	3.26±35.12 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	1.25±18.14 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	0.03 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction
TSH (µu/ml)	0.23±2.02 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	0.26±2.41 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	0.54±10.16 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	0.79±12.80 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction	0.001 The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction. The studied cases indicated that the concentration of this vitamin has a strong correlation with some diseases, such as thyroid dysfunction
T3 (nmol/L)	0.190±3.72	0.16±3.52	0.11±1.11	0.10±1.09	0.05
T4 (nmol/L)	1.53±20.32	0.49±18.25	0.20±9.57	0.26±9.64	0.04

In the hypothyroid patients the linear regression analysis showed there was a significant negative correlation between TSH(µu/ml) and 25(OH) vit D(ng/ml) ($r = -0.41, P=0.007$), as shown in Figure 1, and between TSH(µu/ml) and ferritin (ng/ml) ($r = -0.35, P=0.02$), as shown in Figure 2.

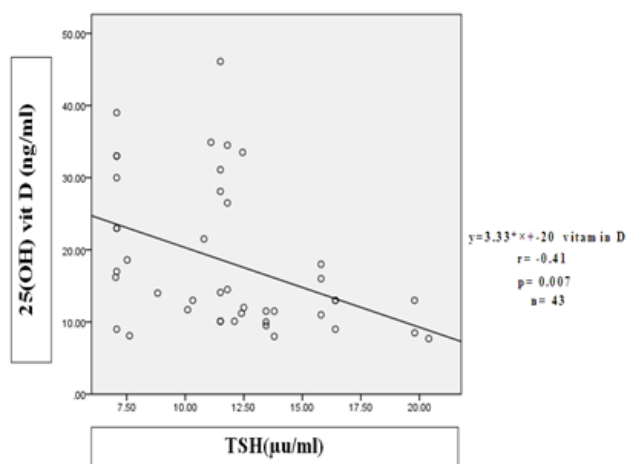


Figure 1: The linear regression analysis of the thyroid-stimulating hormone (TSH) (µ/ml) with 25(OH) vit D (ng/ml) for hypothyroid patients.

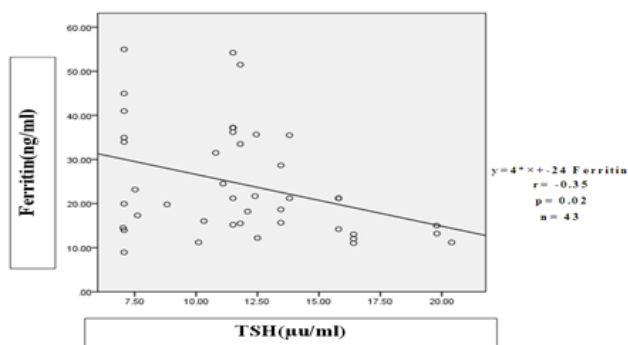


Figure 2: The linear regression analysis of the thyroid-stimulating hormone (TSH) (µ/ml) with ferritin (ng/ml) for hypothyroid patients.

Discussion

The outcomes indicated a significant correlation between the level of vitamin D and the thyroid disorder. A decrease in the average of vitamin D was noticed as the average of TSH increased. This relationship could be related to the increase in bone turnover in hyperthyroid patients that increases the calcium level, which in turn alters the synthesis of both parathyroid hormone and vitamin D¹⁹.

The outcomes of the current study agree with those of²⁰, which indicated that deficiency of vitamin D is responsible for low thyroid hormones. Mackawy, Al-Ayed²¹ found two facts, firstly the level of serum 25(OH) vit D in hypothyroid patients is less than its level in healthy people. Secondly, the authors noticed a clear correlation between serum 25(OH) vit D and TSH., which agrees with the results of Shilpa, Mishra²² that showed a clear reduction in the level of vitamin D in hypothyroid patients (≤ 20 ng/ml). Additionally, the literature showed that treatment of the vitamin D

deficiency in thyroid patients has enhanced thyroid functions²³. The literature also indicated an inverse relationship between the levels of vitamin D and TSH^{24,25}.

Conclusion

The results showed that hypothyroidism, represented by the high level of TSH, was associated with high BMI and low level of 25(OH) vit D, ferritin, TSH, T3 and T4, and age does not play a significant role.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Kirkuk University and all experiments were carried out in accordance with approved guidelines.

References

1. Stenzel D, Huttner WB. Role of maternal thyroid hormones in the developing neocortex and during human evolution. *Frontiers in neuroanatomy*.2013;7:19.
2. Moreno M, de Lange P, Lombardi A, Silvestri E, Lanni A, Goglia F. Metabolic effects of thyroid hormone derivatives. *Thyroid* .2008;18(2):239-53.
3. Chaker L, Bianco A, Jonklaas J, Peeters R. Hypothyroidism. *Lancet* .2017;390(23).
4. Zimmermann MB. Iodine deficiency. *Endocrine reviews* .2009;30(4):376-408.
5. Hadlow NC, Rothacker KM, Wardrop R, Brown SJ, Lim EM, Walsh JP. The relationship between TSH and free T4 in a large population is complex and nonlinear and differs by age and sex. *The Journal of Clinical Endocrinology & Metabolism* .2013;98(7):2936-43.
6. Leese G, Flynn R, Jung R, Macdonald T, Murphy M, Morris A. Increasing prevalence and incidence of thyroid disease in Tayside, Scotland: the Thyroid Epidemiology Audit and Research Study (TEARS). *Clinical endocrinology* .2008;68(2):311-16.
7. Caty SA, Marta OB, Jordi R, Leonardo G, Inaki G, Elisabeth M. Factors Associated with the Stability of Thyroid-stimulating Hormone Values in Hypothyroidism. *Archives of Medicine* .2017;9(2:13).

8. Melmed S. Williams textbook of endocrinology: Elsevier Health Sciences; 2016.
9. Hess SY, Zimmermann MB, Arnold M, Langhans W, Hurrell RF. Iron deficiency anemia reduces thyroid peroxidase activity in rats. *The Journal of nutrition* .2002;132(7):1951-55.
10. Sachdeva A, Singh V, Malik I, Roy PS, Madaan H, Nair R. Association between serum ferritin and thyroid hormone profile in hypothyroidism. *International Journal of Medical Science and Public Health* .2015;4(6):863-65.
11. Takamatsu J, Majima M, Miki K, Kuma K, Mozai T. Serum ferritin as a marker of thyroid hormone action on peripheral tissues. *The Journal of Clinical Endocrinology & Metabolism* .1985;61(4):672-76.
12. Sarin M, Arora P, Mohapatra S. Association between Serum Ferritin and Thyroid profile in Radiologically proven patients with Goitre with Thyroiditis. *The Journal of Community Health Management* .2017;4(2):50-52.
13. Theil EC. Ferritin protein nanocages—The story. *Nanotechnology perceptions* .2012;8(1):7.
14. Knovich MA, Storey JA, Coffman LG, Torti SV, Torti FM. Ferritin for the clinician. *Blood reviews* .2009;23(3):95-104.
15. Yilmaz R, Ozkayit S. VITAMIN D DEFICIENCY AND CHRONIC WIDESPREAD PAIN. *RHEUMATOLOGY* .2017.
16. Makariou S, Liberopoulos EN, Elisaf M, Challa A. Novel roles of vitamin D in disease: what is new in 2011? *European journal of internal medicine* .2011;22(4):355-62.
17. Kmiec P, Sworczak K. Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association. Official journal of German Society of Endocrinology [and] German Diabetes Association .2015;7(123).
18. Muscogiuri G, Tirabassi G, Bizzaro G, Orio F, Paschou S, Vryonidou A *et al*. Vitamin D and thyroid disease: to D or not to D? *European journal of clinical nutrition* .2015;69(3):291.
19. Iqbal AA, Burgess EH, Gallina DL, Nanes MS, Cook CB. Hypercalcemia in hyperthyroidism: patterns of serum calcium, parathyroid hormone, and 1, 25-dihydroxyvitamin D3 levels during management of thyrotoxicosis. *Endocrine practice* .2003;9(6):517-21.
20. Richards B. Low Vitamin D Contributes to Thyroid Problems. *Health news* .2008.
21. Mackawy AMH, Al-Ayed BM, Al-Rashidi BM. Vitamin D deficiency and its association with thyroid disease. *International journal of health sciences* .2013;7(3):267.
22. Shilpa H, Mishra B, Yadav S. Vitamin D levels correlated with hypothyroidism in Indian population: a pilot study. *Int J Rec Sci Res* .2014;5(5):984-7.
23. Talaei A, Ghorbani F, Naseri P, Chehrea A. The Study the Effect of Vitamin D on Hypothyroidism. *ISMJ* .2017;20(3):301-07.
24. Sonawane S, Bora B, Shrikhande D, Bansal S, Kumar P. Vitamin D deficiency and its association with thyroid diseases. *International Journal of Contemporary Medical Research* .2017;4(8):1765-67.
25. Hashemipour S, Larijani B, Adibi H, Javadi E, Sedaghat M, Pajouhi M *et al*. Vitamin D deficiency and causative factors in the population of Tehran. *BMC Public health* .2004;4(1):38.