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Changes in the before and after thyroxine treatment levels of adipose tissue, leptin, and resistin in subclinical hypothyroid patients

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Summary
Background Subclinical hypothyroidism (SH) occurs when serum thyroid stimulating hormone (TSH) concentrations are raised and serum thyroid hormone concentrations are normal. The effect of SH on the proinflammatory adipose cytokine releasing visceral adipose tissue (VAT) is not clear. The aim of this study is to identify the difference between the pre and posttreatment levels of VAT, leptin, and resistin in SH patients.

Methods There were 51 SH patients and 43 age- and gender-matched healthy subjects included in the study. Thyroid functions, biochemical tests, leptin, resistin, and visceral and subcutaneous fat measurements were made. The measurements were repeated in the SH group in the third month following L-thyroxin treatment.

Results Initially, high sensitivity C-reactive protein, carotid artery intima-media thickness (mm), leptin, and resistin levels were significantly higher in the SH group compared to the controls, while the other parameters were similar. While no correlation was observed between TSH levels and adipokines, a positive correlation was detected between waist circumference and leptin levels ($r=0.549$, $p<0.01$). Visceral adipose tissue was positively correlated to age, waist circumference, and leptin levels, but negatively correlated to free thyroxin (T4) levels ($r=0.419$, $p=0.009$; $r=0.794$, $p<0.01$; $r=0.515$, $p<0.01$ and $r=-0.416$, $p=0.009$, respectively). A significant decrease was observed in VAT volume, leptin, and resistin levels of SH patients following levothyroxine treatment.

Conclusion The reduced VAT volume, leptin, and resistin levels in SH patients following treatment may support the idea that TSH affects adipose tissue functions.

Keywords Subclinical hypothyroidism · Visceral adipose tissue · Thyroid stimulating hormone · Leptin · Resistin

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Introduction

Abdominal obesity is an independent risk factor for the development of cardiovascular diseases (CVD). It is associated with an increased volume of visceral adipose tissue (VAT) [1]. VAT is the predominant adipose tissue compartment that produces various proinflammatory cytokines and adipokines [2]. Increased VAT is strongly related to metabolic complications such as dyslipidemia, hypertension, and insulin resistance [3]. Visceral fat thickness can be evaluated accurately with computed tomography (CT) and magnetic resonance imaging (MRI). Both techniques have some limitations, like radiation exposure for CT and cost-effectiveness for MRI. Abdominal ultrasound (US) is an accurate, noninvasive, and cost-effective method for VF evaluation. When compared with the CT, it has been found that visceral fat volume measured by US has similar accuracy [4].

Subclinical hypothyroidism (SH) occurs when serum thyroid stimulating hormone (TSH) concentrations are raised while serum thyroid hormone concentrations are normal [5]. Several publications have demonstrated a positive correlation between SH and CVD [6, 7]. One study has shown that even small increases in serum TSH concentrations within normal reference ranges may be associated with increased weight [8], as thyroid hormones, leptin, and resistin are involved in energy metabolism and weight changes. While a majority of studies report normal leptin levels among hypothyroid patients [9–12], there are studies reporting low [13–16] or high [17–19] levels of leptin as well. Similarly, low [10, 13], normal [20], and high [18] resistin levels have been reported in hypothyroid cases. Resistin levels among these patients did not change with treatment for hypothyroidism [13, 20].

One study demonstrated that, among patients with known vascular disorders, high TSH levels within normal TSH ranges are associated with increased VAT [21]. Another study reported that epicardial adipose tissue (EAT) is increased among SH patients [22]. Another study analyzed fatty tissue changes after treatment in SH patients and evaluated fatty tissues throughout the entire body [23]. Therefore, we aimed to identify the changes in VAT, as it is the predominant adipose tissue compartment that produces various proinflammatory cytokines and adipokines, leptin, and resistin, with treatment compared to pretreatment levels in SH patients.

Methods and materials

Study population

Fifty-one patients who presented at the Endocrinology Clinic of Ankara Numune Training and Research Hospital and received SH diagnosis were included in the study. TSH measurements were conducted at the same time of day, in the morning, and blood was drawn sequentially on two different days. The etiology of hypothyroidism was autoimmune thyroiditis in 90.1% of the patients. None of them had any known or suspected cardiovascular disease, based on their clinical histories and laboratory evaluations, such as electrocardiography and echocardiography, nor had any taken any thyroid medications. A total of 43 age- and gender-matched healthy subjects with no thyroid dysfunctions were enrolled. The institutional Ethics Committee approved the study, and informed consent was obtained from all subjects enrolled. Body mass index (BMI) was calculated by dividing subjects' weight in kilograms by the square of their height in meters. Treatment with L-thyroxine was started in patients with dyslipidemia, obesity, planned pregnancy, goiter, or hypothyroidism. L-thyroxine of 25–50 μg/day was started, and the dose was adjusted by monthly TSH controls. Euthyroidism was provided with an average dose of 50–75 μg of L-thyroxine. Our study was designed prospectively. Measurements were repeated in the SH group 3 months after achieving euthyroid levels.

Biochemical analyses

Thyroid function tests: the Abbott Architect 2000 device and chemiluminescence micro-particle immunoassay approach were used to detect free triiodothyronine (fT3), freeT4 (fT4), and TSH concentrations. Patients with TSH levels between 4.0–10 mIU/mL with normal fT4 values are accepted to have SH [24].

Serum lipids: Serum lipids are measured by enzymatic calorimetric method. Low-density lipoprotein-cholesterol (LDL-C) is calculated with the Friedwald formula.

Plasma glucose and insulin: Plasma glucose is measured with a spectrometric analyzer using the glucose oxidase method, and insulin levels are measured with immunoradiometric assay (Immunotech IRMA, Czech Republic) (intra-assay coefficient of variation (CV) 4.3%, inter-assay CV 3.4%). Insulin sensitivity upon homeostasis model assessment (HOMA) is calculated as "fasting plasma glucose (mmol/l) × fasting plasma insulin]/22.5" [25].

High sensitivity C-reactive protein (hsCRP): HsCRP concentrations were determined using the Behring BN100 and the N hsCRP reagent (Dade-Behring, Mississauga, Ontario, Canada).

Leptin and resistin levels: Venous blood samples were collected in vacutainer tubes and centrifuged at 1300 g for 10 min. Sera were separated and stored at –20 °C until analysis. Human leptin and resistin levels were determined quantitatively by enzyme-linked immunosorbent assay (ELISA) with an ELISA microplate strip washer (ELX50; BioTek Instruments, USA) and ELISA microplate reader (Chromate; Awareness Technology, USA). Human resistin concentrations were determined with an eBioscience ELISA kit (Bender MedSystems GmbH; Austria). Intra- and inter-assay precisions were 5.1 and 8.1% for resistin, respectively. Leptin concentrations were measured with a DRG ELISA kit (DRG Instruments GmbH, Germany). The range of the assay was 1.0–100 ng/mL.

Mean intra- and inter-assay precisions were 6.43 and 10 %, respectively.

Measurements of visceral and subcutaneous fat

Ultrasonography (Toshiba Aplio Ultrasound Imaging System, Japan) was performed independent of a fasting state, and visceral fat was measured at the end of a normal exhalation in the supine position. For each patient, a total of four measurements were obtained as follows: (i) the distance between the internal surface of the splenic vein and the abdominal muscle, (ii) thickness of the fat layer of the posterior right renal wall in the right posterior perinephric space, (iii) distance between the internal surface of the abdominal muscle and the posterior wall of the aorta on the umbilicus, (iv) the thickness of preperitoneal and subcutaneous fat layers in the xiphoid process [4]. The visceral fat volume was calculated by using the following equation: "[visceral fat volume] = [−9.008] + [1.191 × distance between the internal surface of the abdominal muscle and the splenic vein (mm)] + [0.987 × distance between the internal surface of the abdominal muscle and the posterior wall of the aorta on the umbilicus (mm)] + [3.644 × thickness of the fat layer of the posterior right renal wall (mm)]"[4]. A 3.75-MHz convex-array probe was used to measure each parameter except the thickness of both the subcutaneous and the preperitoneal fat layers, which was measured using a 7.5-MHz linear-array probe by performing a longitudinal scan. The procedures were performed by two radiologists with similar levels of experience.

Measurement of carotid artery intima-media thickness

All SH patients and control subjects received one measurement of the intima-media thickness (IMT) of the carotid arteries. This was measured by ultrasound in the supine position and by the same experienced investigator. High-resolution B-mode ultrasound images (Loqic 3, General Electric, USA) with an 11-MHz linear array transducer were obtained for IMT measurement. Three arterial wall segments in each carotid artery were imaged from a fixed lateral transducer angle at the far wall. The mean IMT over the three segments of both carotid arteries was calculated and designated as the mean IMT.

Statistical analyses

Analyses of the data were performed using Statistical Package for Social Sciences (SPSS) for Windows 20 software (Chicago, IL). Definitive statistics were expressed as mean ± standard deviation or median (minimum–maximum) for continuous variables, and they were shown as the number of cases and percent for categorical variables. Chi-square tests were used to assess the statistical significance of differences between groups in the frequency distribution of categorical variables, unless the expected cell size was less than five when Fisher's exact test was used. Medians were compared by using the Mann–Whitney U test when the number of independent groups was two. Differences between the medians of more than two groups were evaluated by using the Kruskal–Wallis test. To evaluate the correlation between the parameters, we used the Spearman correlation. Multivariate logistic regression analyses were performed in order to evaluate whether factors that are considered to be effective on visceral adipose tissue were statistically significant or not. A p-value less than 0.05 was considered statistically significant.

Results

Clinical and laboratory characteristics of the study population are presented in Table 1. In all, 51 patients were diagnosed with SH. Their mean age was 36.9 ± 10.6 years, and most of the subjects were female. The mean age of the control subjects was 34.9 ± 8.4 years, and the gender distribution was similar to that of the SH group. While TSH ($p<0.01$), hsCRP ($p=0.011$), carotid artery IMT (mm) ($p<0.01$), leptin ($p<0.01$), and resistin ($p<0.01$) levels were significantly higher in the SH group compared to the control group, fT4 ($p<0.01$) levels were significantly lower. No significant correlation was observed between pre-treatment TSH and the VAT volume ($r=0.292$, $p=0.76$), hsCRP ($r=0.110$, $p=0.511$), leptin ($r=0.207$, $p=0.213$), and resistin ($r=0.105$, $p=0.530$) levels. While VAT was positively correlated to age ($r=0.419$, $p<0.01$), waist circumference ($r=0.794$, $p<0.01$), antithyroid peroxidase (antiTPO) ($r=0.435$, $p<0.01$), and leptin ($r=0.515$, $p<0.01$) levels, there was a negative correlation between VAT and fT4 ($r=-0.416$, $p<0.01$). No correlation was determined between VAT and resistin ($r=0.004$, $p=0.980$) (Table 2). Age was observed to have a positive correlation with waist circumference and leptin ($r=0.345$, $p=0.034$; $r=0.549$, $p<0.01$, respectively), but it did not have a significant correlation with resistin.

No changes were observed in the subcutaneous fat tissue of the SH patients following L-thyroxin treatment compared to pre-treatment values, though a significant decrease was observed in VAT (141.3 ± 44.7 vs. 130.7 ± 44.0 mm^3, $p=0.022$) (Table 3). While this decrease occurred in abdominal muscle-aorta distance fat distribution ($p<0.01$), no significant change was observed in the abdominal muscle-splenic vein distance ($p=0.09$) or the pararenal fat distribution ($p=0.452$). HsCRP ($p<0.01$), leptin ($p<0.01$), and resistin ($p=0.013$) levels in SH patients significantly improved after the treatment.

When analyzed after treatment, TSH was not correlated with VAT volume ($r=-0.351$, $p=0.140$), resistin ($r=0.221$, $p=0.182$), or leptin ($r=0.103$, $p=0.537$) levels. No correlation was observed between VAT volume and resistin ($r=0.138$, $p=0.409$), while VAT was correlated positively to leptin ($r=0.365$, $p=0.024$) and anti-TPO

Table 1 Clinical and laboratory characteristics of the study population

	Patients ($n=51$)	Control ($n=43$)	*P*-value
Age, years	36.9 ± 10.6	34.9 ± 8.4	0.427
Male/female	10/41	11/32	0.076
BMI, kg/m^2	26.1 ± 5.5	25.7 ± 4.2	0.715
Smoking (%)	29.4	20.9	0.477
HOMA-IR	1.81 ± 1.34	1.47 ± 0.88	0.224
Triglyceride (mg/dL)	111.9 ± 67.6	136.7 ± 42.0	0.07
HDL-cholesterol (mg/dL)	46.9 ± 14.9	49.1 ± 17.0	0.501
LDL- cholesterol (mg/dL)	114.3 ± 5.5	120.9 ± 48	0.366
fT4, ng/dL	0.8 ± 0.1	1.02 ± 0.2	<**0.01**
TSH, mU/L	6.2 ± 1.3	1.9 ± 0.8	<**0.01**
hs-CRP (mg/dL)	0.79 ± 0.3	0.49 ± 0.47	**0.011**
Carotid artery IMT (mm)	0.74 ± 0.3	0.47 ± 0.5	<**0.01**
Subcutaneous fat thickness (mm)	22.6 ± 7.6	24.9 ± 8.2	0.258
Abdominal muscle-splenic vein distance (mm)	40.0 ± 12.2	40.5 ± 7.3	0.313
Abdominal muscle-aorta distance (mm)	55.9 ± 19.6	48.1 ± 15.5	0.086
Para-renal fat thickness (mm)	13.0 ± 4.9	10.7 ± 5.0	0,07
Visceral fat volume (mm^3)	141.3 ± 44.7	125.8 ± 36.9	0.139
Leptin (ng/mL)	19.9 ± 9.6	10.5 ± 4.9	<**0.01**
Resistin (ng/mL)	5830.4 ± 2089.9	4072.1 ± 1523.2	<**0.01**

Variables are expressed as mean ± standard deviation
BMI body mass index, *HOMA-IR* homeostatic model of assessment-insulin resistance, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *T4* thyroxin, *TSH* thyroid stimulation hormone, *hs-CRP* high-sensitivity C-reactive protein, *IMT* intima-media thickness (A p-value less than 0.05 was considered statistically significant).

Table 2 Baseline visceral adipose tissue correlation table ($n=94$)

Variables	Visceral adipose tissue, mm^3	
	r	*p*
Age, years	0.419	<**0.01**
Waist circumference, cm	0.794	<**0.01**
TSH, mU/L	0.292	0.760
fT4, ng/dL	−0.416	<**0.01**
AntiTPO (IU/L)	0.435	<**0.01**
Leptin (ng/mL)	0.515	<**0.01**
Resistin (ng/mL)	0.004	0.980

TSH thyroid stimulating hormone, *T4* thyroxin, *TPO* thyroid peroxidase (A p-value less than 0.05 was considered statistically significant).

($r=0.451$, $p=0.004$), and negatively correlated to fT4 ($r=-0.351$, $p=0.03$).

In regression analyses, when the effect of baseline clinical and laboratory characteristics on visceral fat volume was assessed, waist circumference and triglycerides were found to be statistically significant (Table 4).

Table 3 Changes in adiposity markers and levels of adipokinine and lipid before and after treatment in the subclinical hypothyroid (SH) group

Variable	SH (before treatment) ($n=51$)	SH (after treatment) ($n=51$)	*P*-value
BMI, kg/m^2	26.1 ± 5.5	25.7 ± 4.2	0.789
Subcutaneous fat thickness (mm)	22.6 ± 7.6	21.8 ± 9.3	0.435
Abdominal muscle-splenic vein distance (mm)	40.0 ± 12.2	37.6 ± 13.3	0.099
Abdominal muscle-aorta distance (mm)	55.9 ± 19.6	50.6 ± 18.2	**0.005**
Pararenal fat thickness (mm)	13.0 ± 4.9	12.3 ± 6.0	0.452
Visceral fat volume (mm^3)	141.3 ± 44.7	130.7 ± 44.0	**0.022**
fT4, ng/dL	0.8 ± 0.1	1.2 ± 0.5	<**0.01**
TSH, mU/L	6.2 ± 1.3	2.3 ± 0.8	<**0.01**
Triglyceride (mg/dL)	111.9 ± 67.6	110.2 ± 42.4	0.752
LDL-cholesterol (mg/dL)	114.3 ± 5.5	110.8 ± 16.2	0.568
hs-CRP (mg/dL)	0.79 ± 0.3	0.58 ± 0.27	<**0.01**
Leptin (ng/mL)	19.9 ± 9.6	16.0 ± 9.3	<**0.01**
Resistin (ng/mL)	5830.4 ± 2089.9	5380 ± 2131	**0.013**

Variables are expressed as mean ± standard deviation
BMI body mass index, *T4* thyroxin, *TSH* throid stimulation hormone, *LDL* low-density lipoprotein, *hs-CRP* high-sensitivity C-reactive protein (A p-value less than 0.05 was considered statistically significant)

Discussion

This study found that the carotid artery IMT, hsCRP, leptin, and resistin levels were significantly higher in SH patients with no cardiovascular disease than in the control group. Though VAT volume was also higher than the control group, the difference was not statistically significant. However, we demonstrated that the VAT volume, hsCRP, leptin, and resistin levels significantly decrease after euthyroidism was achieved in the SH group. This is the first study, to our knowledge, that investigates the VAT change in SH patients after euthyroidism is achieved.

Abdominal obesity is known to increase VAT [1]. In line with this finding, we detected a positive correlation between VAT and waist circumference. SH was associated with increased coronary heart disease (CHD) prevalence [26, 27] and all-cause mortality independent of CHD risk factors [27]. Even though studies have revealed an association between SH and CHD and its related complications, the underlying pathological mechanisms are not well understood. Furthermore, there is a relationship between visceral adipose tissue and TSH levels. Abdominal adipose tissue is metabolically active by producing

Table 4 Effect of baseline clinical and laboratory characteristics on visceral fat volume ($n = 94$)

Coefficients[a]						
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	−97.509	57.429		−1.698	0.096
	Age, years	−0.023	0.446	−0.005	−0.053	0.958
	Gender	26.703	13.855	0.286	1.927	0.06
	BMI, kg/m^2	0.637	1.738	0.082	0.366	0.716
	Waist circumference, cm	1.898	0.656	0.549	2.891	*0.006*
	fT3, pg/ml	−4.027	9.269	−0.052	−0.434	0.666
	fT4, ng/dL	−7.256	23.079	−0.039	−0.314	0.755
	TSH, mU/L	0.899	2.704	0.052	0.333	0.741
	AntiTPO (IU/L)	0.036	0.019	0.207	1.871	0.068
	hs-CRP (mg/dL)	−9.559	9.659	−0.099	−0.99	0.328
	Resistin (ng/mL)	−0.002	0.002	−0.1	−0.899	0.374
	Leptin (ng/mL)	0.796	0.772	0.174	1.031	0.308
	Carotid artery IMT (mm)	15.794	17.243	0.099	0.916	0.364
	HOMA-IR	−1.358	3.825	−0.038	−0.355	0.724
	LDL-cholesterol (mg/dL)	−0.132	0.132	−0.093	−1.001	0.322
	Triglyceride (mg/dL)	0.161	0.068	0.238	2,369	*0.022*
	HDL-cholesterol (mg/dL)	0.323	0.245	0.126	1.318	0.194

BMI body mass index, *T3* triiodothyronine, *T4* thyroxin, *TSH* thyroid stimulation hormone, *TPO* thyroid peroxidase, *hs-CRP* high-sensitivity C-reactive protein, *IMT* intima-media thickness, *HOMA-IR* homeostatic model of assessment-insulin resistance, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein (A p-value less than 0.05 was considered statistically significant)

various adipokines and inflammatory cytokines involved in atherogenesis, atherothrombosis, and arterial plaque rupture [2, 28, 29]. Adipocytes express TSH receptors, and VAT proliferation can take place based on TSH expression in visceral and adipose tissue [30]. TSH may also be capable of increasing adipogenesis in embryonic stem cells [31]. A study has demonstrated that, even within the normal range, increase in TSH in women with no known history of CVD increased fatal coronary incidences [32]. Another study reported that increased TSH levels within the normal range increased visceral adipose thickness among patients over 66 years of age who have a history of vascular diseases [21]. In light of these studies, it can be said that TSH levels can increase in older age populations, which in turn increases the risk of CVD. A positive correlation was detected between age and VAT in this study. Because the mean age of the subclinical hypothyroid patients in this study are younger, we may have failed to observe a significant difference in VAT volume across patient and control groups, or a correlation between TSH and VAT. Similarly, Westerink et al. [21] have also failed to demonstrate a significant association between TSH and VAT among patients who were under 66 years of age.

While studies have reported that low fT4 levels were associated with coronary atherosclerosis [33] and that low fT4 levels were associated with increased pericardial fat tissue and VAT even in euthyroid patients, no association was observed between TSH and fat tissue compartments [34]. In this study, we have also failed to demonstrate an association between pre and posttreatment TSH and VAT, but determined a negative correlation between fT4 and VAT. This result suggests that low fT4 levels may increase VAT even when it is in normal reference ranges and leads to an increase in inflammation due to the increase in adipose tissue. Moreover, we also believe that autoimmunity may be responsible for the changes in the adipocyte functions observed in SH, as we detected a positive correlation between anti-TPO and VAT.

A recent meta-analysis (based on the Cochrane methodology) including 12 randomized, controlled trials of 6–14 months of duration showed that significant decreases in LDL-C levels were noticed only in the subgroup of patients with LDL-C values >155 mg/dl after L-thyroxine treatment [35]. As compared with those individuals with normal or near-normal lipid profiles, those with high lipid levels may have a greater lowering effect on their lipid levels with thyroid hormone treatment. We did not find a significant change in the lipid values of SH patients after treatment; their lipid values were similar to those of the control group. Increased values of carotid artery IMT have been reported in patients with SH compared with euthyroid individuals [36], though there is evidence suggesting a beneficial effect of levothyroxine replacement therapy on carotid artery IMT in subjects with SH [37, 38]. In this study BMI, smoking habits, and lipid profiles of the SH group were similar to those in the control group; carotid artery IMT and VAT volume, early indicators of atherosclerosis, were higher in the SH group than in the control group, but the difference was statistically significant for IMT only. After 3 months of euthyroidism was achieved, a significant decrease was observed in the VAT volume. Since the follow-up period was relatively short, we did not evaluate the change in IMT.

While there are studies reporting increased hsCRP levels among SH patients [39, 40], some studies also reported similar hsCRP levels as well [41–43]. In this study, we determined that hsCRP levels in the SH group were significantly higher than in the control group, and that significantly decreased after euthyroidism was achieved.

Prior studies reported normal, decreased, and increased leptin levels in hypothyroid patients [13]. There are also studies reporting L-thyroxin treatment to have caused increased [11, 44], not changed [45, 46], or lowered [17, 19, 23] leptin levels. We observed a significant decrease in leptin levels after euthyroidism was achieved. Study by Yildiz BO et al. demonstrated a decrease in leptin levels without a change in fat mass after euthyroid-

ism was achieved [23], but the fat mass was evaluated via Tanita scales; subcutaneous and adipose tissue were not measured separately in this study, which makes it likely that a failure to detect a decrease in the fat mass may be due to measurement methods. In our study, we separately examined the fat tissue and the VAT, which is the predominant adipose tissue compartment that produces various proinflammatory cytokines and adipokines, and observed that leptin levels, along with VAT, significantly decreased after treatment, while no change occurred in subcutaneous fat tissue. We identified a positive correlation between pre and posttreatment leptin and VAT volume. The posttreatment decrease in leptin levels is suggestive of a possible leptin resistance in SH patients. Leptin sensitivity may increase with the decrease in VAT volume.

Although resistin was first postulated to contribute to insulin resistance, it has recently been shown that resistin can trigger a proinflammatory state in vitro as well as in vivo [47]. Resistin's role in the inflammatory process is defined completely, but resistin has some features of the proinflammatory cytokines and plays a role in inflammation and immunity regulation irrespective of its role in insulin resistance [41, 48]. There are studies reporting increased [18], decreased [10, 13], and similar [20, 41] resistin levels in hypothyroid patients, compared to euthyroid individuals. In the present study, it was observed that resistin levels were higher in the SH group than in the control group without insulin resistance, and they significantly decreased following treatment. We did not detect a correlation between pre and posttreatment VAT and resistin. The changes in energy metabolism, even in SH status, may affect adipokine levels. The thyrotropin-releasing hormone (TRH)-TSH pathway affects fat metabolism through a complex interaction between hypothalamus, pituitary, thyroid, and adipose tissues [49]. Our results suggest that inflammation and related hsCRP and resistin levels increase in the case of SH; after euthyroidism is achieved, inflammation and related hsCRP and resistin levels decrease.

Limitations of the study

The duration of subclinical hypothyroidism can have an effect on both VAT and adipocytokine levels. One of the limitations of our study was the lack of knowledge of the patients' duration of subclinical hypothyroidism. In addition, the short follow-up time after achieving euthyroid levels may have restricted our ability to assess subjects' VAT and adipocytokine levels.

Conclusion

The conflicting results related to the relationship between the thyroid and adipocytokine noted in several studies may be related to gender and patient characteristics, the degree and duration of thyroid dysfunction, antibody concentrations, the metabolic effects of other hormones, and the possible effects of intermediate metabolism.

This study was designed prospectively, so that we could investigate the changes in VAT and adipokinine within the same patients who achieved euthyroidism following L-thyroxin treatment after an SH diagnosis. However, the small number of patients and the short follow-up period after achieving euthyroidism may not be sufficient to fully observe the changes in VAT.

Conflicts of interest

The authors have nothing to disclose.

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