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The relationships between selected serum adipokines and thyroid function in patients with obesity

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Abstract

Introduction: The study was designed to evaluate the effect of thyroid function on serum levels of different adipokines in obesity. We investigated relationships between the thyroid axis and serum levels of leptin, adiponectin, and chemerin, and we assessed the influence of autoimmune thyroiditis (AIT) on those relations.

Material and methods: The participants of this study included 181 euthyroid patients (147 women and 34 men) with obesity [body mass index (BMI) 30–39.9 kg/m^2] and severe (morbid) obesity (BMI ≥ 40 kg/m^2), aged 18 to 65 years. We divided all obese patients by thyrotropic hormone (TSH) tertiles, and we compared all participants according to BMI. Patients were further divided into the following subgroups: with chronic autoimmune thyroiditis and without autoimmune thyroiditis.

Results: Comparison of obese patients according to TSH tertile showed significantly higher serum concentrations of leptin, chemerin, and thyroid antibodies and an increased leptin/adiponectin ratio in the group with high normal TSH. We observed statistically significant correlations between serum TSH and BMI, leptin, chemerin, thyroid peroxidase antibodies, and the leptin/adiponectin ratio. In patients diagnosed with autoimmune thyroiditis, higher levels of antibodies and TSH were found, but there were no differences in homeostatic model assessment index (HOMA-I), the leptin/adiponectin ratio, and adipokine levels. In obese patients the relationships between serum leptin, chemerin, the leptin/adiponectin ratio, and BMI were dependent on each other.

Conclusion: Serum leptin, chemerin, the leptin/adiponectin ratio, and BMI are significantly higher in patients with high normal TSH; however, selected adipokines are not related to the presence of autoimmune thyroiditis. There are interplays between TSH, adipokines, and obesity, but how these relationships are related remains unknown. **(Endokrynol Pol 2022; 73 (2): 353–360)**

Key words: *adipokines; thyroid; obesity*

Introduction

There are interrelationships between adipose tissue and the hypothalamic–pituitary–thyroid axis. Leptin stimulates the activity of thyrotropin-releasing hormone (TRH) neurons and consequently the synthesis of thyrotropic hormone (TSH) and thyroid hormones (THs). It promotes energy expenditure by enhancing lipolysis and thermogenesis through central and peripheral mechanisms [1, 2]. Hyperthyrotropinaemia observed in obese individuals may be a compensatory mechanism. Higher levels of the TSH observed in obese individuals may also result from impaired hormonal function of thyroid gland. Even slight thyroid dysfunction can lead to a reduction in thermogenesis and the basal metabolic rate, which promotes weight gain [3]. Adipocytes contain receptors for THs [2] and for TSH [4]; therefore, thyrotropin and THs, independently, may influence the function of adipose tissue. It was shown that at the level of adipocytes, TSH stimulates production of leptin and other cytokines: interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α). Recombinant TSH administered to patients with differentiated thyroid cancer increased serum leptin concentration [5]. Leptin signals the amount of stored energy and regulates the metabolism of lipids and carbohydrates. The effect of TSH on the production and secretion of other adipokines is not known. Adiponectin exerts favourable metabolic effects and has anti-inflammatory properties. Chemerin and its receptors are increased in obesity. The activity of chemerin is regulated by proinflammatory cytokines, and it presents immunomodulating properties.

The relationships between thyroid function and serum levels of selected adipokines: leptin, adiponectin, and chemerin in obesity are the focus of this study.

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Material and methods

The participants of this study included 181 patients (147 women and 34 men) with obesity [body mass index (BMI) 30–39.9 kg/m^2] and severe (morbid) obesity (BMI ≥ 40 kg/m^2), aged 18 to 65 years. We enrolled only euthyroid subjects, as inferred from TSH and free thyroxine (fT4) concentrations within reference ranges. The normal reference range for TSH was 0.35–4.50 mIU/L, and for fT4 it was 0.7–2.2 ng/dL.

Exclusion criteria were as follows: diagnosed or already treated hypothyroidism with levothyroxine, history of thyroid surgery, presence of cancer, kidney failure, and liver disorders. The project was carried out with the permission of the Bioethics Committee. Written informed consent was obtained from all participants before the study. Height and weight were measured, and BMI was calculated by dividing the weight (kg) by the height squared (m^2). Waist circumference and blood pressure were measured. Venous fasting blood samples were obtained from each participant in the morning at rest. The blood samples were centrifuged at 3000 g for 10 min, and the samples of serum were stored at –70°C until assays were performed. We assessed the concentrations of leptin, adiponectin, chemerin, TSH, fT4, antithyroid peroxidase (ATPO) antibodies, anti-thyroglobulin (ATG) antibodies, glucose, total cholesterol, high density lipoprotein (HDL), triglycerides, and insulin. The leptin/adiponectin ratio was calculated. Insulin resistance was estimated by homeostatic model assessment index (HOMA-I) and calculated as [serum glucose (mg/dL)/18.1 × insulin concentration (mU/L)/22.5]. Serum levels of adipokines, hormones, and antibodies were determined by Enzyme Linked Immunosorbent Assay ELISA using commercial assays (Leptin BioVendor, Adiponectin BioVendor, Chemerin BioVendor, TSH DiaMetra, ATPO IBL International, ATG IBL International, Insulin LDN). Intra- and extra-assay errors did not exceed 10%. Tests of glucose, total cholesterol, HDL, and triglycerides were carried out using standard biochemical methods.

We divided all obese patients by TSH tertiles and we compared subjects with upper tertile of TSH (3rd tertile/high-normal TSH) and low tertile (1st tertile) of TSH. We also compared all participants according to BMI (subjects with BMI ≥ 40 kg/m^2 *vs.* BMI 30.0–39.9 kg/m^2). Patients were further divided into the following subgroups: with chronic autoimmune thyroiditis and without autoimmune thyroiditis. Chronic autoimmune thyroid disease was diagnosed by the presence of autoantibodies to thyroid peroxidase and/or thyroglobulin, and thyroid ultrasound was used as a complementary tool to biochemistry tests.

Results

Characteristics of participants

Baseline characteristics of study participants and the comparison of clinical and biochemical characteristics of women and men are summarized in Table 1. The mean BMI in the total group of participants was 42.91 (SD 6.69): in women 42.91 (SD 6.84) and in men 42.89 (SD 6.08). There were no differences between age and BMI between women and men.

The mean TSH was 2.34 (SD 1.10), and there were no differences between women (2.53, SD 1.46) and men (2.14, SD 1.11). In the studied group 57 participants were diagnosed with autoimmune thyroiditis (51 women, 6 men).

Waist circumference and glucose level were higher in men than in women, whereas HDL, leptin, and the leptin/adiponectin ratio were statistically higher in

Table 1. *The clinical, metabolic, and hormonal parameters of all participants with obesity, and a comparison between the women and men*

	All participants (n = 181)	Women (n = 147)	Men (n = 34)	p
Age	38.31 ± 9.86	38.39 ± 9.56	37.94 ± 11.22	NS
BMI [kg/m^2]	42.91 ± 6.69	42.91 ± 6.84	42.89 ± 6.08	NS
Waist [m]	1.25 ± 0.15	1.24 ± 0.14	1.34 ± 0.15	< 0.001
Glucose [mg/dL]	110.01 ± 30.12	107.78 ± 26.51	119.62 ± 41.51	< 0.05
Triglycerides [mg/dL]	149.73 ± 72.07	146.22 ± 71.81	165.24 ± 72.26	NS
HDL [mg/dL]	55.42 ± 13.49	56.78 ± 13.59	49.46 ± 11.42	< 0.01
Cholesterol [mg/dL]	207.87 ± 37.51	207.53 ± 37.95	209.35 ± 36.08	NS
HOMA-I	4.27 [2.89; 6.13]	4.03 [2.76; 5.99]	4.79 [3.46; 6.95]	NS
TSH [mIU/L]	2.34 ± 1.10	2.53 ± 1.46	2.14 ± 1.11	NS
fT4 [ng/dL]	1.25 ± 0.38	1.24 ± 0.37	1.31 ± 0.44	NS
ATPO [IU/mL]	7.85 [6.93; 81.25]	7.97 [6.87; 99.66]	7.54 [7.05; 8.74]	NS
ATG [IU/mL]	19.93 [16.21;26.89]	20.52 [15.93;28.78]	18.63 [16.49; 0.52]	NS
Adiponectin [μg/mL]	10.80 ± 6.03	11.21 ± 6.37	8.82 ± 3.44	NS
Leptin [ng/mL]	51.54 ± 22.43	55.57 ± 20.33	32.24 ± 22.30	< 0.001
Leptin/adiponectin ratio	5.85 ± 3.67	6.18 ± 3.68	4.25 ± 3.22	< 0.01
Chemerin [ng/mL]	289.72 ± 80.75	293.42 ± 84.73	272.09 ± 56.06	NS
AIT n (%)	57 (31.49)	51 (34.69)	6 (17.65)	< 0.05

Normally distributed data are given as mean ± standard deviation (SD). Skewed data are given as median and percentiles [25th; 75th]. BMI — body mass index; HDL — high-density lipoprotein; HOMA-I — homeostatic model assessment index; TSH — thyroid stimulating hormone; fT4 — free thyroxine; ATPO — anti-thyroid peroxidase antibody; ATG — anti-thyroglobulin antibody; AIT — autoimmune thyroiditis; NS — non significant

Table 2. *The comparison of clinical, metabolic, and hormonal parameters between participants with severe obesity [body mass index (BMI) ≥ 40 kg/m²] and with obesity (BMI 30.0–39.9 kg/m²)*

	BMI ≥ 40 kg/m² (n = 115)	BMI 30.0–39.9 kg/m² (n = 66)	p
Age	38.40 ± 10.36	38.15 ± 8.98	NS
Waist [m]	1.31 ± 0.15	1.15 ± 0.09	NS
Glucose [mg/dL]	110.90 ± 26.42	108.44 ± 35.84	NS
Triglycerides [mg/dL]	150.24 ± 69.59	148.83 ± 76.76	NS
HDL [mg/dL]	53.73 ± 13.34	58.42 ± 13.32	NS
Cholesterol [mg/dL]	205.66 ± 36.43	211.72 ± 39.29	NS
HOMA-I	4.78 [3.31; 6.80]	3.37 [2.50; 4.84]	< 0.05
TSH [mIU/L]	2.46 ± 1.36	2.43 ± 1.49	NS
fT4 [ng/dL]	1.25 ± 0.36	1.23 ± 0.41	NS
ATPO [IU/mL]	12.70 [7.60; 304.42]	8.04 [6.99; 171.90]	NS
ATG [IU/mL]	19.49 [16.21; 26.58]	20.52 [16.21; 28.78]	NS
Adiponectin [μg/mL]	10.39 ± 6.08	11.49 ± 5.92	NS
Leptin [ng/mL]	58.27 ± 22.45	40.03 ± 17.21	< 0.001
Leptin/adiponectin ratio	6.83 ± 3.93	4.15 ± 2.35	< 0.001
Chemerin [ng/mL]	301.67 ± 84.07	269.46 ± 70.94	< 0.05
Prevalence of autoimmune thyroiditis, n (%)	35 (30.43)	8 (12.12)	< 0.01

Normally distributed data are given as mean ± standard deviation (SD). Skewed data are given as median and percentiles [25th; 75th]. HDL — high-density lipoprotein; HOMA-I — homeostatic model assessment index; TSH — thyroid stimulating hormone; fT4 — free thyroxine; ATPO — anti-thyroid peroxidase antibody; ATG — anti-thyroglobulin antibody; NS — non significant

women. Serum antibodies were not significantly different between the groups; however, the prevalence of autoimmune thyroiditis was higher among women (34.69%) than among men (17.65%), $p < 0.05$.

Subgroup analyses

When stratified by BMI, subjects were classified as obese (BMI 30-39.9 kg/m²) or severe obese (BMI ≥ 40 kg/m²). Overall, 62.59% of women (n = 92) and 67.65% of men (n = 23) had severe obesity; the proportion among women and men was similar. The characteristics of the participants according to BMI are described in Table 2.

The HOMA-I, serum leptin, chemerin concentrations, leptin/adiponectin ratio, and the prevalence of autoimmune thyroiditis in subjects with BMI ≥ 40 kg/m² were greater than in subjects with BMI 30–39.9 kg/m².

In the next step, we analysed subjects according to tertiles of TSH. We compared the patients with high and low tertiles of TSH. Table 3 shows the results of this comparison.

Patients with upper tertile of TSH (52 women, 8 men) had higher BMI and higher prevalence of autoimmune thyroiditis when compared with subjects with low tertile of TSH (45 women, 15 men). Between the 1st and 3rd tertiles of TSH values the BMI differed by 2.45 kg/m². The data also demonstrated significant differences in serum concentrations of leptin and chemerin, and the leptin/adiponectin ratio. There were no differences in adiponectin and HOMA-I.

Patients with and without autoimmune thyroiditis were then compared. In the group diagnosed with autoimmune thyroiditis, higher levels of antibodies and TSH were found (3.28 ± 1.82 mIU/L *vs.* 2.07 ± 0.96 mIU/L), but there were no differences in HOMA-I, leptin/adiponectin ratio, and adipokine levels.

In the next stage, the correlations of TSH with anthropometric and biochemical variables among all patients were assessed (Tab. 4). Statistically significant positive relationships with BMI, ATPO antibodies, leptin, the leptin/adiponectin ratio, and chemerin were observed.

We then analysed the correlation between TSH and other parameters separately for morbidly obese patients. Serum levels of TSH correlated positively with BMI ($R = 0.21$, $p < 0.05$) and with waist circumference ($R = 0.16$, $p < 0.05$) in severe obesity. However, no significant correlation was found between TSH and anthropometrical parameters in the group of BMI between 30 and 39.9 kg/m². The remaining analysed parameters (ATPO antibodies, leptin, leptin/adiponectin ratio and chemerin) correlated with TSH in both groups. We also investigated the relationships between leptin, adiponectin, the leptin/adiponectin ratio, chemerin, and selected anthropometric, metabolic, as well as hormonal parameters. The results are given in Table 4.

Table 3. *Comparison of clinical, hormonal, and biochemical parameters in patients with upper and lower tertiles of thyroid-stimulating hormone (TSH)*

	TSH > 2.65 mIU/L (n = 60)	TSH < 1.64 mIU/L (n = 60)	p
BMI [kg/m^2]	44.35 ± 8.38	41.90 ± 6.23	< 0.05
Age	38.68 ± 11.37	39.95 ± 6.71	NS
Waist [m]	1.27 ± 0.18	1.25 ± 0.12	NS
Glucose [mg/dL]	115.03 ± 36.88	109.57 ± 31.49	NS
Triglycerides [mg/dL]	153.93 ± 67.92	146.21 ± 77.15	NS
HDL [mg/dL]	54.71 ± 11.44	56.57 ± 17.25	NS
Cholesterol [mg/dL]	204.02 ± 37.83	210.48 ± 38.26	NS
HOMA-I	3.95 [2.89; 6.79]	4.31 [2.83; 6.25]	NS
fT4 [ng/dL]	1.24 ± 0.40	1.24 ± 0.38	NS
ATPO [IU/mL]	12.70 [7.60; 304.42]	7.29 [6.9; 8.57]	< 0.001
ATG [IU/mL]	24.88 [18.20; 43.05]	17.91 [15.25; 21.71]	< 0.05
Adiponectin [μg/mL]	10.67 ± 7.16	10.96 ± 5.86	NS
Leptin [ng/mL]	55.13 ± 22.44	46.06 ± 21.24	< 0.01
Leptin/adiponectin ratio	6.65 ± 4.34	5.08 ± 3.02	< 0.01
Chemerin [ng/mL]	310.00 ± 81.47	270.59 ± 86.36	< 0.05
Prevalence of autoimmune thyroiditis, n (%)	33 (55)	8 (13.33)	< 0.01

Normally distributed data are given as mean ± standard deviation (SD). Skewed data are given as median and percentiles [25th; 75th]. BMI — body mass index; HDL — high-density lipoprotein; HOMA-I — homeostatic model assessment index; fT4 — free thyroxine; ATPO — anti-thyroid peroxidase antibody; ATG — anti-thyroglobulin antibody; NS — non significant

Table 4. *Spearman's coefficients of the relationships between serum adipokines, thyroid-stimulating hormone (TSH), homeostatic model assessment index (HOMA-I), and selected anthropometric, metabolic, and hormonal variables for all obese participants*

Variable	Adiponectin	Leptin	Leptin/adiponectin	Chemerin	TSH	HOMA-I
BMI	NS	–0.65***	0.41***	0.24***	0.18*	0.30***
Waist	–0.21***	0.18**	0.26***	0.16*	NS	0.34***
HDL	0.26**	NS	NS	NS	NS	–0.22**
HOMA-I	–0.43***	NS	0.39***	NS	NS	
TG	–0.28***	NS	0.17**	0.21**	NS	0.36***
TSH	NS	0.19**	0.18**	0.27***		NS
ATPO	NS	NS	NS	0.21*	0.34**	NS
Leptin	NS		NS	0.23**	0.20**	NS
Leptin/adiponectin	–0.65***	0.73***		NS	0.19**	0.39***
Chemerin	NS	0.23**	NS		0.27***	NS

*p < 0.05, **p < 0.01, ***p < 0.001; BMI – body mass index; HDL — high-density lipoprotein; TG — thyroglobulin; ATPO — anti-thyroid peroxidase antibody; NS — non significant

Then, we repeated the analysis between chemerin and other variables separately in men and women. The correlation between chemerin and ATPO remained statistically significant only in women (R = 0.22, p < 0.05) and disappeared in men.

To determine the independent contributions of BMI, serum leptin, chemerin, the leptin/adiponectin ratio, and the presence of autoimmune thyroiditis to the serum TSH concentration, they all were included in the multiple linear regression analysis. After the analysis, we found that the presence of autoimmune thyroiditis, serum chemerin and the leptin/adiponectin ratio were significantly associated with elevated TSH level (Tab. 5).

Discussion

In the present study, we evaluated potential relationships between thyroid function and concentrations of leptin, adiponectin, and chemerin in obese men and women. Obese patients with highly normal TSH were

Table 5. *Multiple regression analysis of serum of thyroid-stimulating hormone (TSH). The analysis was performed for all studied subjects. Dependent variable: TSH*

Independent variable	Regression coefficient	p
BMI	0.10	NS
Leptin	0.10	NS
Leptin/adiponectin	0.18	< 0.05
Chemerin	0.18	< 0.05
Autoimmune thyroiditis Yes/No	0.39	< 0.001

BMI — body mass index; NS — non significant

shown to have elevated leptin levels, and these results are consistent with previous reports [6, 7]. In humans, TSH essentially stimulates lipolysis, as demonstrated in neonatal/childhood and in vitro studies [8]. Studies have shown that TSH via TSH receptor stimulates the protein kinase A (PKA) signalling pathway, leading to a lipolytic response [9]. Thyrotropin also activates perilipin phosphorylation in human and mouse 3T3-L1 adipocytes in a cAMP-dependent manner [9]. Consequently, non-esterified fatty acids and glycerol are released from differentiated adipocytes. In certain situations, however, thyrotropin may exert a pro-lipogenic effect in mature adipocytes. A state of excessive energy supply over a prolonged period of time favours the interference of intracellular TSH signalling with insulin signalling, leading to increased lipogenesis and decreased lipolysis [10]. Enhanced lipogenesis results in both adipocyte hypertrophy and fat mass gain. At lower BMI values, the inhibitory effect of TSH on insulin-stimulated lipogenesis predominates. The opposite effect occurs in obese subjects with insulin resistance. In our study, subjects in the upper TSH tertile had higher BMI and higher leptin levels. There was also a positive correlation between TSH and leptin, and the finding is consistent with results of Delitala et al. [11]; however, in our study leptin could not be found as a significant TSH independent variable. There was also a statistically significant correlation between TSH levels and BMI, but the degree of obesity modulated this effect. The correlation between TSH and BMI was evident in subjects with BMI ≥ 40 kg/m^2, but not in those with BMI 30–39.9 kg/m^2. Furthermore, the correlation between TSH and waist circumference, which is considered a marker of abdominal obesity, was only observed in subjects with severe obesity but not in those with BMI 30–39.9 kg/m^2. These opposing results may be due to greater insulin resistance in morbid obesity. Subjects with morbid obesity had significantly higher HOMA-I than those with BMI 30–39.9 kg/m^2. Our results are consistent with those of Shao et al., who showed that long-term feeding of high-fat feed to rats not only caused obesity but also induced an increase in TSH levels with associated insulin and leptin resistance [12]. Ma et al. [13] showed that TSH promotes fat accumulation through adipocyte hypertrophy and through adipose tissue hyperplasia by differentiating immature preadipocytes into adipocytes and their proliferation. In a human cross-sectional study including 1534 subjects, positive correlations were found between TSH and BMI, waist circumference, and triglyceride levels [14]. However, the results of the above analyses are not consistent with those of other studies. No association between BMI and TSH in euthyroid subjects was found by Layegh et al. [15] and Bjergved et al. [16]

In our study, the upper tertile of TSH was associated not only with leptin secretion but also with an elevated leptin/adiponectin ratio. Studies have shown that an elevated leptin/adiponectin ratio is associated with obesity and may be involved in the pathogenesis of diabetes and vascular disease [17]. The leptin/adiponectin (or adiponectin/leptin) ratio is considered a biomarker of adipose tissue dysfunction [18]. Some authors believe that it may be a more accurate predictor of insulin resistance than leptin and adiponectin alone [19]. In our study the association between the leptin/adiponectin ratio and HOMA-I has been found. We speculate that obese individuals in the highest TSH tertile may represent poorer adipose tissue function. Elevated TSH has been shown to promote adipose tissue hyperplasia and adipocyte hypertrophy, which is especially advanced when TSH and insulin act together for a long time [10]. Furthermore, elevated TSH stimulates inflammation, which contributes to adipose tissue dysfunction [20] and subsequently may facilitate weight gain.

Our results seem to be consistent with the observations of van Tienhoven-Wind et al., who found a significant positive correlation between TSH and the leptin/adiponectin ratio in euthyroid and metabolic syndrome subjects [21]. A correlation between the leptin/adiponectin ratio and TSH was also observed in Saudi Arabian subjects without obesity, while in the group with giant obesity, the authors found no statistically significant correlation [22]. The discrepancy between the results of our study and that of Al Mohareb et al. [22] may be due to the small size of the Saudi population and the different study design. The proportion of women in our study was significantly higher than that in the study of Al Mohareb et al. (81.2% *vs.* 45.7%), and these different proportions may influence the results because gender is known to modulate leptin and adiponectin levels.

When we extended the study to antithyroid autoantibodies, we revealed that obese patients with higher TSH in the euthyroid range had significantly higher

levels of thyroid antibodies than those with lower TSH, and they also had significantly higher prevalence of autoimmune thyroiditis. We also found positive correlations between TSH and ATPO in all obese study participants, and our results are consistent with previously published data [23, 24].

Antithyroid antibodies induce cellular cytotoxicity and activate complement, which may lead to impaired thyroid function, followed by a decrease in basal metabolism and subsequent weight gain and an increase in TSH. However, some authors have speculated that obesity itself may be a risk factor for thyroid autoimmunity [25–27], but the association of obesity with the occurrence of autoimmune thyroid diseases is still under debate. In our study, the incidence of autoimmune thyroiditis was significantly higher in subjects with severe obesity than in patients with a BMI of 30.0–39.9 kg/m^2.

There are many theories regarding the relationship between excess body fat and immune dysfunction [28]. It has been documented that various adipokines and cytokines secreted by adipose tissue may lead to the promotion of Th2 to Th1 immune response transition, which is associated with autoimmune processes. Moreover, chronic inflammation in obesity may act as a trigger for autoimmunity [28]. Marzullo et al. believe that high leptin levels in obesity may be associated with thyroid autoimmunity [25], and the results of different experimental studies suggest that leptin plays a role in the initiation of autoimmune thyroid disease [29]. It is speculated that toll-like receptors expressed in adipocytes and pro-inflammatory cells could be a link between obesity and the immune system [30]. However, the connections between hyperleptinaemia and autoimmune thyroiditis are not clear. Although Marzullo et al. demonstrated that leptin was elevated in patients with chronic thyroiditis [25], our study failed to confirm these findings, and this is in agreement with the results obtained by Adamska et al. [31].

In the present study, we observed that obese subjects with upper TSH tertile had elevated chemerin levels compared to those with low TSH tertile. There are few studies on the relationship between chemerin levels and thyroid function, and the results are controversial. Higher chemerin levels have been found in thyroid cancer patients with high normal TSH [32]. Positive correlations between TSH and chemerin were found in an animal model [33, 34]. The researchers demonstrated significantly higher chemerin levels in rats treated with methimazole compared to baseline. These results suggest that increased TSH levels or induced hypothyroidism may affect chemerin secretion. However, the effect of thyroid status on chemerin concentrations remains unclear because the results of other studies are inconsistent. In a human study by Alshaikh et al. [35] involving 70 euthyroid and 70 hyperthyroid subjects, chemerin levels were found to be higher in the latter group compared to subjects with normal TSH. The authors observed positive correlations between chemerin and free triiodothyronine (fT3) and negative correlations between chemerin and TSH in both groups [35]. In our study, chemerin correlated positively with TSH and with BMI, leptin, and triglycerides, whereas no correlation was found with metabolic parameters such as HOMA-I, glucose, and cholesterol. Our observations suggest that not only leptin but also chemerin may be a link between adipose tissue and thyroid function. Higher serum chemerin levels and increased expression of receptors for chemerin in obesity have been previously described, as well as positive correlations between chemerin and BMI [36] and between chemerin and triglycerides [37, 38]. Chemerin is mainly expressed in visceral adipose tissue, and this adipokine through chemokine-like receptor 1 (CMKLR1) signalling affects adipogenesis and promotes lipogenesis [39]. It is speculated that increased chemokine release allows hyperplasia of adipose mass. The observation made in the current study, that elevated serum chemerin levels in obese patients were positively associated with increased leptin levels, was also supported by previous studies [40–42]. Complex relationships between obesity, leptin resistance, and increased chemerin secretion have been considered [43]. Furthermore, chemerin, like leptin, contributes to low-grade inflammation. This adipokine is involved in the immune response by regulating infiltration of adipose tissue by macrophages and other immune cells [44]. The role of chemerin in the pathogenesis of various autoimmune diseases has been documented [45, 46]. Chemerin levels have been found to be elevated in rheumatoid arthritis [47], and high levels correlate with disease activity [48]. Elevated chemerin levels in multiple sclerosis patients have been associated with obesity [49]. Elevated chemerin levels have also been described in psoriasis [50]. A local effect of chemerin in lupus nephritis has been demonstrated [51]. Chemerin levels were also evaluated in asthmatic patients and found to be elevated in serum [52]. It has been documented that chemerin can promote Th17 cell activation in asthma [52]. It is worth mentioning that the same population of Th lymphocytes is involved in the development of autoimmune thyroid disease. In autoimmune thyroiditis, high levels of Th17 cells and Th17-related proinflammatory cytokines have been observed in both serum and thyroid tissue. The role of Th17-related cytokines is to stimulate epithelial cells, macrophages, and fibroblasts involved in thyroid injury. Chemerin not only stimulates Th17 cells but also recruits cells expressing chemerin receptor 23 (ChemR23)

receptors, including plasmacytoid dendritic cells. The role of dendritic cells in the pathogenesis of many autoimmune diseases is well documented [53], and they have been particularly demonstrated in autoimmune thyroid disease [54–56].

Although the role of chemerin as a ChemR23+ dendritic cell ligand is well documented in lupus nephritis [51], it is unclear whether chemerin can increase the dendritic cell population in autoimmune thyroid disease. In the present study, correlations between serum chemerin levels and thyroid autoantibody levels were analysed. Positive correlations were found between chemerin and ATPO levels in the whole group of patients. It is not known whether the observed correlation between chemerin and ATPO concentrations is involved in the initiation of the immune response. When evaluating women and men separately, the correlation remained significant only in women. There was also no correlation between chemerin and ATG antibodies. As far as we know, only one study has evaluated chemerin levels in patients with autoimmune thyroiditis [57]. In contrast to our results, the authors were not able to demonstrate a correlation between chemerin and ATPO. However, the number of patients in the previous study was smaller. Further studies with a larger number of patients of both sexes are needed to verify our observations and determine the exact role of chemerin in autoimmune thyroid disease.

Conclusions

Comparison of obese patients according to TSH tertile showed significantly higher serum concentrations of leptin, chemerin, and thyroid antibodies and increased leptin/adiponectin ratio in the group with high normal TSH. We provided evidence that leptin, chemerin, and the leptin/adiponectin ratio were correlated to the serum TSH, but were not related to the presence of autoimmune thyroiditis. There are interrelationships between TSH, adipokines, and obesity, but how these relationships are related remains unknown, so further investigations are needed.

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