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RESEARCH ARTICLE

SERUM LEPTIN AND ADIPONECTIN IN INDIAN FEMALE POPULATION WITH THYROID DYSFUNCTION

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Abstract

Thyroid dysfunction is associated with metabolic changes that affect mass and adipocyte function. Adipose tissue is confirmed to be a gland that secretes several molecules with multiple metabolic functions. Both adipokines (Leptin and adiponectin) and thyroid hormone may be affected by energy balance and body weight. A relationship between these 2 endocrine systems seems intuitive.. In recent years an extensive research is under way to explore the mutual roles of different adipokines and thyroid hormones. The aim of this study was to evaluate the relationships between thyroid status and circulating levels of the two adipose tissue hormones in Indian female population. We studied 38 female patients with hyperthyroidism, 38 female patients with hypothyroidism and 38 euthyroid female subjects, all matched by age and body mass index (BMI). Serum concentrations of thyroxine, triiodothyronine, TSH, leptin and adiponectin were assessed. The study showed that serum adiponectin is statistically increased in hyperthyroid females while serum leptin concentration was significantly increased in hypothyroid females. We concluded that changes associated with thyroid dysfunction in Indian female population are related to variations in serum levels of adiponectin and leptin independent of BMI.

INTRODUCTION

Adipose tissue is a complex organ including adipocytes, immune cells, fibroblasts, blood vessels, and collagen fibers. Over the past decade, it has been recognized that adipose tissue has important functions other than energy storage, such as secreting a variety of endocrine, paracrine, and autocrine hormones; cytokines; and growth factors which influence local adipose tissue and different organs/tissues. These include CNS, liver, pancreas, and the skeletal muscles.

Thyroid hormones are involved in the regulation of body metabolism. Their effects include the stimulation of resting metabolic rate, increase in energy expenditure, modulation of responsiveness to catecholamines, and thermogenesis in adipose tissue (12, 13). Disturbances in thyroid function lead to changes in body weight, muscle mass, and fat

tissue. Thyroid-stimulating hormone (TSH) receptors have been found in the adipose tissues, indicating that they play a role in the regulation of the adipocytokines which are involved in the regulation of energy balance (7).
Thyroid hormones are also crucial for the regulation of total energy consumption and body composition besides their roles in normal growth, development, and reproduction. A positive correlation between serum thyroid stimulating hormone (TSH) levels and body mass index (BMI) is suggested as thyroid dysfunction is associated with weight changes [14, 3]. High-energy intake results in an increase of plasma T3 levels, and starvation causes a decrease in plasma T3 (triiodothyronine) levels [17]. Leptin is considered to play a wide range of functions in humans such as decreasing appetite and thereby food intake, stimulating and maintaining energy expenditure and acting as a metabolic hormone in a wide range of processes by binding to receptors in the brain.(19) Leptin functions primarily as an anti-obesity hormone. In most obese subjects, leptin levels are high and correlate with the Body Mass Index (BMI) and the percentage of body fat (6). Leptin levels are found to be correlated with a number of endocrine substances such as insulin, glucocorticoids, thyroid hormones and testosterone. (10) Hence study was designed to evaluate the relationship of thyroid hormones with adipokines without the influence of BMI. Hyperthyroidism and hypothyroidism are also both associated with insulin resistance [20].
Several reports indicate that leptin regulates thyroid function at hypothalamic – hypophyseal level and conversely, thyroid hormones might control leptin metabolism at least in some animal studies. Both adiponectin and thyroid hormones share some physiological actions as reduction of body fat by increasing thermogenesis and lipid oxidation affect serum leptin concentrations. Serum levels of adiponectin are not influenced by thyroid hypofunction; however, hyperthyroidism is associated with normal or elevated adiponectin levels. This suggests a complex interaction between thyroid hormones and adipocytokines.
Statistics show that one in eight women between the ages of 35 and 65 and one in five women over the age of 65 have some form of thyroid disease. Hence, the aim of this study is to document the adipokines and thyroid profile in Indian female population with thyroid dysfunction.

Material and Methods

The study has been conducted on 114 female subjects with age group 30 to 65 years attending OPD of. Department of Medicine/Surgery/E.N.T, Jawaharlal Nehru Medical College and Associated Group of Hospitals, Ajmer (Rajasthan). These were further divided into 3 groups of 38 subjects each: (Control) Group - A ,Group B (hypothyroid) subjects and Group C (hyperthyroid) subjects). Basic anthropometric measurements including weight, height, BMI were carried out and those with BMI ranging from 20 to 30 kg/m^2 were considered.
Subjects diagnosed with thyroid function on the basis of history and clinical examination were included in the study. Subjects who had history of using drug like corticosteroid, thyroid disease drugs, had received any iodinated contrast agents within previous two weeks or had established diseases such as malignancy, chronic obstructive pulmonary disease, chronic renal failure, cirrhosis of liver, active infection or uncontrolled diabetes mellitus were excluded from the study. Subjects not willing to participate were also excluded.
Subjects were further investigated by blood sample for thyroid profile and adipokines. Adipokines namely Serum leptin and serum adiponectin were determined using ELISA kit. In this study Thyroid profile included Serum T_3, T_4 and TSH which was estimated by Radioimmunoassay (RIA) method.

Statistical method

All statistical analysis including mean ± s.d., p value and pearson's correlation coefficient was performed using excel spreadsheet and graph pad software (Quick calcs).

Result

In our study the levels of T_3 (**0.45 ± 0.18** ng/ml) & T_4 (**3.78 ± 0.98** µg/dl) in group B were low as compared to the group A (T_3 = **0.98 ± 0.26** ng/ml & T_4 = **7.44 ± 1.64** µg/dl) and this decrease was statistically significant. The increase in TSH (**26.25 ± 23.52** µIU/ml) level was statistically significant in hypothyroid patients as compared to the controls (**2.78 ± 1.27** µIU/ml) (Table 1). Similarly, the levels of T_3 (**2.34 ± 0.18** ng/ml) & T_4 (**16.13 ± 1.17** µg/dl) in group C were high as compared to the group A (T_3 = **0.98 ± 0.26** ng/ml & T_4 = **7.44 ± 1.64** µg/dl) and this increase was statistically significant. The decrease in TSH (**0.10 ± 0.05** µIU/ml) level was statistically significant in hyperthyroid patients as compared to the controls (**2.78 ± 1.27** µIU/ml) (Table 1).

The increase in leptin in hypothyroid patients (**28.84 ± 3.81**ng/ml) and decrease in hyperthyroid patients (**8.89 ± 0.82** ng/ml) was highly significant statistically as compared to the controls (**10.96 ± 2.29** ng/ml) (Table 2). The levels of adiponectin were low in hypothyroid (**6.87 ± 1.63** ng/ml) and high in hyperthyroid (**18.02 ± 2.56** ng/ml) as compared to controls (**11.82 ± 1.94** ng/ml)
(Table 2).

Correlation analysis of TSH, T_3 & T_4 with leptin and adiponectin of both hypothyroid and hyperthyroid showed that TSH was negatively correlated with adiponectin (p=0.77) and positively correlated with leptin (p= 0.03), but this was not significant statistically (Table 3). The levels of T_3 and T_4 were negatively correlated with leptin and positively correlated with adiponectin. This was highly significant statistically (p<0.001) (Table 3).

Table 1 Comparison between the TSH, T_4 and T_3 values obtained in control, hypothyroid and hyperthyroid female subjects.

Parameters	Group-A (Control)	Group- B (Hypothyroid)	Group- C (Hyperthyroid)
T_3	0.98 ± 0.26	0.45 ± 0.18**	2.34 ± 0.18*
T_4	7.44 ± 1.64	3.78 ± 0.98*	16.13 ± 1.17*
TSH	2.78 ± 1.27	26.25 ± 23.52*	0.10 ± 0.05*

Values represent mean ± S.D. **p<0.0001, *p<0.001

Table 2 Comparison between Leptin and Adiponectin values obtained in control, hypothyroid and hyperthyroid female subjects.

Parameters	Group-A (Control)	Group- B (Hypothyroid)	Group- C (Hyperthyroid)
Leptin	10.96 ± 2.29*	28.84 ± 3.81*	8.89 ± 0.82*
Adiponectin	11.82 ± 1.94*	6.87 ± 1.63*	18.02 ± 2.56*

Values represent mean ± S.D. *p<0.0001

Table 3 Correlation of Leptin and Adiponectin values with T_3,T_4 and TSH obtained in both (hypothyroid and hyperthyroid) female subjects.

Parameters	T_3	T_4	TSH
Leptin	-0.94**	-0.94**	0.56
Adiponectin	0.92**	0.92*	-0.61

Values represent mean ± S.D. **p<0.0001,*p<0.01

Discussion

Our study demonstrates that keeping no significant difference in BMI among the three groups, serum leptin concentrations are statistically increased in hypothyroid patients and decreased in hyperthyroid patients in comparison to the control group. Both thyroid hormones and leptin affect each other and may regulate body composition and metabolism by complex mechanisms**.** The mechanism of leptin's effects on appetite and energy consumption is not only due to central neural regulation. Leptin regulates central and peripheral iodothyronine deiodinase activity and conversion of T4 to T3 [18]. According to P. Cettour-Rose et. al (16) Leptin also increases D2 activity centrally and leads to an increase of T3. Increased serum leptin in hypothyroidism may be due to decreased effect of thyroid hormone on adipocyte and leptin receptor (Leptin resistance), the decreased serum leptin in hyperthyroidism may be due to the increased effect of thyroid hormone by stimulating sympathetic system specifically of adrenergic receptors which tend to inhibit leptin secretion by blocking leptin receptors in adipose tissue. Besides this TSH stimulates leptin secretion by a direct effect on adipocytes, probably via TSH-receptors on the surface of adipocytes. C. Menendez et. al [5] showed Positive association between leptin and TSH can be caused by this direct effect of TSH on leptin secretion by adipocytes which is in agreement to our study. Given that thyroid hormones share some physiological actions with ADP (i.e. such as reduction of body fat by increased thermogenesis and lipid oxidation) (1), it is conceivable that ADP may interact with thyroid axis. Brenta G. (4) suggested that Thyroid hormones are associated with insulin resistance and a relationship between ADP and thyroid hormones may exist via either direct or indirect interactions between them. Fernandez-Real JM et.al (8) demonstrated that Adiponectin may influence thyroid hormone production through interaction with gC1q receptor, whereas changes in the pituitary – thyroid axis may alter serum adiponectin levels through different mechanism. Our study found that serum adiponectin concentrations are statistically increased in hyperthyroid patients and decreased in hypothyroid patients in comparison to control group. Insulin resistance in the liver and peripheral tissues is observed in hyperthyroid patients. Therefore, increased ADP levels might represent a compensatory mechanism against the insulin resistance observed in the hyperthyroid state. Further studies are needed to confirm all these hypotheses. Controversial results are reported for the experimental studies on hypo/hyperthyroid animals, concerning the association between ADP levels and thyroid hormones. (11, 2)

Leptin correlated negatively with T3 and T4 was in agreement with Oge A.,et al (15) while adiponectin serum adiponectin correlated positively with t3 and t4 and negative with TSH was in agreement with Iglesias P.Diez JJ (9).

Conclusion

Serum Leptin were significantly increased in hypothyroid female patients and significantly decreased in hyperthyroid female patients. Serum Adiponectin were significantly increased in hyperthyroid female patients and significantly decreased in hypothyroid female patients. Both leptin and adiponectin correlated significantly with thyroid hormones (T_3 and T_4) than TSH independent of BMI. Hence, it produces an insight on the mechanisms linking adipocytes with thyroid hormones other than insulin resistance or obesity.

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