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Effects of thyroid autoimmunity on abdominal obesity and hyperlipidaemia

Wpływ chorób autoimmunologicznych tarczycy na rozwój otyłości brzusznej i hiperlipidemii

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Abstract

Background: Thyroid autoimmunity has been suggested as a risk factor for atherosclerosis independent of thyroid function in several studies. The aim of this study was to investigate whether thyroid autoimmunity had any effect on hyperlipidaemia, obesity and abdominal obesity independent of thyroid function.

Material and methods: 184 premenopausal female patients with Hashimoto's thyroiditis (HT) and 150 healthy premenopausal female volunteers as control group (CG) were included in the study. According to thyroid function status, the patients were divided into three subgroups: overt hypothyroid patients (ohp), subclinical hypothyroid patients (shp) and euthyroid patients (ep). Body mass index (BMI), waist to hip ratios, waist circumference (WC), and serum lipid levels of all the participants were determined. These parameters of ep were compared with those of ohp, shp and CG. Relationships among thyroid stimulating hormone (TSH), thyroid autoantibodies and lipid levels were investigated.

Results: There were no significant differences between serum total cholesterol and low density lipoprotein cholesterol (LDL-C) levels of ohp and ep with HT ($P = 0.18$, $P = 0.07$ respectively) and LDL-C levels of ep were higher than those of CG ($P = 0.03$, $P = 0.042$, respectively). Although TSH levels did not correlate with serum lipid levels, levels of anti-thyroid peroxidase antibody correlated with triglyceride levels and WCs (r = 0.158; $P = 0.013$, r = 0.128; $P = 0.048$ respectively) and negatively correlated with high density lipoprotein cholesterol (HDL-C) levels (r = –0.137; $P = 0.031$). Levels of anti-thyroglobulin antibody also correlated with triglyceride and nonHDL-C levels (r = 0.208; $P = 0.007$, r = 0.158; $P = 0.043$ respectively).

Conclusion: Thyroid autoimmunity may have some effects on hyperlipidaemia and abdominal obesity independent of thyroid function. **(Pol J Endocrinol 2011; 62 (5): 421–428)**

Key words: *autoimmune thyroiditis, atherosclerosis, hyperlipidaemia, abdominal obesity, LDL-C*

Streszczenie

Wstęp: Wyniki badań wskazują, że choroby autoimmunologiczne tarczycy są czynnikiem ryzyka miażdżycy, bez względu na czynność tego narządu. Celem badania było ustalenie, czy obecność chorób autoimmunologicznch tarczycy niezależnie od jej funkcji wpływa na rozwój hiperlipidemii, otyłości i otyłości brzusznej.

Materiał i metody: Do badania włączono 184 kobiet przed menopauzą z zapaleniem tarczycy typu Hashimoto (HT) i 150 zdrowych ochotniczek przed menopauzą, które stanowiły grupę kontrolną (CG). Chore podzielono na 3 podgrupy w zależności od stanu czynnościowego tarczycy: osoby z jawną niedoczynnością tarczycy (ohp), z bezobjawową niewydolnością tarczycy (shp) i osoby z eutyreozą (ep). U wszystkich uczestniczek badania określono wskaźnik masy ciała (BMI), wskaźnik talia/biodra, obwód talii i stężenia lipidów w surowicy. Powyższe parametry porównano między grupą ep i pozostałymi grupami (ohp, shp, CG). Zbadano zależności między stężeniem TSH, przeciwciał przeciwtarczycowych i stężeniami lipidów.

Wyniki: Nie stwierdzono istotnych różnic między stężeniami cholesterolu całkowitego i cholesterolu frakcji LDL między grupami ohp i ep (odpowiednio p = 0,18 i p = 0,07). Stężenia cholesterolu frakcji LDL w grupie ep były wyższe niż w grupie CG (odpowiednio p = 0,03 i p = 0,042). Stężenia TSH nie korelowały ze stężeniami lipidów w surowicy, jednak stwierdzono prostą zależność między stężeniami przeciwciał przeciw peroksydazie tarczycowej i stężeniami triglicerydów oraz obwodem talii (odpowiednio r = 0,158; p = 0,013, r = 0,128; p = 0,048) i odwrotną zależność między cholesterolem frakcji HDL (r = –0,137; p = 0,031). Stężenia przeciwciał przeciw tyreoglobulinie korelowały ze stężeniami triglicerydów i cholesterolu nie-HDL (odpowiednio r = 0,208; p = 0,007, r = 0,158; p = 0,043).

Wnioski: Choroby autoimmunologiczne tarczycy mogą wpływać na rozwój hiperlipidemii i otyłości brzusznej niezależnie od stanu czynnościowego tego narządu. **(Endokrynol Pol 2011; 62 (5): 421–428)**

Słowa kluczowe: *autoimmunologiczne zapalenie tarczycy, miażdżyca, hiperlipidemia, otyłość brzuszna, cholesterol frakcji LDL*

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Introduction

Hypothyroidism is a known common risk factor for obesity and hyperlipidaemia. Hashimoto's thyroiditis (HT) is the commonest cause of hypothyroidism [1–4]. But it is not clear if thyroid autoimmunity is a risk factor for obesity and hyperlipidaemia independent of thyroid function.

The involvement of thyroid autoimmunity in atherosclerosis as a risk factor for coronary heart disease independent of thyroid function has been suggested in some previous studies. Increased serum levels of circulating thyroid and/or other autoantibodies have often been observed in the atherosclerotic process [5–10].

In 1991, Volpe suggested that HT is predominantly a disorder of cell-mediated immunity that is manifested by a genetic defect in the suppressor T-cell function [11]. According to this hypothesis, in HT, helper (CD4) T cells are not suppressed because of the defective suppressor T cells, and therefore are able to produce various cytokines such as interferon (IFN)-γ, interleukin (IL)-2 and tumour necrosis factor (TNF)-α [12].

Recently, a study performed in mice determined that (IFN)-γ regulates fat inflammation and TNF-α promotes lipogenesis and induces lipolysis [13].

There are a few studies suggesting that thyroid autoimmunity is a risk factor for atherosclerosis independent of thyroid function. However in HT, T helper cells may not be suppressed and can produce some cytokines such as IFN-γ and TNF-α as suggested by Volpe [11]. These cytokines might cause weight gain, lipogenesis and lipolysis in humans as in mice, as suggested by Sultan [13].

Combining Volpe's hypothesis with Sultan's finding, it is possible that thyroid autoimmunity might cause weight gain and hyperlipidaemia independent of thyroid function.

In this study, we hypothesised that thyroid autoimmunity may have some effects on hyperlipidaemia, obesity and abdominal obesity independent of thyroid function.

With this aim, we investigated body mass index (BMI), waist circumference (WC), waist to hip ratio (WHR), rates of obesity and abdominal obesity and total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), and non-high density lipoprotein cholesterol (non-HDL-C) levels of euthyroid patients (ep) with Hashimoto's thyroiditis, and compared them with those of overt hypothyroid patients (ohp), subclinical hypothyroid patients (shp) and healthy subjects. We also examined if each one of those lipid parameters, BMIs, WCs and WHRs correlated with serum thyroid stimulating hormone (TSH), autoantibodies against thyroglobulin (TgAb) and thyroid peroxidase (TPOAb) concentrations separately in all the patients with HT.

Material and methods

The study included 184 premenopausal female patients with newly diagnosed and untreated HT and 150 healthy premenopausal female volunteers as the control group (CG). All CG subjects were matched for age with HT patients (Table I). This study was approved by our institutional ethics committee (approval date and number: 21.02.2008, 44/E) and the study subjects have therefore been recruited to the study in accordance with ethical standards announced in the 1964 Declaration of Helsinki. All the subjects in this study gave informed consent prior to their inclusion.

Lymphocytic infiltration of the thyroid gland is present up to 40% of healthy women [3, 14] and it is known that loss of oestrogen at the menopause causes an increase in serum LDL-C levels and weight gain [15]. Therefore, the present study was designed to include premenopausal women. Patients with liver disorders, renal disorders, congestive heart failure, diabetes mellitus, pregnant women, patients on oral contraceptive pills, fibrates and/or statins, steroids, thiazides, beta blockers, or with other medications that might alter or influence body weight, serum lipid levels or thyroid functions were excluded from the study. A diagnosis of HT was made in the presence of elevated antithyroid peroxidase and antithyroglobulin antibodies and ultrasound patterns suggestive of HT [2].

HT patients were classfied into three subgroups according to their thyroid function status. Overt hypothyroid patients (ohp, n = 51; 27.71%) were those with serum TSH > 10 uIU/mL (reference interval was 0.27–4.2 uIU/mL) and free T4 < 0.93 ng/dL (reference interval was 0.93–1.7 ng/dL).

Subclinical hypothyroid patients (shp, n = 49; 26.63%) were those with normal serum free T4 and free T3 levels but with high serum TSH levels.

Euthyroid patients (ep, n = 84; 54.34%) were those with HT but normal free T4 and TSH levels [3, 14].

BMI was calculated as body weight (kg) divided by height (m) squared [16] and obesity was defined as BMI of 30 or more (kg/m^2) [17, 18]. Waist and hip circumferences of all the patients were measured and waist to hip ratios (WHRs) were calculated.

Waist circumferences were measured at the plane between anterior superior iliac spines and lower costal margins at the narrowest part of the waistline while patients were standing during slight expiration [16–18]. For women, WC > 88 cm was accepted as abdominal obesity according to WC [19]. Hip circumferences were measured horizontally over the furthest points

of trochanters while standing with 20–30 cm distance between feet. A measure of WHR > 0.85 was accepted as abdominal obesity for women [17, 19].

Blood samples were taken following 12 hours of fasting, and immediately centrifuged (2,500 rpm) and the sera were separated. TC, HDL-C and TG levels were determined by enzymatic methods and LDL-C levels were determined using the Friedewald formula [20]. Those patients whose TG levels were higher than 400 mg/dL were excluded from the study as they might have limitation of the calculation of LDL-C levels [20]. Serum autoantibodies against thyroglobulin (TgAb) and thyroid peroxidase (TPOAb), TSH, free T3 and free T4 levels were measured by electrochemiluminescence immunoassay ECLIA (Modular Analytics E170; Roche Diagnostics). The normal ranges were 0–34 IU/mL for TPOAb levels and 0–115 IU/mL for TgAb levels.

Statistical analysis

All statistical analyses were made using SPSS 13.0. Normality of the distribution of variables was tested by Shapiro-Wilk and Kolmogorov-Smirnov tests. Waist circumference, total cholesterol, non-HDL cholesterol, HDL-C and LDL-C were compared by independent samples t — test in all hypothyroidism patients and control group, in ohp and control group, in shp and control group, and in ep and control group. The same parameters were compared by one-way analysis of variance (ANOVA) for more than two categories. TG, BMI, WHR, TSH, TPOAb and TgAb were compared by the Wilcoxon–Mann–Whitney U test in all hypothyroidism patients and control group, in ohp and control group, in shp and control group, and in ep and control group. The same parameters were compared by Kruskal Wallis test for groups with more than two levels. A factorial logistic regression was used when we had two or more categorical independent variables but a dichotomous dependent variable. Pearson's correlation coefficients among TSH, TPOAb, Tg Ab, BMI, WC, WHR, lipid parameters were determined using regression analyses. Data was reported as means ± SD. Significant differences were assumed for $p < 0.05$.

Results

Characteristics of all subjects are shown in Tables I–IV. Serum TC, LDL-C, TG and non-HDL-C levels of all the patients with HT were significantly higher than those of CG ($P = 0.01$, $P = 0.002$, $P = 0.001$, $P < 0.0001$, respectively) (Table I). Means of BMI and WC, rates of obesity and abdominal obesity according to WC, serum TC, LDL-C, TG and non-HDL-C levels of ohp were significantly higher than those of CG ($P = 0.026$, $P = 0.01$, $P = 0.013$, $P = 0.029$, $P = 0.01$, $P = 0.001$, $P = 0.001$, respectively) (Table II). We interestingly

Table I. *Comparison of the characteristics of patients with Hashimoto's thyroiditis [HT] and the control group*
Tabela I. *Porównanie parametrów między chorymi na zapalenie tarczycy typu Hashimoto (HT) i kobietami z grupy kontrolnej*

	Patients with HT (n = 184)	Control group (n = 150)	p
Age	35.48 ± 7.92	35.71 ± 7.85	NS
TSH [uIU/mL]	15.51 ± 44.88	1.69 ± 0.93	0.0005
TPOAb [IU/mL]	292.47 ± 361.7	11.7 ± 33.6	0.0005
TgAb [IU/mL]	461.22 ± 788.46	21.95 ± 43.38	0.0005
BMI	28.30 ± 6.21	27.98 ± 7.09	NS
Rate of obesity	60 [34.3%]	44 [29.7%]	NS
WC [cm]	88.89 ± 3.14	86.27 ± 14.80	NS
Rate of abdominal obesity according to WC	88 [53.3%]	66 [47.1%]	NS
WHR [cm]	0.809 ± 0.06	0.801 ± 0.7	NS
Rate of abdominal obesity according to WHR	47 [28.7%]	40 [28.6%]	NS
TC [mg/dL]	197.12 ± 38.96	184.79 ± 36.23	0.01
LDL-C [mg/dL]	129.55 ± 30.63	116.39 ± 28.57	0.002
HDL-C [mg/dL]	54.84 ± 13.09	56.19 ± 14.88	NS
TG [mg/dL]	118.20 ± 66.85	97.92 ± 58.95	0.001
non-HDL-C [mg/dL]	142.28 ± 36.40	128.60 ± 3413	< 0.0001

BMI — body mass index; WC — waist circumference; WHR — waist-to-hip ratio; TC — total cholesterol; LDL-C — low-density lipoprotein cholesterol; HDL-C — high-density lipoprotein cholesterol; TG — triglyceride; non-HDL-C — non-high-density lipoprotein cholesterol; NS — non-significant

Table II. *Comparison of the characteristics of overt hypothyroid patients [ohp] with Hashimoto's thyroiditis (HT) and control group*

Tabela II. *Porównanie parametrów między grupą chorych na zapalenie tarczycy typu Hashimoto (HT) z jawną niedoczynnością tarczycy (ohp) i grupą kontrolną*

	ohp with HT (n = 51)	Control Group (n = 150)	p
Age	35.75 ± 7.75	35.71 ± 7.85	NS
TSH [uIU/mL]	31.83 ± 31.47	1.69 ± 0.93	0.0005
TPOAb [IU/mL]	421.19 ± 551.99	11.70 ± 33.6	0.0005
TgAb [IU/mL]	574.48 ± 1016.6	21.95 ± 43.38	0.0005
BMI	30.34 ± 6.69	27.98 ± 7.09	0.026
Rate of obesity	26 [52%]	44 [29.7%]	0.013
WC [cm]	93.17 ± 13.35	86.27 ± 14.80	0.010
Rate of abdominal obesity according to WC	28 [68.3%]	66 [47.1%]	0.029
WHR [cm]	0.816 ± 0.72	0.801 ± 0.7	NS
Rate of abdominal obesity according to WHR	10 [24.4%]	40 [28.6%]	NS
TC [mg/dL]	202.53 ± 41.41	184.79 ± 36.23	0.01
LDL-C [mg/dL]	136.14 ± 33.55	116.39 ± 28.57	0.001
HDL-C [mg/dL]	51.52 ± 11.86	56.19 ± 14.88	NS
TG [mg/dL]	131.25 ± 73.66	97.92 ± 58.95	0.001
non-HDL-C [mg/dL]	151.31 ± 39.24	128.60 ± 3413	0.001

Table III. *Comparison of the characteristics of subclinical hypothyroid patients [shp] with Hashimoto's thyroiditis (HT) and control group*

Tabela III. *Porównanie parametrów między grupą chorych na zapalenie tarczycy typu Hashimoto (HT) z bezobjawową niedoczynnością tarczycy (shp) i grupą kontrolną*

	shp with HT (n = 49)	Control group (n = 150)	p
Age	35.94 ± 8.75	35.71 ± 7.85	NS
TSH [uIU/mL]	21.04 ± 77.66	1.69 ± 0.93	0.0005
TPOAb [IU/mL]	296.45 ± 312.92	11.7 ± 33.6	0.0005
TgAb [IU/mL]	603.36 ± 974.77	21.95 ± 43.38	0.0005
BMI	26.81 ± 5.81	27.98 ± 7.09	NS
Rate of obesity	12 [26.1%]	44 [29.7%]	NS
WC [cm]	86.27 ± 14.59	86.27 ± 14.80	NS
Rate of abdominal obesity according to WC	21 [47.7%]	66 [47.1%]	NS
WHR [cm]	0.802 ± 0.64	0.801 ± 0.7	NS
Rate of abdominal obesity according to WHR	10 [23.3%]	40 [28.6%]	NS
TC [mg/dL]	196.39 ± 41.03	184.79 ± 36.23	NS
LDL-C [mg/dL]	128.24 ± 33.02	116.39 ± 28.57	0.031
HDL-C [mg/dL]	54.02 ± 13.37	56.19 ± 14.88	NS
TG [mg/dL]	112.11 ± 62.72	97.92 ± 58.95	NS
non-HDL-C [mg/dL]	142.37 ± 40.07	128.60 ± 3413	NS

Table IV. *Comparison of the characteristics of euthyroid patients (ep) with Hashimoto's thyroiditis (HT) and control group*

Tabela IV. *Porównanie parametrów między grupą chorych na zapalenie tarczycy typu Hashimoto (HT) z eutyreozą (ep) i grupą kontrolną*

	ep with HT (n = 84)	Control group (n = 150)	p
Age	35.05 ± 7.58	35.71 ± 7.85	NS
TSH [uIU/mL]	2.38 ± 1.05	1.69 ± 0.93	0.0005
TPOAb [IU/mL]	212.77 ± 176.78	11.70 ± 33.60	0.0005
TgAb [IU/mL]	305.14 ± 378.74	21.95 ± 43.38	0.0005
BMI	27.88 ± 7.09	27.98 ± 7.09	NS
Rate of obesity	22 [27.8%]	44 [29.7%]	NS
WC [cm]	88.13 ± 11.77	86.27 ± 14.80	NS
Rate of abdominal obesity according to WC	39 [48.8%]	66 [47.1%]	NS
WHR [cm]	0.81 ± 0.58	0.801 ± 0.7	NS
Rate of abdominal obesity according to WHR	27 [33.8%]	40 [28.6%]	NS
TC [mg/dL]	194.17 ± 36.26	184.79 ± 36.23	NS
LDL-C [mg/dL]	126.27 ± 26.92	116.39 ± 28.57	0.0042
HDL-C [mg/dL]	57.56 ± 13.2	56.19 ± 14.88	NS
TG [mg/dL]	113.5 ± 64.31	97.92 ± 58.95	NS
non-HDL-C [mg/dL]	136.61 ± 31.39	128.60 ± 3413	NS

Table V. *Comparison of the characteristics of overt hypothyroid patients [ohp], subclinical hypothyroid patients (shp) and euthyroid patients (ep)*

Tabela V. *Porównanie parametrów między grupami chorych na zapalenie tarczycy typu Hashimoto (HT) z jawną niewydolnością tarczycy (ohp), bezobjawową niewydolnością tarczycy (shp) i eutyreozą (ep)*

	ohp (n = 51)	shp (n = 49)	ep (n = 84)	p
Age	35.75 ± 7.75	35.94 ± 8.75	35.5 ± 7.58	NS
TSH [uIU/mL]	31.83 ± 31.47	21.044 ± 77.66	2.38 ± 1.05	0.0005
TPOAb [IU/mL]	421.19 ± 551.99	296.45 ± 312.92	212.77 ± 176.78	0.001
TgAb [IU/mL]	574.48 ± 1016.61	603.36 ± 974.77	305.14 ± 378.74	NS
BMI	30.34 ± 6.69	26.81 ± 5.81	27.88 ± 7.09	0.03
Rate of obesity	26 (52%)	12 (26.1%)	22 (27.8%)	NS
WC [cm]	93.17 ± 13.35	86.27 ± 14.59	88.13 ± 11.77	0.04
Rate of abdominal obesity according to WC	28 (68.3%)	21 (47.7%)	39 (48.8%)	NS
WHR [cm]	0.816 ± 0.72	0.802 ± 0.64	0.81 ± 0.58	NS
Rate of abdominal obesity according to WHR	10 (24.4%)	10 (23.3%)	27 (33.8%)	NS
TC [mg/dL]	202.53 ± 41.41	196.39 ± 41.03	194.17 ± 36.26	NS
LDL-C [mg/dL]	136.14 ± 33.55	128.24 ± 33.02	126.27 ± 26.92	0.01
HDL-C [mg/dL]	51.52 ± 11.86	54.02 ± 13.37	57.56 ± 13.2	NS
TG [mg/dL]	131.25 ± 73.66	112.11 ± 62.72	113.5 ± 64.31	0.01
non-HDL-C [mg/dL]	151.31 ± 39.24	142.37 ± 40.07	136.61 ± 31.39	NS

determined that LDL-C levels of ep were significantly higher than those of CG ($P = 0.042$) (Table IV). LDL levels of shp were also significantly higher than those of CG ($P = 0.031$) (Table III). Contrary to expectations, TSH levels did not correlate with LDL-C levels in all the patients with HT (r = 0.045; $P = 0.551$). Total cholesterol, TG, nonHDL-C, and HDL-C levels did not correlate with TSH levels either (r = 0.039; $P = 0.606$, r = 0.063; $P = 0.399$, r = 0.044; $P = 0.554$, r = –0.008; $P = 0.914$ respectively). We surprisingly observed that serum TPOAb concentrations correlated with TG levels and WCs (r = 0.158; $P = 0.013$, r = 0.128; $P = 0.048$ respectively) and negatively correlated with HDL-C levels in all the patients with HT (r = –0.137; $P = 0.031$). Serum TgAb concentrations also correlated with TG and nonHDL-C levels in all the patients with HT (r = 0.208; $P = 0.007$, r = 0.158; $P = 0.043$ respectively). TSH levels correlated with TgAb levels (r = 0.187; $P = 0.015$), but did not correlate with TPOAb levels in all the patients with HT (r = 0.081; $P = 0.280$).

Serum TSH and TPOAb levels of ohp were significantly higher than those of ep ($P = 0.0005$, $P = 0.0005$, respectively), and those of shp ($P = 0.0005$, $P = 0.044$, respectively). However, there was no significant difference among TgAb levels of ohp, shp and ep ($P = 0.19$).

Body mass index, WC and rate of obesity of ohp were higher than those of shp ($P = 0.006$, $P = 0.023$, $P = 0.009$, respectively). Between ohp and shp, there was no significant difference concerning serum TC, LDL-C, HDL-C, TG and non-HDL-C levels, and rates of abdominal obesity according to WC and WHR. ($P = 0.40$, $P = 0.27$, $P = 0.37$, $P = 0.11$, and $P = 0.25$, $P = 0.054$, $P = 0.903$, respectively). Body mass index and WC and rates of obesity and abdominal obesity according to WC of ohp were significantly higher than ep ($P = 0.037$, $P = 0.035$, $P = 0.006$, $P = 0.039$, respectively). Serum TG and non-HDL levels of ohp were also higher than those of ep ($P = 0.04$, $P = 0.02$, respectively) and serum HDL-C levels of ep with HT were higher than those of ohp ($P = 0.02$). But there was no significant difference between serum TC and LDL-C levels of ohp and ep with HT ($P = 0.18$, $P = 0.07$ respectively).

Discussion

Unlike most previous studies, in the present study serum LDL-C levels of ep with HT were determined to be higher than those of healthy subjects and there was no significant difference between serum TC and LDL-C levels of ohp and of ep with HT. Not only ohp but also all the patients with HT had higher serum TC, LDL-C, TG, and non HDL-C levels compared to healthy subjects. There were no correlations between TSH and LDL-C levels or between TSH and other lipid parameters in all the patients with HT. However, TPOAb concentrations negatively correlated with HDL-C and positively correlated with TG levels and WCs in all the patients with HT. Serum TgAb concentrations also correlated with TG and nonHDL-C levels.

These findings suggest that thyroid autoimmunity may be associated with hyperlipidaemia independent of thyroid function, as suggested in the old studies by the Bastenie et al. [8–10]. Overt hypothyroidism (OH) is not only one of the causes of obesity but also a risk factor for atherosclerotic cardiovascular disease and hyperlipidaemia as well. Moreover, OH has been found to be associated with insulin resistance [21].

It is known that serum TC, LDL-C, TG, free fatty acid (FFA) levels and BMIs of ohp are higher than those of healthy subjects [3, 21–25]. Elevated levels of FFAs stimulate insulin secretion, placing a further burden on genetically compromised and stressed -cell function in individuals susceptible to type 2 diabetes. Furthermore, elevated FFAs have been reported to impair early insulin secretion, a characteristic B-cell abnormality in type 2 diabetes. In addition, increased flux of FFA to the liver increases hepatic gluconeogenesis and hepatic glucose output, adding to already existing abnormalities in hepatic glucose metabolism in type 2 diabetes [1]. Recently, it has been demonstrated that insulin resistance may modify the relationship between lipids and thyroid function and the association between elevated TSH and LDL-C levels varies depending on the degree of insulin sensitivity [26–31].

In the present study, BMI, WC, rates of obesity and abdominal obesity according to WC, serum TC, TG, LDL-C and non-HDL-C levels of ohp with HT were higher than those of healthy subjects, but there was no significant difference between HDL-C levels of ohp and those of healthy people.

Many studies have investigated the relationship between thyroid function and serum lipid levels and determined various findings. A large cross-sectional survey of 3,410 elderly subjects in Maryland noted significantly elevated LDL-C levels in subjects with subclinical hypothyroidism, but no increased frequency of diagnosed atherosclerotic disease could be found in the entire cohort of shp [32]. McDermott et al. found that overt hypothyroidism and also subclinical hypothyroidism (SH) lead to increased blood pressure and triglyceride levels and decreased HDL-C levels [33]. Canaris determined that shp had higher serum cholesterol levels than ep [34], and in another study it was observed that LDL-C levels were higher and HDL-C levels were lower in shp than those in healthy subjects [35].

A report from Rotterdam noted that shp actually had lower TC levels than controls, but manifested inc-

reased atherosclerotic cardiovascular disease [36], This finding suggests that some other factors contribute to the increased risk of atherosclerosis independent of serum TC levels [36]. In another large study, no difference could be determined between serum cholesterol levels of shp and those of healty subjects [37]. Uzunlulu et al. did not observe any difference between serum TG, HDL-C levels of 36 shp and of 190 healthy subjects [38]. Shantha et al. also could not determine any difference among serum TC, TG, HDL-C levels of 92 shp, 31 ohp and 406 healthy subjects [39].

In the present study, serum LDL-C levels of shp and ep were higher than healthy subjects. However, there was no significant difference between serum TC, TG, HDL-C and non-HDL-C levels of shp with HT and healthy people, and also between those of ep with HT and healthy subjects.

Contrary to the studies which determined the association between high TSH levels and hyperlipidaemia, another study has identified subclinical hypothyroidism as an independent risk factor for aortic atherosclerosis and myocardial infarction in elderly women [36].

In the present study, it was determined that TSH levels suprisingly did not correlate with LDL-C levels or other lipid parameters.

Based on the data, the association between overt hypothyroidism and cardiovascular disease or between subclinical hypothyroidism and cardiovascular disease may not be entirely explained by dyslipidaemia alone. The involvement of the immune system in atherosclerosis is mainly suggested by the presence of activated T cells within the atherosclerotic lesions and of circulating autoantibodies to plaque components. Two studies focused on the involvement of two major autoantigenic determinants in the atherogenic process, namely, the heat shock protein and oxi LDL-C [5, 6]. According to this view, after early activation of the immune system, the progression of the atherosclerotic lesions would be enhanced by focal secretion of cytokine and growth factor networks. In the framework of the above scenario, the increased serum levels of circulating thyroid and/or other autoantibodies are often observed in the elderly and reflect an ongoing autoimmune activation involved in the atherosclerotic process leading to increased risk of coronary heart disease. No direct support to this hypothesis has been provided. However, in one of the few studies addressing this question more directly, a significant correlation was found in humans between atherosclerotic lesions and circulating anti-hsp 65 antibodies, while in the same patients, the arterial damage was unrelated to serum thyroid and other autoantibodies [5, 7].

On the epidemiological basis, thyroid autoimmunity as a risk factor for coronary heart disease independent of thyroid function, as suggested by Bastenie et al. [8–10], has not been confirmed in more recent investigations [40].

Many studies determined that elevated serum lipid levels were associated with TSH elevations. In the HUNT study, the association of hypothyroidism with high serum lipids was linear across the entire reference range of TSH [41]. Tagami et al. determined positive correlation between serum TSH and lipid levels [42]. However, the Whickham study showed that elevated serum lipid levels were not associated with TSH elevations [43] and during the follow up of the Whickham survey, investigators found no association between elevated serum TSH and the increased risk of ischaemic heart disease or dyslipidaemia [44].

Complying with the Whickam study, in the present study, TSH levels did not correlate with serum lipid levels, BMI and WC. However, it was suprisingly found that TPOAb concentrations correlated with TG levels and WC and negatively correlated with HDL-C levels and TgAb concentrations correlated with TG and nonHDL-C levels. Besides, serum LDL-C levels of ep with HT were found to be higher than those of healthy subjects and there was no significant difference between serum TC and LDL-C levels of ohp and ep with HT. It was another notable finding in the study that there was no significant difference between TgAb levels of ohp and those of ep.

These findings support the idea that thyroid autoimmunity is a risk factor for hyperlipidaemia independent of the thyroid function.

It is not clear how thyroid autoimmunity affects obesity, abdominal obesity and serum lipid levels. However, in HT it is possible that increased IFN-γ and TNF-α may cause obesity and hyperlipidaemia without elevated TSH levels.

In conclusion, although overt hypothyroidism has more effect on hyperlipidaemia and obesity, thyroid autoimmunity may have some effects on hyperlipidaemia and abdominal obesity independent of thyroid function. Therefore it may be beneficial to determine the TC, LDL-C, HDL-C, TG, nonHDL-C levels and WCs of all patients with HT, even if they are euthyroid. Further studies are needed to investigate the relationships between thyroid autoantibodies and hyperlipidaemia and between thyroid autoantibodies and abdominal obesity.

Conflict of interest

The authors have disclosed that they have no significant relationships with, or financial interests in, any commercial company that pertains to this educational activity.

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