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ORIGINAL ARTICLE

Vitamin D Status in Sample of Iraqi Women with Autoimmune Thyroiditis

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ABSTRACT

The most common cause of acquired thyroid dysfunction is autoimmune thyroid disease (AITD), which most commonly manifests as Hashimoto's thyroiditis (HT) or Graves' disease (GD). The importance of vitamin D (vit D) as an immune modulator has recently been emphasized in several types of disorders. However, its significance in thyroid illnesses is not fully understood. The purpose of this study is to investigate how vitamin D affects the pathophysiology of hyperthyroidism and hypothyroidism in Iraqi women. One hundred Iraqi women with age ranged from 18 to 60 years participate in this research, 50 of them were hypothyroidism patients, 30 were hyperthyroidism patients and the other 20 were euthyroidism served as controls. Blood samples were collected from the studied subjects to determine thyroid profile [free triiodothyronine (FT3), free tetraiodothyronine (FT4) and thyroid stimulating hormone (TSH)], thyroid antibodies [anti-thyroid peroxidase (anti-TPO), anti-thyroglobulin (anti-Tg), and anti-thyroid stimulating hormone receptor (anti-TSHR)], vit D, calcium (Ca), and phosphorus (P) using different analysis techniques.

Levels of FT3 and FT4 revealed a significant ($P<0.01$) increase in hyperthyroidism patients and a significant ($P<0.01$) decrease in hypothyroidism patients compared with euthyroidism control. While level of TSH was significantly ($P<0.01$) decreased in hyperthyroidism patients and significantly ($P<0.01$) increased in hypothyroidism compared with euthyroidism control. When a comparison was made between hyperthyroidism group and hypothyroidism group, the results showed that levels of FT3 and FT4 were significantly ($P<0.01$) higher in hyerthyroidism than hyporthyroidism while level of TSH was significantly ($P<0.01$) lower in hyperthyroidism than hyporthyroidism.

Levels of anti-TPO and anti-Tg significantly ($P<0.01$) increased in hyperthyroidism and hypothyroidism patients compared with euthyroidism individuals, while level of anti-TSHR was significantly ($P<0.01$) decreased in hyperthyroidism patients and significantly ($P<0.01$) increased in hypothyroidism patients compared with euthyroidism individuals. On the other hand, the findings revealed that level of anti-TPO was significantly ($P<0.01$) higher while levels of anti-Tg and anti-TSHR were significantly ($P<0.01$) higher in hypothyroidism than hyperthyroidism.

The results revealed a significant ($P<0.01$) decrease in level of vit D in hyperthyroidism patients and hypothyroidism patients compared with euthyroidism control, a significant ($P<0.01$) increase in levels of Ca and P in hyperthyroidism patients compared with euthyroidism control, while non-significant ($P>0.01$) differences were found between hypothyroidism patients and euthyroidism control. Also, the findings revealed that levels of vit D, Ca, and P were significantly ($P<0.01$) higher in hyperthyroidism than hypothyroidism.

Conclusion: It can be concluded that Vit D deficiency may be act as a factor in both hyperthyroidism and hypothyroidism, and the status of vit D impact on autoimmune thyroiditis.

Keyword: Autoimmune thyroiditis, Vitamin D, Hyperthyroidism, Hypothyroidism, Euthyroidism

INTRODUCTION

Thyroid illness is a sex-related disease, with women being naturally predisposed to thyroid disease[1]. The thyroid gland is frequently attacked by autoimmune illnesses, with the most common thyroid gland dysfunctions being hypothyroidism, lymphocytic thyroiditis, Hashimoto's thyroiditis (HT), and hyperthyroidism, Graves' disease (GD). Thyroid disorders are caused by an abnormal immunological response to thyroid auto-antigens[2]. The biochemical feature of the disease is the existence of thyroid autoantibodies against. TPO and Tg are two main thyroid antigens. Anti-TPO and anti-Tg antibodies are detected in more than 90% and 80% of HT patients, respectively[3]. Thyroid autoantibodies that react with key proteins in the thyroid, such as TPO or Tg, can induce a chronic lymphocytic thyroiditis that ultimately results in destruction and loss of thyroid function. In recent year, anti-TPO and anti-Tg antibodies are associated with abnormal TSH levels. However, the effect of dynamic changes in TPOAb and TgAb on incident abnormal TSH is unknown[4].

Thyroid dysfunction is commonly acquiring and can occur at any age. Thyroid autoimmunity is the most common cause of thyroid dysfunction in women of reproductive age. Thyroid autoantibodies that react with thyroid proteins such as TPO or Tg can cause chronic lymphocytic thyroiditis, which leads to thyroid destruction and loss of function. TSH receptor autoantibodies in the blood can activate the TSH receptor in GD, resulting in hyperthyroidism[5].

The primary action of vit D is to enhance intestinal calcium absorption and to promote osteoclast function, thereby maintaining Ca and P homeostasis and bone health[6]. Vit D deficiency is a worldwide health issue, and its significance as an immunological modulator has lately been highlighted. The evidence is mounting that vit D has a substantial role in lowering the occurrence of autoimmune disorders (AID); Nevertheless, studies on its impact in autoimmune and thyroid disorders is inconclusive[7]. The available data from studies on occurrence of vit D deficiency in relation to thyroid diseases mostly prove the association of vita D deficiency with higher incidence of autoimmune thyroiditis[8]. More severe deficiency is often accompanied by thyroid hypofunction[9].

MATERIALS AND METHODS

Subjects and blood samples collection: One hundred Iraqi women with age ranged from 18 to 60 years participated in this study; 30 of them were hyerthyroidism patients, 50 were hypothyroidism patients and the other 20 were euthyroidism served as controls. Blood samples has been collected from the studied women and serum has been collected and kept at (-20°C) until used.

Measurement of the studied parameters: A fluorescence immunoassay (FIA) was used to carry out the thyroid profile assay (FT3, FT4, and TSH) using Boditech kit/ Korea. The electrochemiluminescence immunoassay (ECLIA) is intended for use on Elecsys and cobase immunoassay analyzers to determine levels of the thyroid antibodies (anti-TPO and anti-Tg) using Cobas kit/Germany. Enzyme-linked immunosorbent assay (ELISA) was employed to estimate level of anti-TSHR using BioSource kit/ India. Level of vit D was determined by FIA using Boditech kit/ Korea. Biolab kit/France was used to determine Ca level, according to Moorhead and Briggs derived CPC (O-Cresol Phtalein Complexone) method, and to determine P level according to method without deproteinisation.

Statistical analysis: Statistical analysis was performed using the SPSS software (SPSS, Inc., Evanston, IL, USA). All data were

expressed as mean ± standard error (SE) and the level of significance was determined at P<0.05. Differences between the groups were analyzed using the analysis of variance (ANOVA) test.

RESULTS

Anthropometric variables of the studied groups: The data present in table (1) shows the anthropometric variables of the studied groups (hyperthyroidism, hypothyroidism, and euthyroidism). Non-significant (P>0.05) differences were noticed in age among the three groups (41.53±2.16, 39.56±1.55 and 35.5±2.82 years), respectively. A significant (P<0.05) increase was found in BMI of hypothyroidism patients (25.86±0.48 kg/m²) compared with hyperthyroidism patients (24.09±0.57 kg/m²) and euthyroidism (24.20±0.87 kg/m²), while non-significant (P>0.05) difference was found between hyperthyroidism patients and euthyroidism.

Table 1: Anthropometric variables of the studied groups

Groups	Mean ± SE	
	Age (year)	BMI(kg/m^2)
Hyperthyroidism	41.53±2.16^a	24.09±0.57^b
Hypothyroidism	39.56±1.55^a	25.86±0.48^a
Euthyroidism	35.5±2.82^a	24.20±0.87^b
P value	0.2	0.04*

Means in row carrying different small letters indicate a significant difference (P<0.05).
Means in row carrying similar small letters indicate a non-significant difference (P>0.05).

Thyroid profile of the studied groups: As shown in table (2), the result demonstrated that level of FT3 significantly (P<0.01) increased in hyperthyroidism patients (4.58±0.21 pmol/L) while decreased in hypothyroidism patients (0.83±0.04 pmol/L) compared with the euthyroidism (1.54±0.09 pmol/L). Also, level of FT4 significantly (P<0.01) increased in hyperthyroidism patients (14.45±0.29 pmol/L) while decreased in hypothyroidism patients (1.88±0.11 pmol/L) compared with euthyroidism (4.57±0.39 pmol/L). Level of TSH significantly (P<0.01) decreased in hyperthyroidism patients (0.12±0.03 µIU/ml) while increased in hypothyroidism patients (8.04±0.51 µIU /ml) compared with the euthyroidism (1.75±0.23 µIU/ml). On the other hand, levels of FT3 and FT4 were significantly (P<0.01) higher in hyerthyroidism than hyporthyroidism while level of TSH was significantly (P<0.01) lower in hyperthyroidism than hyporthyroidism.

Table 2: Thyroid profile of the studied groups

Groups	Mean ± SE		
	FT3 (pmol/L)	FT4 (pmol/L)	TSH (µIU/ml)
Hyperthyroidism	4.58±0.21^a	14.45±0.29^a	0.12±0.03^c
Hypothyroidism	0.83±0.04^c	1.88±0.11^c	8.04±0.51^a
Euthyroidism	1.54±0.09^b	4.57±0.39^b	1.75±0.23^b
P value	<0.001*	<0.001*	<0.001*

Means in row carrying different small letters indicate a significant difference (P<0.05).
Means in row carrying similar small letters indicate a non-significant difference (P>0.05).

Thyroid autoantibodies of the studied groups: As shown in table (3), levels of anti-TPO significantly (P<0.01) increased in hyperthyroidism patients (347.69±15.59 IU/ml) and hypothyroidism patients (242.088±23.96 IU/ml) compared with euthyroidism (12.45±1.24 IU/ml), while it was significantly (P<0.01) higher in hyperthyroidism than hypothyroidism. Also, levels of anti-Tg significantly (P<0.01) increased in hyperthyroidism patients (135.23±2.57 IU/ml) and hypothyroidism patients (211.2±10.43 IU/ml) compared with euthyroidism (14.5±1.71 IU/ml), while it was significantly (P<0.01) higher in hypothyroidism than hyperthyroidism. The results showed a significant (P<0.01) decrease in level of anti-TSHR in hyperthyroidism patients (1.321±0.05 ng/ml) and a significant (P<0.01) increase in hypothyroidism patients (29.56±0.64 ng/ml) compared with euthyroidism (12.92±0.43 ng/ml), while it was significantly (P<0.01) higher in hypothyroidism than hyperthyroidism.

Table 3: Thyroid autoantibodies of the studied groups

Groups	Mean ± SE		
	Anti- TPO (IU/ml)	Anti- Tg (IU/ml)	Anti-TSHR (ng/ml)
Hyperthyroidism	347.69±15.59^a	135.23±2.57^b	1.321±0.05^c
Hypothyroidism	242.088±23.96^b	211.2±10.43^a	29.56±0.64^a
Euthyroidism	12.45±1.24^c	14.5±1.71^c	12.92±0.43^b
P value	<0.001*	<0.001*	<0.001*

Means in row carrying different small letters indicate a significant difference (P<0.05).
Means in row carrying similar small letters indicate a non-significant difference (P>0.05).

Levels of vitamin D, calcium, and phosphorus of the studied groups: The data present in table (4) illustrate levels of vit D, Ca, and P in the studied groups. A significant (P<0.01) decrease was found in vit D level in hyperthyroidism patients (20.51±1.25 ng/ml) and hypothyroidism patients (19.74±1.30 ng/ml) compared with euthyroidism (46±1.14 ng/ml). Levels of Ca and P revealed significant (P<0.01) increase in hyperthyroidism patients (10.67±0.12 mg/dl and 6.19±0.48 mg/dl), respectively compared with euthyroidism (9.32±0.49 mg/dl and 3.42±0.11mg/dl), respectively; while non-significant (P>0.05) differences were found between hypothyroidism patients (9.08±0.12 mg/dl and 2.42±0.11 mg/dl), respectively and euthyroidism. When a comparison was made between hyperthyroidism group and hypothyroidism group, the findings revealed that levels of vit D, Ca, and P were significantly (P<0.01) higher in hyperthyroidism than hypothyroidism.

Table 4: Levels of vitamin D, calcium, and phosphorus of the studied groups

Groups	Mean ± SE		
	Vit D (ng/ml)	Ca (mg/dl)	P (mg/dl)
Hyperthyroidism	20.51±1.25^b	10.67±0.12^a	6.19±0.48^a
Hypothyroidism	19.74±1.30^c	9.08±0.12^b	2.42±0.11^b
Euthyroidism	46±1.14^a	9.32±0.11^b	3.42±0.11^b
P value	<0.001*	0.006*	<0.001*

Means in row carrying different small letters indicate a significant difference (P<0.05).
Means in row carrying similar small letters indicate a non-significant difference (P>0.05).

DISCUSSION

Non-significant differences in the mean of age between hyperthyroidism, hypothyroidism and euthyroidism groups could be attributed to the matching of the age range between the subjects of the three studied groups. These results are similar to that reported by other authors[10,11] who observed no significant difference with respect to age among the study groups. The present finding that the significant differences in BMI between hypothyroidism, euthyroidism, and hyperthyroidism have been reported in several previous studies[13,14] ; while they are disagreement with other study[11]. This finding due to the fact that thyroid hormones regulate energy metabolism and thermogenesis and play a critical role in glucose and lipid metabolism, food intake, and the oxidation of fatty acids[14]. Hypothyroidism is associated with decreased thermogenesis, decreased metabolic rate, and has also been shown to correlate with a higher BMI and a higher prevalence of obesity[15]. Also, BMI can be used in clinical diagnosis of thyroid autoimmune diseases but not indicator which was depended on only.

The findings that low TSH level in hyperthyroidism patients, in the present study, have been reported by[16]. A high level of TSH in hypothyroidism patients may be caused by the pituitary gland secreting more TSH in an attempt to stimulate the thyroid gland to produce more thyroid hormones (T3, T4). As for patients with hyperthyroidism, the opposite happens, as the level of thyroid hormone decreases to reduce the level of thyroid hormone secretion[17]. In agreement with[18], the present results showed that

hypothyroidism, caused by an underactive thyroid gland, hyperthyroidism caused by increased thyroid gland function. Because TSH secretion is so sensitive to minor changes in FT4 through this negative feedback loop, abnormal TSH levels are detected earlier than those of FT4 in hyperhyroidism and hypothyroidism. There is a log-linear relationship between T3/T4 and TSH, and minor changes in T3/T4 lead to significant changes in TSH[17].

The current results agree with several previous studies[19,20] which stated that anti-TPO and anti-TG levels were significantly higher in both subclinical hyperthyroid and hyporthyroid groups than euthyroidism. Also, this finding is agreement with[21] who reported that anti-TSHR are specific biomarkers for hyperthyroidism which are found in GD patients and responsible for many of its clinical manifestations. Anti-TSHR may also be found in patients with HT in whom they may contribute to the hypothyroidism of the disease. As some TSHR-Ab have a blocking effect, they may contribute to hypothyroidism[22], or be associated with a fluctuating course between hyper and hypothyroidism[23]. The explanation behind these results is that dynamic thyroid antibody changes may be related to incident abnormal TSH levels[4]. According to the current knowledge, a complex interaction between genetic and non-genetic factors presumably results in enhanced thyroid antigen presentation and reduced immune tolerance leading to predominantly Th1-type (T-helper) autoimmunity, thyroid destruction, and clinical disease[24].

The present findings are agreement with that reported by previous researcher[25] who demonstrated an association between low vit D status and autoimmune thyroid diseases such as HT and GD, and impaired vita D signaling has been reported in thyroid cancers. In patients with autoimmune thyroiditis, with special attention to hypothyroidism, deficiencies of many vitamins are observed include vit D. The current finding could be attributed to mechanisms of vit D in function of the immune system suggest that its deficiency may be disrupting the immune balance and be one of the environmental factors important in the development of hypothyroidism. There are also indications of the role of the VDR polymorphisms of disease etiology, which may also be one of the genetic factors[24].

It has been suggested that abnormal levels of vit D in serum may be the cause of dysfunction in the intestinal absorption of Ca in patients with AITD[26]. In agreement with other investigations[27,28], the current study found that serum Ca and P levels in hyperthyroid patients were increased while in hypothyroid patients they were decreased. In subclinical hypothyroidism and hyperthyroidism, serum Ca and serum P levels are significantly altered. Thyroid hormone is a central regulator of body hemodynamics, thermoregulation and metabolism. Therefore, it has an influence on renal hemodynamics, glomerular filtration and electrolyte handling[29]. Ca, magnesium (Mg) and P homeostasis were frequently disturbed in thyroid dysfunctions. Thyroid hormone affects the glomerular filtration rate and blood flow and has a direct effect on Ca and Mg resorption[30].

CONCLUSION

It can be concluded that anti-TPO and anti-Tg increase in both hyperthyroidism and hypothyroidism, while anti-TSHR increases in hypothyroidism and decreases in hyperthyroidism. Additionally, it can also be concluded that Vit D deficiency may be act as a factor in both hyperthyroidism and hypothyroidism.

REFERENCES

1 Merrill SJ, Mu Y. Thyroid autoimmunity as a window to autoimmunity: an explanation for sex differences in the prevalence of thyroid autoimmunity. Journal of Theoretical Biology 2015; 375: 95-100.

2 Przybylik-Mazurek E, Hubalewska-Dydejczyk A, Huszno B. Autoimmune hypothyroidism. Immunulogia 2007; 3-4: 64-69.

3 Zaletel K. Determinants of thyroid autoantibody production in Hashimoto's thyroiditis. Expert Review of Clinical Immunology 2007; 3(2): 217-223.

4 Li Y, Teng D, Guan H, LiY, Teng X, Yu X, Mao J, Shi X, Fan C, Shan Z, Teng W. Dynamic changes in antithyroperoxidase and antithyroglobulin antibodies suggest an increased risk for abnormal thyrotropin levels. Frontiers in Endocrinology 2020; 11: 521.

5 van den Boogaard E, Vissenberg R, Land JA, van Wely M, van der Post JA, Goddijn M, Bisschop PH. Significance of (sub) clinical thyroid dysfunction and thyroid autoimmunity before conception and in early pregnancy: a systematic review. Human Reproduction Update 2011; 17(5: 605-619.

6 Muscogiuri G, Mitri J, Mathieu C, Badenhoop K, Tamer G, Orio F., Mezza, T, Vieth R, Colao A, Pittas A. Mechanisms in endocrinology: vitamin D as a potential contributor in endocrine health and disease. European Journal of Endocrinology 2014; 171(3): R101-R110.

7 Mackawy AM, Al-Ayed BM, Al-Rashidi BM. Vitamin D deficiency and its association with thyroid disease. International Journal of Health Sciences 2013; 7(3): 267.

8 Bizzaro G, Shoenfeld Y. Vitamin D and thyroid autoimmune diseases: The known and the obscure. Immunol. Res. 2015; 61:107-109.

9 Bozkurt NC, Karbek B, Ucan B, Sahin M, Cakal E, Ozbek M, Delibasi T. The association between severity of vitamin D deficiency and Hashimoto's thyroiditis. Endocrine Practice 2013; 19(3): 479-484.

10 Cikim AS, Oflaz H, Ozbey N, Cikim K, Umman S, Meric M, Sencer E, Molvalilar S. Evaluation of endothelial function in subclinical hypothyroidism and subclinical hyperthyroidism. Thyroid 2004; 14(8): 605-609.

11 Korevaar TI, Mínguez-Alarcón L, Messerlian C, de Poortere RA, Williams PL, Broeren MA, Hauser R, Souter IC. Association of thyroid function and autoimmunity with ovarian reserve in women seeking infertility care. Thyroid 2018; 28(10):1349-1358.

12 Song RH, Wang B, Yao QM, Li Q, Jia X, Zhang JA. The impact of obesity on thyroid autoimmunity and dysfunction: a systematic review and meta-analysis. Frontiers in Immunology 2019; 10: 2349.

13 Mahdavi M, Amouzegar A, Mehran L, Madreseh E, Tohidi M, Azizi F. Investigating the prevalence of primary thyroid dysfunction in obese and overweight individuals: Tehran thyroid study. BMC Endocrine Disorders 2021; 21: 1-12.

14 Reinehr T. Obesity and thyroid function. Molecular and Cellular Endocrinology 2021; 316(2): 165-171.

15 Danforth E, Horton ES, O'Connell, M, Sims EA, Burger AG, Ingbar SH, Braverman L, Vagenakis AG. Dietary-induced alterations in thyroid hormone metabolism during overnutrition. J Clin Invest 1979; 64(5): 1336-1347.

16 Lillevang-Johansen M, Abrahamsen B, Jørgensen HL, Brix TH, Hegedüs L. Excess mortality in treated and untreated hyperthyroidism is related to cumulative periods of low serum TSH. The Journal of Clinical Endocrinology and Metabolism 2017; 102(7):2301-2309.

17 Shahid MA, Ashraf MA, Sharma S. (2022). Physiology, Thyroid Hormone. StatPearls Publishing, Treasure Island. 2018.

18 Pirahanchi Y, Toro F, Jialal I. Physiology, Thyroid Stimulating Hormone. StatPearls Publishing. Treasure Island. 2018.

19 Tipu HN, Ahmed D, Bashir MM, Asif N. Significance of testing anti-thyroid autoantibodies in patients with deranged thyroid profile. Journal of Thyroid Research 2018.

20 El Din LMT, El Melegy TTH, Hussien SAE (2021). Serum levels of anti-thyroid autoantibodies in different thyroid function status. Journal of Current Medical Research and Practice 2021; 6(3):298.

21 Kahaly GJ, Diana T, Olivo PD (2020). TSH receptor antibodies: relevance and utility. Endocrine Practice 2020; 26(1): 97-106.

22 Michalek K, Morshed SA, Latif R, Davies TF .TSH receptor autoantibodies. Autoimmunity reviews 2009; 9(2): 113-116.

23 Napolitano G, Bucci I, Di Dalmazi G, Giuliani C. Non-conventional clinical uses of TSH receptor antibodies: the case of chronic autoimmune thyroiditis. Frontiers in Endocrinology 2021; 12: 769084.

24 Zaletel K, Gaberscek S. Hashimoto's thyroiditis: from genes to the disease. Current Genomics 2011; 12(8): 576-588.

25 Mele C, Caputo M, Bisceglia A, Samà MT, Zavattaro M, Aimaretti G, Pagano L, Prodam F, Marzullo P. Immunomodulatory effects of vitamin D in thyroid diseases. Nutrients 2020; 12(5): 1444.

26 Bouillon R, De Moor P. Influence of thyroid function on the serum concentration of 1, 25-dihydroxyvitamin D3. The Journal of Clinical Endocrinology and Metabolism 1980; 51(4): 793-797.

27 Jat RK, Panwar AK, Agarwal P, Sharma C, Bansal DP, Pareek A, Tyagi A, Mathur M. (2021). Assessment of serum minerals in subclinical hypothyroid and overt hypothyroid patients. Cureus 2021; 13(8): e16944.

28 Babu BS, Azmatulla Shaik A, Khan SA, Altaf N. Study of serum calcium, magnesium and phosphorous levels in hypothyroidism. European Journal of Molecular and Clinical Medicine 2022; 9(3):1286-1292.

29 Mariani LH, Berns JS. The renal manifestations of thyroid disease. Journal of the American Society of Nephrology 2012; 23(1): 22-26.

30 McCaffrey C, Quamme GA. Effects of thyroid status on renal calcium and magnesium handling. Canadian Journal of Comparative Medicine 1984. 48(1): 51.