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Effect of Age and Body Mass Index on some Physiological Parameters in Women with Thyroid Disorders

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Abstract

Age and BMI may be used to diagnosis of thyroid autoimmune disease. 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)], and levels of vitamin D (vit D), calcium (Ca), and phosphorus (P) using different analysis techniques.

When the effect of age on the studied parameters was investigated, the findings of hyperthyroidism revealed a significant ($P<0.05$) decrease in levels of FT4, anti-TPO, anti-TG, vit D, and Ca with increase of age. The findings of hypothyroidism revealed a significant ($P<0.05$) increase in levels of TSH, anti-TPO, and anti-TG with progress of age; while a significant ($P<0.05$) decrease was found in levels of anti-TSHR, vit D, and Ca with progress of age. The findings of euthyroidism revealed a significant ($P<0.05$) increase in levels of TSH and anti-TG with progress of age. Also, a high significant ($P<0.01$) increase was found in levels of anti-TPO and anti-TSHR with progress of age. While a significant ($P<0.05$) decrease was found in levels of vit D with progress of age.

On the other hand, when the effect of BMI on the studied parameters was investigated, the results of hyperthyroidism revealed a high significant ($P<0.01$) decrease in level of TSH with increase of BMI value. Also, levels of anti-TSHR, Ca, and P decreased significantly ($P<0.05$) with increase of BMI value. In hypothyroidism, the results showed a high significant ($P<0.01$) increase in levels of TSH, anti-TPO, and anti-TG with increase of BMI value; while levels of anti-TSHR, Ca, and P decreased significantly ($P<0.05$) with increase of BMI value.

Conclusion: Both of age and body mass index affect on levels of thyroid hormones and thyroid autoantibodied in patients with thyroid disorders (hyperthyroidism and hypothyroidism).

Keyword: Age, Body mass index, Hyperthyroidism, Hypothyroidism, Euthyroidism.

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Introduction

A euthyroid state is said to be in an individual whose thyroid function is normal. The clinical state resulting from an alteration in thyroid function is classified as either hypothyroidism (low thyroid function) or hyperthyroidism (excessive thyroid function). Autoimmune diseases play an important role in thyroid disease [1].

The major secretory products of the thyroid gland are triiodothyronine (T3) and tetraiodothyronine (T4), consisting of 10% T3 and 90% T4 [2]. Thyroid stimulating hormone (TSH) is the main regulator of thyroid growth and function from late fetal life to adulthood [3]. Levels of free T3 (FT3), free T4 (FT4), and (TSH) vary significantly by gender and age. In women of reproductive age, the most prevalent cause of thyroid dysfunction is thyroid autoimmunity [4].

The major antigens driving the appearance of thyroid autoantibodies are thyroid peroxidase (TPO), thyroglobulin (TG), and thyroid stimulating hormone receptor (TSHR) [5]. It has been reported that anti-TPO and anti-TG can cause chronic lymphocytic thyroiditis, which leads to thyroid destruction and loss of function, while anti-TSHR can activate the TSHR in Graves' disease (GD), resulting in hyperthyroidism [6].

Vitamin D (vit D) has major biologic function in human to maintain serum calcium (Ca) and phosphorus (P) concentrations within the normal range by enhancing the efficiency of the small intestine to absorb these minerals from the diet [7]. Recent studies have revealed that the prevalence of low vit D status is higher in patients with autoimmune thyroid disease (AITD), particularly those with Hashimoto's thyroiditis (HT), than in patients without AITD. These studies revealed that low vita D status was associated with TPOAb positivity, subclinical hypothyroidism, or overt hypothyroidism [8].

Some previous studies reported that high number of total thyroid dysfunction was observed with progress of age [9]. Also, it has been reported that prevalence of thyroid autoantibodies increases with age, reaching up to 20% in women over the age of 60 years, and may be partly responsible for the anatomic changes in the thyroid gland [10].

The incidence of obesity in AITD has been estimated as 12.4% in children and 10-60% in adult population [11]. Hyperthyroidism causes weight loss in the majority, but its effect is variable and 10% of patients gain weight with it [12].

The causes of increased body mass index (BMI) in hypothyroidism patients and the relation between TSH and BMI, as well as body composition have not been fully elucidated so far. In the previous study, TSH concentration correlated significantly with waist-hip ratio (WHR) and the percentage of body fat [13]. On the other hand, hyperthyroidism induces increased basal energy expenditure that leads to weight loss as a result of a decrease in the body's lean and fat mass [14].

Materials and Methods

Subjects and blood samples collection

This study includes one hundred Iraqi women with age ranged from 18 to 60 years; 30 of them were hyperthyroidism patients, 50 were hypothyroidism patients and 20 were euthyroidism served as control group. 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

The thyroid profile assay (FT3, FT4, and TSH) was carried out by a fluorescence immunoassay (FIA) using Boditech kit/ Korea. Levels of the thyroid antibodies (anti-TPO and anti-Tg) were determined by the electrochemiluminescence immunoassay (ECLIA) and cobase immunoassay analyzers using Cobas kit/Germany. Level of anti-TSHR was estimated by enzyme-linked immunosorbent assay (ELISA) 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 done using the SPSS software (SPSS, Inc., Evanston, IL, USA). The 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

Effect of age on the studied parameters

Effect of age on thyroid profile is shown in table (1). Findings of hyperthyroidism revealed a significant ($P<0.05$) decrease in levels of FT4 with progress of age, while a significan ($P<0.05$) increase was found in level of TSH with progress of age in hypothyroidism and euthyroidism.

Table (1): Effect of age on thyroid profile

Group	Thyroid profile	Age categories (year)			P value
		18-30	31-45	46-60	
Hyperthyroidism	FT3 (pmol/L)	1.76±0.28^{a}	1.64±0.13^{a}	1.30±0.11^{a}	0.13
	FT4 (pmol/L)	6.16±1.18^{a}	4.57±0.48^{b}	3.56±0.33^{c}	0.03*
	TSH (µIU/ml)	0.04±0.02^{a}	0.10±0.08^{a}	0.11±0.03^{a}	0.23
Hypothyroidism	FT3 (pmol/L)	0.92±0.06^{a}	0.79±0.06^{a}	0.79±0.09^{a}	0.43
	FT4 (pmol/L)	1.95±0.22^{a}	1.83±0.20^{a}	1.85±0.16^{a}	0.89
	TSH (µIU/ml)	9.77±0.90^{a}	8.52±0.87^{b}	6.38±0.69^{c}	0.04*
Euthyroidism	FT3 (pmol/L)	4.50±0.33	4.98±0.45	4.32±0.33	0.54
	FT4 (pmol/L)	14.71±0.41	14.80±0.72	14.24±0.49	0.68
	TSH (µIU/ml)	1.45±0.31	2.02±0.55	2.04±0.44	0.04*
* Significant ($P<0.05$).					

- 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 ($P>0.05$).

Table (2) shows effect of age on thyroid autoantibodies. The results of hyperthyroidism revealed a

significant (P<0.05) decrease in levels of anti-TPO and anti-TG with increase of the age. The results of hypothyroidism revealed a significan (P<0.05) increase in levels of anti-TPO and anti-TG; while a significan (P<0.05) decrease was found in level of anti-TSHR with progress of the age. The findings of euthyroidism revealed a significan (P<0.05) increase in level of anti-TG, and a high significan (P<0.01) increase was found in levels of anti-TPO and anti-TSHR with progress of age.

Table (2): Effect of age on thyroid autoantibodies

Group	Thyroid autoantibody	Age groups (Year)			P value
		18-30	31-45	46-60	
Hyperthyroidism	Anti-TPO (IU/ml)	142.50±3.16^{a}	135.38±2.29^{b}	130.45±6.05^{c}	0.02*
	Anti-TG (IU/ml)	383.64±29.25^{a}	359.34±23.63^{b}	312.11±26.51^{c}	0.02*
	Anti-TSHR (ng/ml)	1.32±0.10^{a}	1.40±0.05^{a}	1.23±0.09^{a}	0.25
Hypothyroidism	Anti-TPO (IU/ml)	209.21±17.41^{c}	211.42±18.39^{b}	214.24±18.74^{a}	0.01*
	Anti-Tg (IU/ml)	199.61±40.58^{c}	252.54±41.24^{b}	265.39±42.37^{a}	0.05*
	Anti-TSHR (ng/ml)	33.74±1.36^{a}	28.58±0.88^{b}	27.22±0.41^{c}	0.03*
Euthyroidism	Anti-TPO (IU/ml)	11.00±1.53^{c}	15.00±3.21^{b}	16±4.51^{a}	0.001**
	Anti-TG (IU/ml)	9.00±1.24^{c}	13.00±2.07^{b}	18.80±1.46^{a}	0.04*
	Anti-TSHR (ng/ml)	11.56±0.43^{c}	13.07±0.40^{b}	15.48±0.15^{a}	0.001**
* Significant (P<0.05), ** High Significant (P<0.01).					

- Means in row carrying different small letters indicate a significant difference (P<0.05) or (P<0.01).
- Means in row carrying similler small letters indicate a non-significant difference (P>0.05) or (P>0.01).

Table (3) shows effect of age on levels of vit D, Ca, and P. Findings of hyperthyroidism revealed a significant (P<0.05) decrease in levels of vit D and Ca with increase of age. Findings of hypothyroidism revealed a significan (P<0.05) decrease in levels of vit D and Ca with progress of age. Findings of euthyroidism revealed a significan (P<0.05) decrease in levels of vit D with progress of age.

Table (3): Effect of age on levels of vitamin D, calcium and phosphorus

Group	Parameter	Age categories (Year)			P value
		18-30	31-45	46-60	
Hyperthyroidism	Vit D (ng/ml)	22.79±2.22^{a}	21.82±1.87^{b}	17.63±2.2^{c}	0.02*
	Ca (mg/dl)	8.74±0.27^{a}	8.50±0.23^{b}	7.82±0.12^{c}	0.04*
	P (mg/dl)	5.81±0.42^{a}	6.12±0.5^{a}	6.50±1.19^{a}	0.86

Hypothyroidism	**Vit D (ng/ml)**	21.21±3.47[a]	20.90±1.91[b]	17.61±1.49[c]	0.03*
	Ca (mg/dl)	9.84±0.25[a]	8.13±0.21[b]	7.22±0.14[c]	0.04*
	P (mg/dl)	4.44±0.32[a]	4.28±0.39[a]	4.69±0.41[a]	0.73
Euthyroidism	**Vit D (ng/ml)**	47.90±0.99[a]	41.20±3.09[b]	40±1.67[c]	0.03*
	Ca (mg/dl)	9.56±0.13[a]	9.12±0.25[a]	9.04±0.15[a]	0.07
	P (mg/dl)	3.62±0.14[a]	3.30±0.18[a]	3.12±0.23[a]	0.13
* Significant (P<0.05).					

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

Effect of BMI on the studied parameters

Effect BMI on thyroid profile is shown table (4). In hyperthyrodism and hypothyroidism groups, the results revealed a high significant (P<0.01) decrease in level of TSH with increase of BMI values; while the findings showed a non-significant (p>0.05) differences between the BMI categorise regards to FT3, FT4 and TSH in euthyroidism group.

Table (4): Effect of BMI on thyroid profile

Group	**Thyroid profile**	**BMI categories (Kg/m^2)**			**P value**
		18.5-24.9	**25.0-29.9**	**≥ 30**	
Hyperthyroidism	**FT3 (pmol/L)**	1.63±.12[a]	1.40±0.18[a]	1.26±0.13[a]	0.42
	FT4 (pmol/L)	5.04±0.53[a]	1.26±0.13[a]	2.95±0.08[a]	0.20
	TSH (µIU/ml)	0.08±0.02[c]	0.11±0.03[b]	2.95±0.08[a]	0.001**
Hypothyroidism	**FT3 (pmol/L)**	0.82±0.08[a]	0.86±0.06[a]	0.70±0.05[a]	0.59
	FT4 (pmol/L)	1.84±0.17[a]	1.87±.155[a]	2.09±0.44[a]	0.82
	TSH (µIU/ml)	7.45±0.49[c]	8.71±0.81[b]	9.86±2.36[a]	0.001**
Euthyroidism	**FT3 (pmol/L)**	4.45±0.29[a]	5.14±0.25[a]	4.00±0.20[a]	0.27
	FT4 (pmol/L)	15.13±0.40[a]	14.30±0.21[a]	13.45±0.65[a]	0.24
	TSH (µIU/ml)	1.68±0.31[a]	1.99±0.52[a]	1.59±0.25[a]	0.84
** High significant (P<0.01).					

- Means in row carrying different small letters indicate a significant difference (P<0.01).
- Means in row carrying similler small letters indicate a non-significant difference (P<0.01).

Effect BMI on thyroid autoantibodies is shown table (5). In hyperthyroidism, the results revealed that level of anti-TSHR decreased significantly (P<0.05) with increase of BMI values. In hypothyroidism, the results revealed a high significant (P<0.01) increase in levels of anti-TPO and anti-TG with increase of BMI values; while level of anti-TSHR decreased significantly (P<0.05) with increase of BMI values. On other hand, the findings of euthyroidism group showed a non-significant (P>0.05) differences between BMI categories regards to anti-TPO, anti TG and anti TSHR.

Table (5): Effect of BMI on thyroid autoantibodies

Group	Thyroid antibody	BMI categories (Kg/m^2)			P value
		18.5-24.9	25.0-29.9	≥ 30	
Hyperthyroidism	Anti-TPO (IU/ml)	135.16±2.14^c	137.79±8.08^b	138.80±8.20^a	0.06
	Anti-TG (IU/ml)	360.20±19.34^a	334.96±30.85^b	273.55±19.45^c	0.36
	Anti-TSHR (ng/ml)	1.36± 0.05^a	1.25±0.12^b	1.22±0.12^c	0.05*
Hypothyroidism	Anti-TPO (IU/ml)	139.47±16.96^c	189.58±13.42^b	216.20±34.39^a	0.007**
	Anti-TG (IU/ml)	172.44±25.09^c	299.52±101.30^b	322.29±39.25^a	0.008**
	Anti-TSHR (ng/ml)	30.36±1.19^a	29.46±2.56^b	28.99±0.76^c	0.03*
Euthyroidism	Anti-TPO (IU/ml)	13±1.94^a	16.60±3.04^a	19.00±11.00^a	0.480
	Anti-TG (IU/ml)	11.69±1.49^a	12.00±2.72^a	18.50±2.50^a	0.281
	Anti-TSHR (ng/ml)	12.67±0.58^a	13.18±0.84^a	13.91±1.00^a	0.683
* Significant (P<0.05), ** High significant (P<0.01).					

- Means in row carrying different small letters indicate a significant difference (P <0.05) or (P<0.01).
- Means in row carrying similler small letters indicate a non-significant difference (P >0.05) or (P<0.01).

Effect of BMI on levels of vit D, Ca, and P, as shown in table (6), revealed non-significant (P>0.05) differences in levels of vit D and Ca among the BMI categories in the three studied groups; while level of P decreased significantly (P<0.05) with increasing BMI values in hyperthyroidism and hypothyroidism.

Table (6): Effect of BMI on levels of vitamin D, calcium and phosphorus

Group	Parameter	BMI categories (Kg/m^2)			P value
		18.5-24.9	25.0-29.9	≥ 30	
Hyperthyroidism	Vit D (ng/ml)	21.55±1.61^a	17.71±2.20^a	21.31±3.50^a	4.17
	Ca (mg/dl)	8.61±0.17^a	7.88±0.11^a	6.55±0.05^a	0.02

	P (mg/dl)	5.92±0.30[a]	4.28±1.62[b]	3.50±0.70[c]	0.03*
Hypothyroidism	**Vit D (ng/ml)**	21.60±2.67[a]	18.57±1.43[a]	18.81±3.73[a]	0.54
	Ca (mg/dl)	9.99±0.18[a]	9.13±0.16[a]	7.14±0.41[a]	0.04
	P (mg/dl)	5.36±0.31[a]	4.36±0.32[b]	3.42±0.82[c]	0.03*
Euthyroidism	**Vit D (ng/ml)**	46.77±0.96[a]	42.60±3.59[a]	49.50±0.50[a]	0.18
	Ca (mg/dl)	9.39±0.13[a]	9.14±0.23[a]	9.30±0.50[a]	0.62
	P (mg/dl)	3.35±0.13[a]	3.60±0.23[a]	3.40±0.40[a]	0.62
* Significant (P<0.05).					

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

Disscusion

Regarding the effect of age on the studied parameters, same findings were reported by previous researchers [15,16] which stated that in older age groups, increasing TSH was not associated with an increased FT3/FT4 ratio. As TSH levels increase, FT3/FT4 ratios increase until age 40, but this differential increase does not occur in older age groups. This may reflect a decrease in T4 to T3 conversion with age, which may be part of the aging process. Age-related subtle thyroid hypofunction (either due to a familial component or due to a reset of the thyroid function occurring between the sixth and the eighth decade of life) appears to be related to longevity [17]. On the other hand, the clinical impact of severe iodine deficiency is well-known, but even small differences in iodine status can affect the population distribution of TSH and alter the relationship between TSH and age [18].

It has been reported by Whickham survey that with increasing age, the incidence of positive antithyroid antibodies and hypothyroidism also increased [19]. The current results are similar to that stated by [20] who reported a higher prevalence of TPO and/ or TG autoantibodies in the serum of females with advanced age.

The present results agree with several previous studies [21,22]. All age-related changes in vit D metabolism are magnified if there is concomitant vit D deficiency, because it limits the substrate supply for 25OHD and ultimately $1,25(OH)_2D$. Substrate deficiency is a common problem in the elderly and is important to recognize because it is preventable and treatable. Serum $1,25(OH)_2D$ levels decrease when the serum 25OHD level falls below 10 ng/mL in both younger and older people [23]. There is a decrease in the concentration of 7-dehydrocholesterol in the epidermis in old compared with young individuals and a reduced response to UV light, resulting in a 50% decrease in the formation of previtamin D3 [22]. Also, there is a decrease in intestinal absorption of Ca with age and a decrease in the capacity to adapt to a low-caliber diet [24]. However, it has been stated that adults aged 30-90 years have similar phosphorus concentrations [25]. Over 30 years, an increase in phosphate consumption by 12% was observed. Thyroxine therapy normalized the deranged lipids and minerals, but not glucose. Results indicate that thyroid function tests should be considered when diagnosing those metabolic disorders [26].

Concerning the effect of BMI on the studied parameters, the current results are similar to that reported by previous researchers such as [27,28]. Obesity and thyroid disorders are two common conditions and there is an intriguing relationship between these two entities [29]. Extreme obesity is associated with thyroid

dysfunction due to HPT axis abnormality causing increased serum TSH. The association between serum TSH and body weight is caused by signals from adipose tissue. Leptin produced by adipocytes directly stimulates TRH neurons in the paraventricular nucleus increasing TSH level [30]. Neuro-transmitters and hormones that regulate body weight and satiety are also involved indirectly in regulation of TSH production [31].

The present results agree with several previous studies [32,29] which stated that obesity may be a contributing factor for hypothyroidism, HT and positive TPOAb, and suggested that thyroid functions in obese population needs extra attention. Unlike other auto immune diseases where autoantibodies may be epiphenomena (e.g., Hashimoto's thyroiditis, type 1 diabetes), TRAb plays an important role in the pathogenesis of the disease. Hence, it is expected that the presence of TRAb is diagnostic of GD [33]. Antibodies often present in the serum of patients with GD that are directed against the TSH receptor, often causing stimulation of this receptor with resulting hyperthyroidism [34]. Similarly, other observational researches also provide evidence that dysfunction in adipokines is associated with thyroid autoimmunity [35]. Meanwhile, meta-analysis of thyroid antibodies showed the correlation between TPOAb positive and obesity, and obesity is associated with a 93% increased risk of developing positive TPOAb. Autoimmune thyroiditis, mainly HT, is believed to be the main cause of hypothyroidism in iodine sufficient regions, and thyroid auto-antibodies (TPOAb and TgAb) are the hallmarks of this disease [36]. This may be another interpretation to explain the mechanism why obesity induces hypothyroidism.

The current findings are in agreement with previous studies [37,38] wich reported no evidence of a relation between vit D and BMI. Obesity is multifactorial. It is a subject of controversy whether the vit D deficiency is a consequence or a factor predisposing to obesity [39]. However, it has been suggested that adiposity phenotypes were strongly linked to serum 25-hydroxyvitamin D levels [40]. A previous study [41] reported that body weight did not change by increasing intake of calcium from different sources. Calcium supplementation could reduce body weight gain in children and adolescents and increase body weight loss in adult men and premenopausal women but not in postmenopausal women [42]. On the other hand, a previous study [43] reported that phosphorus status inversely related to body weight and waist circumference. The mechanisms by which phosphorus affected body weight may have been related to its involvement in food intake control and/or energy metabolism. Phosphorus availability is known to stimulate ATP production, in particular hepatic ATP , that is believed to transmit afferent neural signals to the central nervous system resulting in a decrease in food intake through the stimulation of satiation. Such effect was believed to be behind the impact of phosphorus addition to different carbohydrate preloads on the suppression of ad libitum energy intake at subsequent meal [44].

It can be concluded that both of age and body mass index affect on levels of thyroid hormones and thyroid autoantibodied in patients with thyroid disorders (hyperthyroidism and hypothyroidism).

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