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Original Article

The potential influence of hyperthyroidism on circulating adipokines chemerin, visfatin, and omentin

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ABSTRACT

Objectives: The aim of this study was to investigate the potential influence of hyperthyroidism on serum chemerin, visfatin, and omentin concentrations. The relationship between these adipokines and thyroid profile values was also investigated.

Methods: A total of 140 female Saudi participants aged 20–45 years were recruited and divided into two groups, the euthyroid control group (n = 70) and the hyperthyroidism group (n = 70). Chemerin, visfatin, omentin, and thyroid profile including thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), total triiodothyronine (TT3), total thyroxine (TT4), and thyroglobulin were measured for all participants.

Results: Serum chemerin levels were significantly higher in patients with hyperthyroidism compared to the controls. In contrast, serum visfatin and omentin concentrations were significantly lower in hyperthyroid patients than controls. Moreover, serum chemerin concentrations were positively correlated with TT3, TT4, and FT3 and negatively correlated with TSH and FT4. A negative correlation was also found between FT4 and TT4 and serum visfatin concentrations. Inversely, TSH correlated positively with serum visfatin levels. No significant correlation was observed between serum omentin concentrations and any of the thyroid profile variables except FT3.

Conclusion: Hyperthyroidism influences serum chemerin, visfatin, and omentin concentrations, and these adipokines are correlated with thyroid hormones.

Keywords: Adipokines, chemerin, hyperthyroidism, omentin, thyroid profile, visfatin

Introduction

Hyperthyroidism refers to the classic manifestations of excessive quantities of the thyroid hormones such as thyroxine (T4) and triiodothyronine (T3). It affects 2% of females between the ages of 20 and 40 years and is 10 times less common in males.[1] Thyroid hormone changes in patients with thyroid dysfunction have been reported to alter secretion of adipokines such as leptin, adiponectin, and resistin.[2-5] These adipokines are secreted from white adipose tissue in addition to chemerin, visfatin, and omentin.[6-9]

Chemerin is a multifunction protein that was first discovered in 1997 as a retinoid (tazarotene)-responsive gene in the skin.[10] In 2003, chemerin was rediscovered as an adipocyte signaling molecule (chemoattractant protein) important in adipogenesis and was described as an adipokine in 2007.[9,11] In addition to chemerin, visfatin is another adipokine that was previously identified as a growth factor for early B-lymphocytes and named as a pre-B cell colony-enhancing factor.[12] It is also called nicotinamide phosphoribosyltransferase due to its biochemical and functional homology with nicotinamide adenine dinucleotide, which is synthesized from nicotinamide [13] Fukuhara *et al*.[14] used the term "visfatin" for this protein due to its predominant production in the visceral adipose tissue (VAT). Moreover, omentin is also secreted from human VAT. Omentin mRNA encodes a peptide of 313 amino acids, containing a secretory signal sequence and a fibrinogen-related domain.[15]

There is a lack of concordance in the literature concerning differences in plasma or serum visfatin concentrations between hyperthyroid patients and controls. Chu *et al*.[16] and Caixàs *et al*.[17] reported higher visfatin concentrations in hyperthyroid patients compared with the control group, while Ozkaya *et al* [18] reported lower visfatin concentrations in hyperthyroid patients than controls. To the best of our knowledge, the direct effect of hyperthyroidism on serum adipokines including chemerin and omentin has not been studied. Thus, the aim of this study was to investigate the potential influence of

hyperthyroidism on serum chemerin, visfatin, and omentin concentrations. In addition, the relationship between these adipokines and thyroid profile values was also investigated.

Methods

Patients

A total of 140 female Saudi participants between 20 and 45 years old were recruited from the King Abdulaziz University Hospital, King Fahad Hospital, and King Fahad Armed Forces Hospital. Participants were divided into two groups: The euthyroid control group (n = 70) and the hyperthyroid group (n = 70). The diagnosis of hyperthyroidism was based on the levels of thyroid-stimulating hormone (TSH) (low) and T3 and T4 (high) hormones. The controls were healthy. Exclusion criteria included the presence of any chronic diseases, treatment with radioactive iodine, pregnancy, non-Saudis, and other age groups. The study was approved by the Ethical Committee of the Faculty of Medicine, King Abdulaziz University (ref.no. 418–16), and the health affairs of Jeddah city (ref. no. 412), and all participants gave informed consent.

Serum adipokines and thyroid profile measurements

All participants donated 5 ml of blood after an overnight fast (12–14 h). Serum samples were separated and stored at −80°C for later measurement. An enzyme-linked immunosorbent assay kit (ab155430-Chemerin Human ELISA Kit) was used to quantitatively determine serum chemerin according to the manufacturer's protocol (Abcam, USA). Serum visfatin and omentin levels were measured quantitatively using a human omentin-1 ELISA kit (cat no. SG-10741, SingoGeneClon Biotech Co. Ltd.) and human visfatin ELISA kit (cat no. SG-10381, SingoGeneClon Biotech Co. Ltd.), respectively. Thyroid hormones including TSH, total triiodothyronine (TT3), total thyroxine (TT4), free triiodothyronine (FT3), free thyroxine (FT4), and thyroglobulin were all measured by the electrochemiluminescence immunoassay method using an COBAS e 411 automated machine analyzer (Roche Company, USA).[19]

Statistical analysis

All statistical analyses were performed using the statistical software GraphPad prism 7. The Student's t-test was used to determine the differences in serum adipokines between the euthyroid control and hyperthyroid patients. The same approach was used to test the differences in thyroid profiles between the two groups. Correlation coefficients between adipokines and thyroid profiles were investigated using the Spearman correlation. $P \leq 0.05$ was considered to be statistically significant.

Results

Table 1 shows the mean difference in thyroid profiles between the control and hyperthyroid females. As expected, mean serum TSH concentrations were significantly lower in females with hyperthyroidism compared with the controls. In contrast, serum TT3, TT4, FT3, and thyroglobulin concentrations were significantly higher in the hyperthyroid females.

Changes in serum adipokines with hyperthyroidism are shown in Figure 1. In control and hyperthyroid patients, mean serum chemerin concentrations were 75 and 88 µg/l, respectively. Serum chemerin concentrations were significantly higher by approximately 13 µg/l in females with hyperthyroidism than the controls. In contrast, mean serum visfatin concentrations were significantly lower by approximately 5 µg/l in hyperthyroid females. Similarly, mean serum omentin concentrations were significantly lower in hyperthyroid females than the control.

The relationship between serum adipokines and thyroid profile variables is shown in Table 2. For all participants, serum chemerin concentrations were positively correlated with TT3, TT4, and FT3 and negatively correlated with TSH and FT4. A negative correlation was also found between FT4 and TT4 and serum visfatin concentrations. Inversely, TSH correlated positively with serum visfatin. No significant correlation was found between serum omentin concentrations and any of the thyroid profile variables, except with FT3.

Discussion

To the best of our knowledge, this is the first study to investigate the potential influence of hyperthyroidism on serum chemerin and omentin concentrations in Saudi females. The results showed that serum chemerin levels were significantly higher

Table 1: Mean serum concentrations of thyroid hormones among control and hyperthyroid females

Biochemical variables	Controls Mean±SEM (n=70)	Hyperthyroid patients Mean±SEM (n=70)	95% Confidence intervals for the difference	
			Lower	Upper
TSH (ng/dl)	0.88±0.06	0.75±0.40***	−0.94	0.614
FT3 (ng/dl)	7.88±0.12	12.8±0.87***	3.14	6.64
FT4 (ng/dl)	1.78±0.02	2.14±0.16	0.03	0.69
TT3 (ng/dl)	107±3.10	187±17.4***	45.21	115.0
TT4 (ng/dl)	7.51±0.20	11.1±0.71***	2.27	5.15
Thyroglobulin (ng/dl)	14.1±2.83	71.7±11.2***	34.70	80.49

Mean values are significantly different from those of controls. ***P<0.01. SEM: Standard error of the mean, TSH: Thyroid-stimulating hormone, FT3: Free triiodothyronine, FT4: Free thyroxine, TT3: Total triiodothyronine, TT4: Total thyroxine

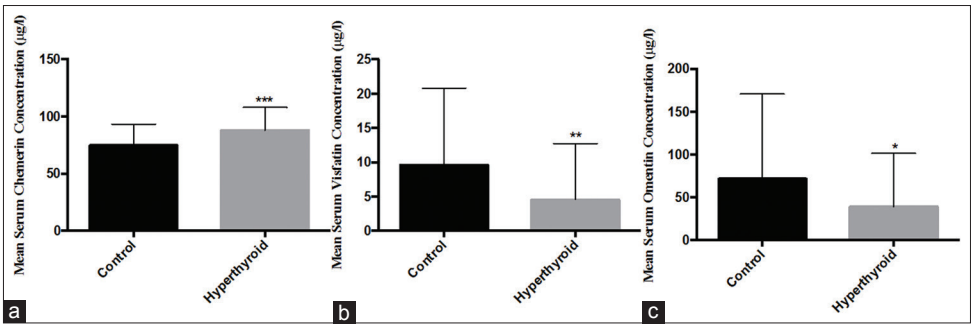

Figure 1: (a-c) Mean serum chemerin, visfatin, and omentin among control and hyperthyroid females (n = 140). Error bars show the standard error of the mean. *P < 0.05, **P < 0.01, ***P < 0.001 compared with controls

Table 2: Spearman correlation coefficients between circulating adipokines and thyroid profile (n=140)

Biochemical variables	Chemerin	Visfatin	Omentin
All			
TSH	−0.186*	0.175*	0.042
TT3	0.253**	0.121	−0.069
TT4	0.261**	−0.198*	−0.064
FT3	0.303***	−0.169	−0.175*
FT4	−0.189*	−0.198*	−0.02
Thyroglobulin	0.156	−0.094	−0.098
Controls			
TSH	0.175	−0.186	−0.04
TT3	0.150	0.036	−0.01
TT4	0.120	0.029	−0.01
FT3	0.220	0.098	−0.306**
FT4	−0.400***	0.08	0.077
Thyroglobulin	0.14	0.028	0.017
Hyperthyroid patients			
TSH	0.05	0.12	0.007
TT3	0.02	0.18	−0.009
TT4	0.03	0.301*	0.064
FT3	−0.004	−0.162	−0.015
FT4	−0.005	0.087	−0.137
Thyroglobulin	−0.18	0.005	−0.138

Significance of the correlation: *P<0.05, **P<0.01, and ***P<0.001. TSH: Thyroid stimulating hormone, FT3: Free triiodothyronine, FT4: Free thyroxine, TT3: Total triiodothyronine, TT4: Total thyroxine

in hyperthyroid patients compared to the euthyroid controls. In addition, serum chemerin concentrations were positively correlated with TT3, TT4, and FT3 and negatively correlated with TSH and FT4. A similar increase in serum chemerin levels was reported by Li *et al*.[20] in patients with Graves' disease. An increase in concentrations of other adipokines such as adiponectin was also reported by Ramadan *et al*.[21] and Yu *et al*.[22] in hyperthyroid patients over the controls. Yu *et al*.[22] also found a similar correlation between adiponectin and FT3 and insulin. They suggested that the increased levels of insulin in hyperthyroid patients may stimulate the secretion of adiponectin. As adiponectin and chemerin have similar effects, we could hypothesize that insulin might also increase the chemerin concentrations of patients in the present study. This hypothesis remains unclear and merits further investigation. In contrast to chemerin, omentin concentrations were lower in hyperthyroid patients compared with the controls. This inverse correlation between plasma chemerin and omentin concentrations observed in the present study was reported by Guzel *et al*.[23] and Jialal *et al*.[24] in obese females with polycystic ovary syndrome and in nascent metabolic syndrome subjects, respectively.

Controversial results were reported concerning the role of thyroid hormones in the regulation of visfatin concentrations. For example, Caixàs *et al*.[17] investigated the change of visfatin concentrations in hyperthyroid patients before and after treatment. The results showed plasma visfatin tended to be higher in hyperthyroid patients than in controls. After normalization of thyroid function, plasma visfatin increased and was higher than those of the controls. Similarly, Chu *et al*.[16] found that visfatin concentrations were higher in patients with hyperthyroidism compared with controls. In addition, they found a positive correlation between visfatin concentration and thyroid hormones, including T3 and T4. The authors suggested that the higher concentrations in hyperthyroid patients may reflect a state of visfatin resistance. In contrast, we observed, in the present study, lower serum visfatin levels in hyperthyroid patients than in controls. Moreover, visfatin levels were positively correlated with TSH and negatively correlated with FT4 and TT4. A similar observation was reported by Ozkaya *et al*.[18] who found that patients with hyperthyroidism had lower concentrations of visfatin than the control group. Furthermore, visfatin was positively correlated with TSH and inversely correlated with FT3 and FT4. This could be explained by the findings of McLaren *et al*.[25] who reported that T3 could induce a downregulation of visfatin mRNA expression in 3T3-L1 adipocytes. Abdelsalam and Edrees[7] reported a similar lowering of serum visfatin in experimentally-induced hyperthyroid rats. Such discrepancies between study results could be explained by different patient characteristics, coexisting autoimmunity, and methodological factors.

Conclusion

The results of the current study showed that hyperthyroid patients have significantly higher levels of chemerin and lower

levels of omentin and visfatin than controls. Moreover, these adipokines showed several correlations with thyroid hormones.

Conflicts of Interest

All authors declare no conflicts of interest.

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