DOI: 10.4274/tjem.2562

Thyroid-Stimulating Hormone, Triiodotyronine and Thyroxine Concentrations and Their Relationship with Metabolic Parameters, Anthropometric Variables and Body Composition in Premenopausal Euthyroid Obese Women

Premenopozal Ötiroid Obez Kadınlarda TSH, T3, T4 Düzeyleri ve Metabolik Parametreler, Antropometrik Değişkenler ve Vücut Kompozisyonu ile Olan İlişkisi

Mahdieh Abbasalizad Farhangi, Mohammadreza Eshraghian*, Seyyed Ali Keshavarz**, Ali Akbar Saboor-Yaraghi***

Tabriz University of Medical Sciences, Nutrition Research Center, Department of Community Nutrition, Tabriz, Iran
*Tehran University of Medical Sciences, Department of Public Health, Division of Biostatistics and Epidemiology, Tehran, Iran
**Tehran University of Medical Sciences, Department of Nutrition and Dietetics, Division of Clinical Nutrition, Tehran, Iran
***Tehran University of Medical Sciences, Department of Nutrition and Dietetics, Division of Cellular and Molecular Nutrition, Tehran, Iran

Abstract

Purpose: This study was performed to evaluate the potential relationships of thyroid hormones, metabolic parameters, and anthropometric variables with body composition in premenopausal women.
Material and Method: A total of 84 women with a mean age of 35.12±8.11 years were investigated. Subjects with a history of diabetes, hyperthyroidism and hypothyroidism, chronic liver, and renal disease were excluded from the study. In all subjects, anthropometric parameters were evaluated and body composition was analyzed by bioelectrical impedance analysis (BIA). Fasting serum thyroid-stimulating hormone (TSH), triiodothyrionine (T3), thyroxine (T4), fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), C-reactive protein (CRP), and interleukin 6 (IL-6) were measured by enzymatic methods. Serum low-density lipoprotein cholesterol (LDL-C) was determined by Friedewald formula.
Results: Serum TSH, CRP and TC levels in obese subjects were significantly higher than in non-obese subjects ($p<0.05$). Serum TSH concentration was positively associated with waist to hip ratio (WHR) and fat mass and, negatively associated with fat-free mass ($p<0.05$). There was also a positive relationship between T3 and TG and between T4 and LDL-C in all participants. In comparison of subjects with different body fat percentage, subjects with higher body fat had also higher amount of TSH concentrations ($p=0.015$).
Discussion: Our results showed a relationship of fat mass and lipid profile with thyroid function in premenopausal women. Further researches are needed to clarify the nature and mechanism of these relationships. *Turk Jem 2015; 19: 1-6*
Key words: Thyroid functions, lipid profile, fat mass, fat free mass

Conflicts of Interest: The authors reported no conflict of interest related to this article.

Özet

Amaç: Bu çalışma premenopozal kadınlarda, tiroid hormonları, metabolik parametreler, antropometrik değişkenler ve vücut kompozisyonu arasındaki olası ilişkiyi tanımlamak için yapılmıştır.
Gereç ve Yöntem: Bu çalışmada ortalama yaşı 35,12±8,11 olan 84 kadın incelenmiştir. Diyabet, hipertiroidi ve hipotiroidi, kronik böbrek veya karaciğer hastalığı olanlar dışlanmıştır. Tüm kişilerde antropometrik parametreler incelenmiş ve vücut kompozisyonu bioelektriksel impedans analizi (BİA) ile analiz edilmiştir. Açlık serum TSH, T3, T4, açlık kan şekeri (AKŞ), total kolesterol (TK), trigliserid (TG), HDL, CRP ve interlökin 6 (IL-6) düzeyleri enzimatik metod ile ölçülmüştür. LDL kolesterol Friedewald formulü ile hesaplanmıştır.
Bulgular: Obezlerde serum TSH, CRP ve TK non-obezlere göre anlamlı olarak yüksek bulunmuştur. Serum TSH düzeyi bel kalça oranı ve yağ kütlesi ile pozitif ve yağsız vücut kütlesi ile negatif korele bulunmuştur. Ayrıca T3 ve trigliserid düzeyi ve T4 ve LDL arasında dapozitif korelasyon saptanmıştır. Farklı vücut yağ yüzdesi olanlar karşılaştırıldığında, vücut kompozisyonunda daha fazla yağ saptanan hastaların daha yüksek TSH düzeyine sahip olduğu görülmüştür (p=0,015).

Address for Correspondence: Ali Akbar Saboor-Yaraghi PhD, Tehran University of Medical Sciences, Department of Nutrition and Dietetics, Division of Cellular and Molecular Nutrition, Tehran, Iran
Phone: +98 021 88774462 E-mail: asaboor@sina.tums.ac.ir **Received:** 14/04/2014 **Accepted:** 05/12/2014

Tartışma: Bizim çalışmamız yağ kütlesi, lipid profili ve tiroid fonksiyonu arasında premenopozal kadınlarda ilişki olduğunu göstermiştir. Bu ilişkilerin aydınlatılabilmesi için ileri araştırmalara gerek vardır. *Turk Jem 2015; 19: 1-6*
Anahtar kelimeler: Tiroid fonksiyonları, lipid profili, yağ kütlesi, yağsız vücut kütlesi

Çıkar Çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemiştir.

Introduction

Thyroid hormones are important regulatory factors involved in energy balance and adaptive thermogenesis (1,2); these hormones (T3, triiodothyronine; T4, thyroxine) increase basal metabolic rate and lipolysis, and suppress the thyroid-stimulating hormone (TSH) concentrations (3). Altered thyroid function is one of the major contributors in developing obesity (1,4). It has been shown that body weight decreases by 15% in hyperthyroidism and increases by 15-30% in hypothyroidism (1). The role of thyroid hormones in energy homeostasis was first described by Magnus Levy in 1895 (5). The underlying mechanisms explaining this role are increased consumption of adenosine triphosphate (ATP) (through some of the intracellular process, such as preserving ion gradients and substrate cycles) and decreased ATP synthesis (6). Thyroid hormones can also influence obesity by acting directly on fat mass (FM) via their nuclear receptors (3,7). It has been reported that thyroid hormones are in relationship with lipid profile; thyroid dysfunction is associated with lipid abnormalities and cardiovascular events (8,9). It has been shown that subclinical hypothyroidism (SCH) is in relationship with cardiovascular risk factors, such as increased low-density lipoprotein cholesterol (LDL-C) and decreased high-density lipoprotein cholesterol (HDL-C) concentrations (9). On the other hand, several reports have declared the possible role of inflammatory biomarkers, such as interleukin 6 (IL-6) (10,11) or C-reactive protein (CRP) (12) in thyroid hormones metabolism. Higher IL-6 concentrations are associated with higher amounts of TSH and lower concentrations of T3 (10).
Data regarding the relationship of thyroid hormones, obesity and lipid profile with proinflammatory cytokines are scarce and conflicting; most of the studies have been carried out in subjects with thyroid dysfunction (4,13), whereas, most cardiovascular events occur in subjects without severe thyroid dysfunction (14). Body weight and body mass index (BMI) were used as obesity indicators in almost all of these studies; whereas, BMI-based definition fails to take body fat into account (15). In the current study, we aimed to investigate the relationship of thyroid hormones with body composition, including FM and fat free mass (FFM), and lipid profile in premenopausal euthyroid women.

Materials and Methods

Participants

In this case-control study, 84 women with a mean age of 35.12±8.11 (mean ± SD) years were investigated; the study was carried out between 22 May and 23 July 2010. Subjects with BMI>30 kg/m^2 were classified as obese and those with BMI values <30 kg/m^2 were considered as non-obese. An informed written consent was obtained from the subjects before participating in the study and the study was approved by the ethics committee of Tehran University of Medical Sciences (TUMS). The exclusion criteria for participation in the study were: presence of diabetes, hyperthyroidism or hypothyroidism, chronic liver and renal disease, autoimmune disease and any other disease that might affect thyroid function. Subjects with a history of hormone replacement therapy, use of lipid-lowering agents, oral contraceptives, thyroid hormone therapy and any other drugs or supplements that might influence thyroid hormone, serum lipids and basal metabolic rate were excluded from the study. Inclusion criteria were: being Iranian, 20-52 years of age and BMI more than 30 kg/m^2 for obese and BMI less than 30 kg/m^2 for non-obese women.

Anthropometric Measurements

Weight was measured with a calibrated Seca scale (Itin Scale Co., Inc. Germany) with the precision of 0.1 kg. Height was measured by a cotton ruler which was attached to the wall. BMI was calculated as weight in kilograms divided by height in meters squared (16). Waist circumference (WC) was obtained by measuring the smallest area below the rib cage and above the umbilicus. Hip circumference (HC) was measured at the intertrochanteric level while the person was standing up (17). Body fat distribution was estimated by waist to hip ratio (WHR) by WC divided by HC. Body composition, including FM and FFM was measured by bioelectrical impedance analysis (BIA) with Human Im-Plus (Human-IM Plus; DS Dietosystem, Milan, Italy). Body composition measurement was performed while the subjects were fasted, have not exercised in the previous 4 to 6 hours, and have not consumed alcohol, caffeine or diuretics in previous 24 hours. The measurement was carried out after a 30-minute rest in room temperature and the measurement pads were attached to the right hand and foot. The subjects were asked to remove any metal jewelry to improve accuracy.

Biochemical Measurements

Serum samples were measured in the fasting state. Serum TSH, T3 and T4 were determined by enzyme-linked immunosorbent assay (ELISA-Pishtaz-Teb, Tehran-Iran). Mean inter and intra assay coefficients of variation (CV) for these tests were obtained as follows: TSH: 5.6 and 7.3 mIU/L, T3: 5.4 and 4.7 ng/mL and T4: 1.5 and 5 µg/mL. Our reference range for thyroid hormones are as follows: TSH: 0.3-3 mIU/L; T4: 64-160 nmol/L and T3: 1.3-3.2 nmol/L. Serum glutamic oxaloacetic transaminase (SGOT) and glutamic pyruvic transaminase (SGPT) were determined by enzymatic methods (Pars-Azmoon, Tehran-Iran). Mean inter and intra assay CV for these tests were 4.40, 3.25 and 3.08, 6.22 respectively. Total cholesterol (TC), triglyceride (TG) and HDL-C were analyzed by enzymatic colorimetric method (Pars-Azmoon, Tehran-Iran). Serum LDL-C was determined by Friedewald formula (18). Fasting blood glucose (FBG) was determined by glucose oxidase-peroxidase (GOD-POD) method using a kit (Pars-Azmoon, Tehran-Iran). Serum high-sensitivity C-reactive protein (hs-CRP) was measured by ELISA (DRG Instruments GmbH, Germany). The reference range for CRP levels was 0.068 to 8.2

mg/L. Mean inter and intra assay CVs for hs-CRP were <4.1% and <7.5%, respectively. Serum IL-6 concentrations were also assayed with ELISA method (e-Bioscience, San Diego, CA). Each assay was performed with recombinant IL-6 standards according to the manufacturer's protocol. This assay has a dynamic range from 2 to 200 pg/mL and a sensitivity of 4 pg/mL.

Statistical Analysis

All data were expressed as mean ± SD. The normality of data was tested by the Kolmogorov-Smirnov test. Comparison of variables between the groups was performed by independent Student's-t test or one-way ANOVA. Relationships between TSH, T3, T4 and other variables were analyzed by Pearson's correlation analysis. A multiple linear regression model was used for controlling the effect of confounding variables. A two-sided P value of less than 0.05 was considered statistically significant. All data were analyzed using SPSS software (version 17, SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics of the study subjects are shown in Table 1. Mean age and height were not significantly different between obese and non-obese subjects, however, other variables, including weight, BMI, WC, HC, WHR, and body composition parameters were significantly different between the groups. Serum TC, CRP and TSH levels in obese women were significantly higher than in non-obese women, whereas other biochemical parameters were not different (Table 2). In simple correlation analysis, TSH was positively correlated with WHR and FM (%) and negatively correlated with FFM (%) in all participants (Table 3); there was also a positive relationship between T3 and TG and between T4 and LDL-C in whole population. In categorization of subjects to obese and non-obese (Table 4), TSH was positively correlated with FM (%) and negatively correlated with FFM (%) in non-obese subjects. A positive relationship between T3 and TG in obese and between T3, TC, LDL-C and HDL-C in non-obese participants was also found. Using multiple linear regression models with TSH, T4 or T3 as dependent variables, and BMI, TC, HDL-C, LDL-C, TG, WHR, FM and FFM as independent variables, a positive relationship was found between WHR and TSH (β=0.28, p=0.049) and between LDL-C and T4 (β=0.3, p=0.049) (data not shown). Thyroid hormones concentrations based on body fat tertiles are shown in Table 5. Serum TSH concentrations in lowest body fat tertile was significantly lower compared with other groups (p=0.015).

Table 1. Subject characteristics

Characteristics	Obese (n=44)	Non-obese (n=40)	Total	p
Age (years)	36.66±6.01	34.13±7.74	35.12±8.11	0.183
Weight (kg)	83.45±8.28	62.35±9.03	73.40±13.65	<0.001
Height (m)	1.57±0.058	1.59±0.048	1.58±0.054	0.088
BMI (kg/m^2)	33.29±4.35	24.82±6.74	29.35±5.74	<0.001
WC (cm)	96.36±6.76	79.58±8.48	88.37±11.33	<0.001
HC (cm)	115.93±8.19	101.15±6.74	108.89±10.55	<0.001
WHR	0.83±0.03	0.78±0.045	0.80±0.04	<0.001
Fat mass (%)	44.26±7.44	31.95±7.09	38.40±9.52	<0.001
Fat mass (kg)	37.06±10.30	20.36±6.95	29.11±12.17	<0.001
Fat free mass (%)	55.49±7.68	67.99±7.17	61.44±9.70	<0.001
Fat free mass (kg)	44.97±4.53	41.64±3.68	43.38±4.45	<0.001

BMI: Body mass index, WC: waist circumference, HC: hip circumference, WHR: waist to hip ratio, Data are presented as mean ± SD.

Discussion

According to our results, obese women have higher TSH concentrations. Serum TSH was also positively associated with percentage of FM and negatively associated with percentage of FFM in our study. Our results were in accordance with the previous findings of a large population-based study performed in Nepalese population (17); a significant positive correlation was found between TSH concentrations and BMI (r=0.376, p=0.011). Similar findings in women have also been reported by Iacobellis et al. (19) and Kumar et al. (20). In the former study, obesity was defined as BMI≥30 kg/m^2 and in the latter, overweight and obese individuals (BMI range 25.7-44.3 kg/m^2) were enrolled in the study. On the other hand, several studies have not found any relationship between obesity and thyroid hormones (14).

Obesity is an independent risk factor for cardiovascular disease and several other causes of morbidity and mortality (21). BMI is the most used measure of obesity because of its simplicity (22), however, a BMI-based definition of obesity fails to take body fat distribution into account (15). In the present study, we found a positive association between FM and TSH concentrations

Table 2. Biochemical variables (mean ± SD) in study subjects

Characteristics	Obese (n=44)	Non-obese (n=40)	Total	p
FBG (mmol/L)	4.32±1.16	4.16±0.94	4.27±0.97	0.091
TC (mmol/L)	4.30±1.08	3.84±0.74	4.08±0.95	0.032
TG (mmol/L)	1.62±0.64	1.27±0.46	1.45±0.58	0.311
LDL-C (mmol/L)	2.11±0.89	1.91±0.60	2.01±0.76	0.257
HDL-C (mmol/L)	1.44±0.25	1.34±0.23	1.39±0.24	0.072
TSH (mIU/L)	3.80±2.65	2.45±1.47	3.30±2.37	0.029
T3 (nmol/L)	1.94±0.40	1.84±0.50	1.90±0.45	0.312
T4 (nmol/L)	125.71±29.63	121.65±22.75	123.78±26.50	0.486
SGOT (U/L)	20.00±8.50	18.00±0.94	19.00±8.00	0.205
SGPT (U/L)	17.00±10.50	18.00±7.00	19.00±7.75	0.641
IL-6 (pg/mL)	30.18±20.00	28.97±27.63	20.57±31.40	0.388
CRP (mg/L)	9.64±5.08	7.51±4.23	8.59±4.77	0.027

FBG: Fasting blood glucose, TC: total cholesterol, TG: triglyceride, LDL-C: low density lipoprotein cholesterol, TSH: thyroid stimulating hormone, T3: triidothyronie, T4: thyroxine, HDL-C: HDL-cholesterol, SGOT: serum glutamic oxaloacetic trans aminase, SGPT: serum glutamic pyrovic trans aminase, IL-6: interleukin 6, CRP: c-reactive protein

(r=0.27, p=0.028). There was also a significant difference in TSH concentrations between the three groups of subjects categorized based on body fat (p=0.015).

In previous reports on adult obese subjects, thyroid hormone and TSH concentrations have been described as normal, elevated or reduced, compared to a control group; increased T3 concentrations has been attributed to increased deiodinase activity and increased conversion of T4 to T3 as a defensive mechanism for preventing FM accumulation by increasing resting energy expenditure (23).

Adipose tissue, the most important compartment of FM, is an endocrine organ with numerous biochemical and metabolic functions (24). Alterations in endocrine roles of adipose tissue are occurred in thyroid dysfunction (25,26,27). Among the adipose tissue hormones, leptin, resistin and adiponectin have regulatory roles in thyroid hormones secretion (25,28). It seems that increased TSH concentrations and changes in body weight and thermogenesis in obesity partly can be explained by alterations in theses hormones secretions (25,26,27). It has also been reported that thyroid hormones prevent FM accumulations by acting directly on adipose tissue via thyroid hormone receptor α and β (3). Another possible mechanism is weakness in target cells receptors in responding to TSH, very similar to that in insulin resistance in type 2 diabetes (29). Additionally, TSH production is regulated by transmitters and hormones which regulate body weight and satiation, such as neuropeptide Y, melanocyte-stimulating hormone (MSH) and agouti-related peptide (30).

In the current study, serum T4 levels were not different between obese and non-obese individuals; it seems that a moderate increase in serum TSH concentrations in obesity is not associated with alterations in serum T4 concentrations and, according to previous reports, serum T4 concentration is independent of body weight status (2).

In this study, we did not find any relationship between TSH and FM or BMI in the obese group. This inconsistency may stem from limiting the obese group to subjects with BMI 30-35 kg/m^2 with excluding morbid obese subjects. Additionally, these relationships were observable in the total population and, when dividing subjects into two groups with lower sample size, they lost their significance in the obese group. Therefore, low sample size of subgroups might be responsible from these findings.

Serum T3 concentrations were positively associated with TC, LDL-C and HDL-C in the non-obese group. Consistent with our findings,

Table 3. Pearson correlation coefficients of thyroid hormones with anthropometric and metabolic parameters in total participants

	TSH		T3		T4	
	r	p	r	p	r	p
WHR	0.32	0.033	0.079	0.925	0.064	0.114
TC (mmol/L)	0.002	0.525	0.21	0.025	0.191	0.369
LDL-C (mmol/L)	0.006	0.856	0.163	0.365	0.23	0.034
TG (mmol/L)	0.051	0.096	0.214	0.042	0.024	0.069
Fat mass (%)	0.27	0.028	0.173	0.369	0.028	0.069
Fat free mass (%)	-0.26	0.011	-0.182	0.968	-0.04	0.693
Fat mass (kg)	0.26	0.049	0.177	0.112	0.08	0.112

WHR: waist to hip ratio, TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, TG: triglyceride, TSH: thyroid stimulating hormone, T3: triidothyronie, T4: thyroxine

Table 4. Pearson correlation coefficients of thyroid hormones with anthropometric and metabolic parameters in obese and non obese subjects

	TSH		T3		T4	
	Obese (n=44) r (p)	Non-obese (n=40) r (p)	Obese (n=44) r (p)	Non-obese (n=40) r (p)	Obese (n=44) r (p)	Non-obese (n=40) r (p)
TC (mmol/L)	-0.03 (0.069)	-0.045 (0.256)	-0.04 (0.852)	0.502 (0.002)	0.157 (0.369)	0.223 (0.985)
LDL-C (mmol/L)	-0.023 (0.235)	0.073 (0.547)	0.04 (0.369)	0.425 (0.009)	0.195 (0.159)	0.245 (0.958)
HDL-C (mmol/L)	-0.098 (0.265)	-0.032 (0.069)	-0.353 (0.049)	0.403 (0.003)	-0.078 (0.247)	0.153 (0.658)
TG (mmol/L)	0.034 (0.365)	-0.118 (0.258)	0.257 (0.036)	0.124 (0.958)	0.05 (0.369)	-0.101 (0.158)
Fat mass (%)	0.187 (0.689)	0.462 (0.025)	0.202 (0.639)	0.07 (0.147)	0.053 (0.548)	-0.153 (0.098)
Fat free mass (%)	-0.001 (0.365)	-0.454 (0.036)	-0.212 (0.968)	-0.08 (0.258)	-0.071 (0.264)	0.147 (0.258)
CRP (mg/L)	-0.38 (0.033)	0.041 (0.954)	0.012 (0.214)	-0.15 (0.789)	0.081(0.954)	-0.005 (0.361)

TC: total cholesterol, LDL-C: low density lipoprotein cholesterol, HDL-C: high density lipoprotein cholesterol, TG: triglyceride, CRP: c-reactive protein, TSH: thyroid stimulating hormone, T3: triidothyronie, T4: thyroxine

Table 5. Thyroid hormones in subject groups based on body fat tertiles (%)

	Body fat (%)			p
	<35.5% (n=28)	35.5-42.5% (n=28)	42.5% < (n=28)	
TSH (mIU/l)	1.89±0.85	4.07±3.14	3.55±1.94	0.015
T3 (nmol/L)	1.78±0.52	1.91±0.44	2.00±0.37	0.901
T4 (nmol/L)	122.77±26.53	122.03±27.82	126.53±25.87	0.348

TSH: thyroid stimulating hormone, T3: triidothyronie, T4: thyroxine

Park et al. (14) found a close relationship of TSH with diastolic blood pressure, LDL-C and TG in euthyroid women. In a study by Kumar et al. (20), T3 positively correlated with TG, LDL-C, TC, insulin and in a negatively correlated with body fat. According to previous reports, hypothyroidism is associated with elevated LDL-C and low HDL-C, as suggested by Kumar et al. (20) with findings similar to our results; this inconsistency could be due to sample being derived from obese females and not from general population as well as small sample size. Changes in lipid profile in thyroid dysfunction is due to decreased fractional clearance of LDL by a reduced number of LDL receptors in the liver and decreased receptor activity and reduced removal rate of triglyceride by the liver which are also operative in euthyroid state (31).

Our study has several limitations: due to the case-control nature of the study, we could not explain the cause-and-effect relationship between variables; in other word, it is not clear for us whether thyroid dysfunction is a result of FM accumulation or vice versa. We did not evaluate the free fractions of thyroid hormones; we also did not evaluate dietary intake of calorie, iodine or other nutrients.

Another important issue is the possible link between thyroid hormone, obesity and inflammation (3,29). In human, infusion of pro-inflammatory cytokines decreases serum T3 concentrations and signals for higher serum TSH levels (10,11). In our study, TSH was negatively associated with CRP in obese individuals. There are conflicting reports about the association of SCH and CRP in previous studies. Christ-Crain and colleagues (32) found elevated levels of CRP in patients with SCH, however, several recent studies have reported that increased CRP levels were not associated with SCH (33,34). Besides, we did not observe any associations between serum IL-6 concentrations and thyroid hormones in the current study. Stourthard et al. have identified IL-6 as a major stimulator of thyroid hormone synthesis and concluded that IL-6 administration induces a transient increase in T3 and T4 concentrations (10). It seems that in individuals with highest IL-6 concentrations, higher prevalence of abnormal thyroid hormones is expected (11). These findings were obtained in patients with certain chronic diseases such as renal disease and heart failure. The difference between their findings and ours might stem from this point. Further studies are needed to investigate the association of thyroid dysfunction with dietary status, low-grade inflammation and presumably adipokines, as discussed earlier.

In conclusion, we found the relationship of thyroid function with FM and lipid profile in premenopausal women. Further researches are needed to clarify the nature and mechanism of these relationships.

Acknowledgement

This work was supported by a grant from Research Undersecretary of Tehran University of Medical Sciences. We thank all of the participants in this study. We would also like to acknowledge the cooperation of Dr. John Raynes for edition of the article.

References

1. Krotkiewski M. Thyroid hormones in the pathogenesis and treatment of obesity. Eur J Pharmacol 2002;440:85-98.
2. Reinehr T. Obesity and thyroid function. Mol Cell Endocrinol. 2010;316:165-17..
3. Villicev CS, Freitas FRS, Aoki MS, Taffarel C, Scanlan TS, Moriscot AS, Ribeiro MO, Bianco AC, Gouveia CH. Thyroid hormone receptor β-specific agonist GC-1 increases energy expenditure and prevents fat-mass accumulation in rats. J Endocrinol 2007;193:21-29.
4. Tagliaferri M, Berselli ME, Cala G, Minocci A, Savia G, Petroni ML, Viberti GC, Liuzzi A. Subclinical hypothyroidism in obese patients: relation to resting energy expenditure, serum leptin, body composition, and lipid profile. Obes Res 2001;9:196-201.
5. Magnus-Levy A. Ueber den respiratorischen gaswechsel unter einfluss de thyroidea sowie unter verschiedenen pathologische zustand. Berlin Klin Wochschr 1895;32:650-652.
6. Leijendekker W, Van Hardeveld C, Elzinga G. Heat production during contraction in skeletal muscle of hypothyroid mice. Am J Physiol 1987;253:214-220.
7. Viguerie N, Millet L, Avizou S, Vidal H, Larrouy D, Langin D. Regulation of human adipocyte gene expression by thyroid hormone. J Clin Endocrinol Metab 2002;87:630-634.
8. Benvenga S, Robbins J. Lipoprotein-thyroid hormone interactions. Trends Endocrinol Metab 1993;4:194-198.
9. Althaus BU, Staub JJ, Ryff-De Lèche A, Oberhänsli A, Stähelin HB. LDL/HDL changes in subclinical hypothyroidism: possible risk factors for coronary heart disease. Clin Endocrinol 1988;28:157-163.
10. Stouthard JM, van der Poll T, Endert E, Bakker PJ, Veenhof CH, Sauerwein HP, Romijn JA. Effects of acute and chronic interleukin-6 administration on thyroid hormone metabolism in humans. J Clin Endocrinol Metab 1994;79:1342-1346.
11. Abozenah H, Shoeb S, Sabry A, Ismail H. Relation between thyroid hormone concentration and serum levels of interleukin-6 and interleukin-10 in patients with nonthyroidal illness including chronic kidney disease. Iran J Kidney Dis 2008;2:16-23.
12. Jublanc C, Bruckert E, Giral P, Chapman MJ, Leenhardt L, Carreau V, Turpin G. Relationship of circulating C-reactive protein levels to thyroid status and cardiovascular risk in hyperlipidemic euthyroid subjects: low free thyroxine is associated with elevated hs-CRP. Atherosclerosis 2004;172:7-11.
13. Meier C, Staub JJ, Roth CB, Guglielmetti M, Kunz M, Miserez AR, Drewe J, Huber P, Herzog R, Müller B. TSH-controlled L-thyroxine therapy reduces cholesterol levels and clinical symptoms in subclinical hypothyroidism: a double blind, placebo-controlled trial (Basel Thyroid Study). J Clin Endocrinol Metab 2001;86:4860-4866.
14. Park HT, Cho GJ, Ahn KH, Shin JH, Hong SC, Kim T, Hur JY, Kim YT, Lee KW, Kim SH. Thyroid stimulating hormone is associated with metabolic syndrome in euthyroid postmenopausal women. Maturitas 2009;62:301-305.
15. Eckel R, Krauss R. American Heart Association Call to Action: Obesity as a major risk factor for coronary heart disease. Circulation 1998;97:2099-2100.
16. Abbasalizad Farhangi M, Ghaemmagami SJ, Ostadrahimi A. The Relationship between serum parathyroid hormone level, nutritional status and body composition in obese and non-obese reproductive age women. Medical Journal of Tabriz University of Science 2008;30:119-124.
17. Nagila A, Bhatt M, Poudel B, et al. Thyroid stimulating hormone and its correlation with lipid profile in the obese Nepalese population. J Clin Diag Res. 2008; 2:932-937.
18. Friedewald W, Levy R, Fredrickson D. Estimation of the concentration of LDL cholesterol in plasma without use of preparative ultracentrifuge. Clin Chem 1972;18:499-502.
19. Iacobellis G, Ribaudo MC, Zappaterreno A, Iannucci CV, Leonetti F. Relationship of thyroid function with body mass index, leptin, insulin sensitivity and adiponectin in euthyroid obese women. Clin Endocrinol 2005;62:487-491.
20. Kumar H, Yadav R, Prajapati J, Reddy CV, Raghunath M, Modi KD. Association between thyroid hormones, insulin resistance, and metabolic syndrome. Saudi Med J 2009;30:907-911.
21. Farhangi MA, Saboor-Yaraghi A.A., Eshraghian M, Ostadrahimi A, Keshavarz SA Serum transforming growth factor β (TGF-β) is associated with body mass index in healthy women. Acta Endocrinologica (Buc) 2013;9:361-368.
22. Taylor RW, Keil D, Gold EJ, Williams SM, Goulding A. Body mass index, waist girth, and waist-to-hip ratio as indexes of total and regional adiposity in women: evaluation using receiver operating characteristic curves. Am J Clin Nutr 1998;67:44-49.
23. Longhi S, Radetti G. Thyroid Function and Obesity. J Clin Res Pediatr Endocrinol 2013;5:40-44.

24. Abbasalizad Farhangi M, Keshavarz SA, Eshraghian M, Ostadrahimi A, Saboor-Yaraghi AA. White blood cell count in women: relation to inflammatory biomarkers, Haematological Profiles, visceral Adiposity, and other cardiovascular risk factors. J Health Popul Nutr 2013;31:58-64.
25. Yaturu S, Prado S, Grimes SR. Changes in adipocyte hormones leptin, resistin, and adiponectin in thyroid dysfunction. J Cell Biochem 2004;93:491-496.
26. Zimmermann-Belsing T, Dreyer M, Holst J, Feldt-Rasmussen U. The relationship between the serum leptin concentrations of thyrotoxic patients during treatment and their total fat mass is different from that of normal subjects. Clin Endocrinol 1998;49:589-595.
27. Yoshida T, Monkawa T, Hayashi M, Saruta T. Regulation of expression of leptin mRNA and secretion of leptin by thyroid hormone in 3T3-L1 adipocytes. Biochem Biophys Res Commun 1997;232:822-826.
28. Cabanelas A, Cordeiro A, Almeida NA, Monteiro de Paula GS, Coelho VM, Ortiga-Carvalho TM, Pazos-Moura CC. Effect of triiodothyronine on adiponectin expression and leptin release by white adipose tissue of normal rats. Horm Metab Res 2010;42:254-260.
29. Kvtny J. Nuclear thyroxine receptors and cellular metabolism of thyroxine in obese subjects before and after fasting. Horm Res 1985;21:60-65.
30. Mihály E, Fekete C, Tatro JB, Liposits Z, Stopa EG, Lechan RM. Hypophysiotropic thyrotropin-releasing hormone-synthesizing neurons in the human hypothalamus are innervated by neuropeptide Y, agouti-related protein, and alpha-melanocyte-stimulating hormone. J Clin Endocrinol Metab 2000;85:2596-2603.
31. Duntas L. Thyroid disease and lipids. Thyroid 2002;12:287-293.
32. Christ-Crain M, Meier C, Guglielmetti M, Huber PR, Riesen W, Staub JJ, Müller B. Elevated C-reactive protein and homocysteine values: cardiovascular risk factors in hypothyroidism? A cross-sectional and a double-blind, placebo-controlled trial. Atherosclerosis 2003;166:379-386.
33. Lee WY, Suh JY, Rhee EJ, Park JS, Sung KC, Kim SW. Plasma CRP, apolipoprotein A-1, apolipoprotein B and Lpa levels according to thyroid function status. Arch Med Res 2004;35:540-545.
34. Hueston WJ, King DE, Geesey ME. Serum biomarkers for cardiovascular inflammation in subclinical hypothyroidism. Clin Endocrinol 2005;63:582-587.