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Investigating the relationship between irisin and cortisol levels in thyroid disease patients

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Abstract

Background: Both thyroid hormones and irisin have profound influences on the metabolism of the human body. Based on their similarities, several studies have been conducted to explore changes in irisin levels in patients with hypothyroidism and hyperthyroidism. Thyroid dysfunction has been reported in hypercortisolism.

Aims: The study aimed to investigate the association between thyroid function and cortisol and to explore the possible interchangeable metabolic roles between irisin and thyroid hormones.

Methods: The studied group consisted of 100 patients in which patients with thyroid dysfunction were formed in two groups as hypothyroid group and hyperthyroid group according to their thyroid hormones' levels and compared to healthy control group. Venous blood samples were analyzed for irisin, thyrotropin (TSH), thyroxine (T4), triiodothyronine (T3) and cortisol serum concentrations by using enzyme linked immunosorbent technique.

Results: The current study showed a significant increase ($P < 0.001$) in the serum level of cortisol in hyperthyroid group (52.36 ± 32.11 mcg/dL) compared to hypothyroid (27.04 ± 20 mcg/dL) and euthyroid group (24.09 ± 3.30 mcg/dL). The serum level of irisin in hyperthyroid group is significantly higher ($P < 0.001$) than that of hypothyroid group, however there is no significant difference between serum level of irisin in hyperthyroid group and that in the euthyroid group.

There is a significant positive correlation between serum level of both T_3 and T_4 with both irisin and cortisol in patient group. Also there is a significant negative correlation between serum level of TSH and both irisin and cortisol in patient group. However, these correlations were not established in the control subjects.

Conclusion: The current study demonstrates that irisin and cortisol concentrations may vary according to the thyrometabolic state. Through the exploration of this issue on group of patients with thyroid dysfunction and healthy subjects, a potentially deeper insight into these significant and evolutionary conserved regulatory mechanisms may be achieved.

Keywords: Irisin; Thyroid Function; Hyperthyroidism; Hypothyroidism; Cortisol

1. Introduction

Endocrine disorders, including thyroid dysfunction, diabetes, and polycystic ovarian syndrome, impair glandular function. Thyroid disorders include hyperthyroidism, characterized by weight loss and tachycardia, and hypothyroidism, which leads to weight gain and bradycardia (1). The thyroid gland secretes essential hormones T4 and

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T3, while TSH regulates their production according to blood T4 concentrations. Thyroid disorders may affect cardiovascular health (2).

Irisin, a hormone secreted during physical activity, influences metabolism and may alleviate stress. Obesity may marginally increase irisin levels, and its association with fibromyalgia and thyroid disorders varies with age, perhaps inhibiting cancer proliferation while regulating energy (3). Irisin has potential for addressing obesity, diabetes, atherosclerosis, and non-alcoholic fatty liver disease; nevertheless, its relationship with thyroid hormones need more research (4).

Cortisol, produced by the adrenal glands, is essential for stress reactions, influencing blood pressure and immune function; prolonged stress may lead to metabolic diseases. Research connects stress with modifications in the endocrine system, where variations in irisin and cortisol influence thyroid disorders (5). Hypothyroidism is associated with a reduced metabolic rate, and research suggests elevated salivary cortisol levels in these individuals. Increased thyroid hormone levels in females suggest irisin's possible involvement in thyroid function and the onset of hypothyroidism via dysregulation (6).

Endocrine system disorders, particularly thyroid diseases, are widespread. Hormonal abnormalities interfere with metabolism and affect fat and glucose levels via insulin. Metabolic abnormalities profoundly impact the liver and muscle as a result of thyroid hormones (7).

Irisin, a myokine, and cortisol, a corticosteroid, have significant roles in thyroid function and muscular activity. Research indicates elevated irisin levels in thyroid disorders, associated with either the illness or surgical intervention (8). Recent studies indicate that thyroid hormone levels influence metabolism via interactions with adipo-myokines and the hypothalamic-pituitary-thyroid axis, emphasizing alterations in cortisol and thyroid hormones, as well as the correlation between irisin and cortisol in a population-based cohort.

The research investigates the impact of irisin and cortisol hormones on individuals with thyroid illness, indicating that thyroid disease affects blood concentrations of these hormones, which mirror alterations in metabolic requirements stemming from endocrine disorders. The objectives include quantifying blood irisin and cortisol levels in diagnosed patients and analyzing their effects in conjunction with other thyroid hormones. This finding supports further investigations into the functions of irisin and cortisol within endocrinology and metabolism.

2. Study Design and Methodology

Participants were precisely chosen on the basis of diagnosis of an overt thyroid disorder. 159 participants (37 with hypothyroidism, 62 with hyperthyroidism, and 60 controls) were recruited. Patients meeting the inclusion criteria and referred to the Department of Endocrinology, Patients were taking aged 40 to 70 years of both sex ,complaining from overt hypothyroidism and hyperthyroidism and excluded immune disease ,pregnancy ,smoker and diabetic patients, pregnancy, patients receiving drugs that could interfere with thyroid function, cortisol and irisin (Amiodarone, Iodine, Lithium, Oral contraceptive pills and antidiabetic drugs) and patients affected by malabsorption-related conditions . Informed consent criteria was established, ensuring personal data confidentiality and voluntary participation. Demographic details, such as age and sex, were recorded, and a reason and information sheet were preceded the distributed materials to ensure participant understanding and consent. All ethical considerations comply with the Helsinki Declaration. The difference between irisin and cortisol serum concentrations in hypothyroid and hyperthyroid patients was evaluated using statistical package for social sciences (SPSS), version 22.

The variables of the study are numerical variables in which analysis of variance test was performed. P values less than 0.05 will be considered significant and the variables of the study are continuous numerical in nature and a peripheral venous line sample drawing between 08.30 and 09.00 a.m., following an overnight fasting and while seated then measured serum T3, T4, TSH, irisin and cortisol. Weight and height were assessed on the day of the blood collection to calculate BMI as kilogram per square meter.

3. Results

The thyroid function tests (T3,T4 and TSH) that used to establish the diagnosis for study groups are illustrated in the table 1.

Table 1 the mean ± SD of the thyroid function parameters in Hypothyroidism group, Hyperthyroidism group and Euthyroid groups

		N	Mean ± SD	Range	Std. Error
T3_conc	Hypothyroidism	37	0.40 ± 0.3 [a ***, b***]	0.40 - 1.88	0.07
	Hyperthyroidism	62	1.10 ± 0.82 [a ***]	1.10 - 5.10	0.10
	Euthyroid	60	0.71 ± 0.45	0.71 - 2.30	0.05
T4_conc	Hypothyroidism	37	44 ± 12.40 [a ***, b***]	44.0 - 88.55	2.03
	Hyperthyroidism	62	77.8 ± 33.69 [a ***]	77.80 - 222.60	4.27
	Euthyroid	60	68.02 ± 9.79	68.02 - 98.00	1.26
TSH conc	Hypothyroidism	37	16.4 ± 10.49 [a ***, b***]	16.40 - 60.00	2.54
	Hyperthyroidism	62	0.05 ± 0.02 [a *]	0.05 - 0.10	0.00
	Euthyroid	60	2.10 ± 0.64	2.10 - 4.60	0.0 8

SD: standard deviation, T3 : triiodothyronin, T4 : thyroxin
[a]: ANOVA test between Hypothyroidism, Hyperthyroidism versus Euthyroid; *** P < 0.001, * P < 0.05.
[b]: ANOVA test between Hypothyroidism versus Hyperthyroidism; *** P < 0.001.

The current study showed a significant increase in the serum level of cortisol in hyperthyroid group compared to hypothyroid and euthyroid group as shown in table 2. The serum level of irisin in hyperthyroid group is significantly higher than that of hypothyroid group, however there is no significant difference between serum level of irisin in hyperthyroid group and that in the euthyroid group as shown in table 2.

Table 2 the mean ± SD of the serum levels of cortisol and irisin in Hypothyroidism group, Hyperthyroidism group and Euthyroid groups

		N	Mean ± SD	Range	Std. Error
Cortisol Conc. (mcg/dL)	Hypothyroidism	37	27.04 ± 20 [a ***, b***]	27.04 - 139.00	3.74
	Hyperthyroidism	62	52.36 ± 32.11 [a ***]	52.36 - 197.00	4.07
	Euthyroid	60	24.09 ± 3.30	3.30 - 98.00	3.11
Irisin conc	Hypothyroidism	37	3.25 ± 2.22 [a ***, b***]	3.25 - 15.00	.53
	Hyperthyroidism	62	5.12 ± 4.25 [a ***]	5.12 - 26.87	.54
	Euthyroid	60	5.80 ± 1.75	5.80 - 16.00	.22

SD: standard deviation,
[a]: ANOVA test between Hypothyroidism, Hyperthyroidism versus Euthyroid; *** P < 0.001, * P < 0.05.
[b]: ANOVA test between Hypothyroidism versus Hyperthyroidism; *** P < 0.001.

The study also explicit no significant difference between males and females regarding serum level of cortisol and irisin in all study groups, as shown in figure 1 and 2.

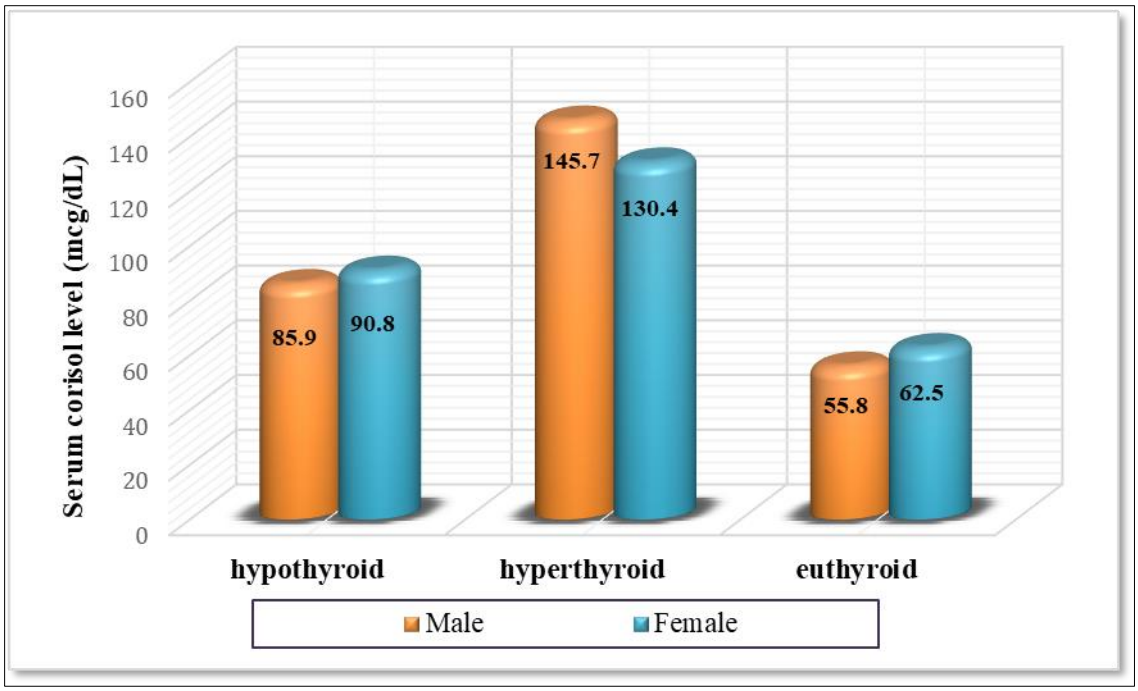

Figure 1 the mean serum levels of cortisol (mcg/dL) of males and females in the study groups.

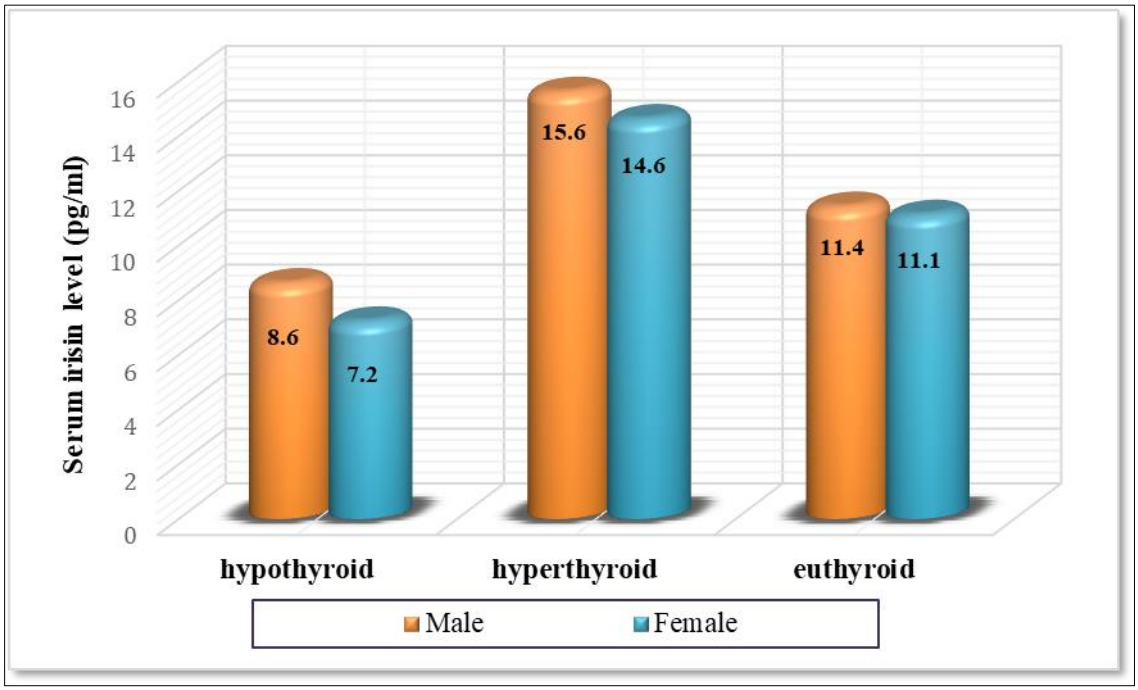

Figure 2 the mean serum levels of irisin (pg/ml) of males and females in the study groups.

There is a significant positive correlation between serum level of both T_3 and T_4 with both irisin and cortisol in patient group as shown table 3. Also there is a significant negative correlation between serum level of TSH and both irisin and cortisol in patient group as shown table 3. However, this correlations were not established in the control subjects.

Table 3 Pearson's correlation coefficient between different parameters in patients group

Parameter	**Serum conc. of TSH (µIU/mL)**	**Serum conc. of T_3 (pg/ml)**	**Serum conc.of T_4 (ng/dl)**	**Serum conc. of Irisin (pg/ml)**	**Serum conc. of cortisol (mcg/dL)**
	R	R	R	R	R
Serum conc. of TSH (µIU/mL)	1	-0.48*	-0.68*	-0.56*	-0.48*
Serum conc. of T_3 (pg/ml)	-0.48*	1	0.57*	0.42*	0.35*
Serum conc. of T_4 (ng/dl)	-0.68*	0.57*	1	0.58*	0.50*
Serum conc. of Irisin (pg/ml)	-0.56*	0.42*	0.58*	1	0.55*
Serum conc.of cortisol (mcg/dL)	-0.48*	0.35*	0.50*	0.55*	1

* Statistical significance regarding Pearson correlation.

4. Discussion

The study found a significant increase in serum cortisol levels in the hyperthyroid group compared to the hypothyroid and euthyroid groups. This finding aligns with the known physiological relationship between thyroid hormones and the hypothalamic-pituitary-adrenal (HPA) axis. Hyperthyroidism is associated with increased metabolic activity and stress on the body, which can stimulate the HPA axis, leading to elevated cortisol levels. Cortisol, a glucocorticoid, is a key stress hormone that regulates metabolism, immune response, and homeostasis (9).

The study reported significantly higher serum irisin levels in the hyperthyroid group compared to the hypothyroid group, but no significant difference between hyperthyroid and euthyroid groups. Irisin is a myokine secreted by skeletal muscle during exercise, and it plays a role in energy metabolism and thermogenesis. Thyroid hormones, particularly T3, are known to influence muscle metabolism and energy expenditure, which may explain the elevated irisin levels in hyperthyroidism (10).

The study found a significant positive correlation between T3/T4 levels and both irisin and cortisol in the patient group, as well as a negative correlation between TSH and these markers. This suggests that thyroid hormones directly or indirectly influence the secretion and regulation of irisin and cortisol. T3, in particular, is a potent regulator of metabolic processes, and its elevation in hyperthyroidism may drive the observed increases in irisin and cortisol (11).

The absence of significant correlations between thyroid hormones, irisin, and cortisol in the euthyroid (control) group suggests that these relationships are specific to pathological thyroid states. In euthyroid individuals, the regulatory mechanisms maintaining homeostasis may prevent extreme fluctuations in irisin and cortisol levels, even with variations in thyroid hormones (12).

The findings of this study have important clinical implications. Elevated cortisol levels in hyperthyroidism may contribute to the metabolic and psychological symptoms observed in these patients, such as anxiety, weight loss, and insulin resistance. Similarly, the increase in irisin levels may reflect an adaptive response to the heightened metabolic demands of hyperthyroidism. Understanding these relationships could help in developing targeted therapies for thyroid disorders and their metabolic complications.

5. Conclusion

Thyrometabolic state and BAT function can be enhanced through the recruitment of multiple pathways. Risin, cortisol, and thyroid hormones may also contribute to the "browning" of white adipose tissue.

In summary, our research indicates that the concentrations of irisin and cortisol may fluctuate in accordance with the thyrometabolic state, which may be associated with the extent of muscle injury. By investigating this matter in a group of patients with thyroid dysfunction and healthy individuals, it is possible to gain a more profound understanding of these evolutionary conserved regulatory mechanisms that are significant.

Our investigation is the initial to quantify the correlation between cortisol and irisin concentrations and thyrometabolic state.

Recommendation

Further studies may be necessary to assess the effect of other energy homeostatic markers such as myoglobin and CK on thyroid function in patients with thyroid disorders.

Compliance with ethical standards

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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