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Research Article

# Levels of serum concentration adiponkines (ghrelin and obestatin) in patient with hypothyroidism

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**Abstract**

**Background**: Hypothyroidism is one of the most widespread disorders affecting the thyroid gland in the world, which associated with hormonal disorders. Objective: the aim of this study to measured adipokines (ghrelin and obestatin) in hypothyroidism patients.

**Patient and method**: A case-control study comprised 60 samples from hypothyroidism patients and 30 healthy samples from female patients ranging in age from 20 to 70 . A questionnaire was designed for collecting patiens as required in criteria of the study and to distinguish them from healthy controls. This questionnaire include Age, hight, weight, BMI, chronic disease and duration of illness for patients.

A thorough clinical history, physical examination, and pertinent laboratory tests were performed on the patients, and an evaluation of laboratory measures for thyroid diseases was used to establish the kind of problem. Serum ghrelin and obestatin concentrations were measured in serum samples using the enzyme-linked immunosorbent assay system (ELISA) using the Competitive-ELISA method

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## Introduction

Hypothyroidism is the One of the conditions affecting the thyroid gland, which is caused by a drop in the blood levels of the hormones T3 and T4. Because of the negative feedback process, the TSH rises to make up for this deficiency [1]. Reduced thyroid hormone production can also be associated with pituitary and hypothalamic problems, in addition to iodine shortage and thyroid diseases. Hypothyroidism symptoms include weight gain, sensitivity to cold, and constipation [2]. Obesity and hypothyroidism are strongly connected diseases [3] [4] [5]. Due to the fact that hypothyroidism is linked to a reduction in thermogenesis and resting energy expenditure [6] [3]. Body weight fluctuations may be caused by thyroid dysfunction; in the past, obesity was thought to be caused by a thyroid hormone shortage. Thyroid function is still often assessed in obese people to identify a possible cause of obesity and/or resistance to weight reduction with a hypocaloric diet. But hypothyroidism only causes a slight increase in weight, which is often brought on by modifications in body composition , TSH levels are correlated with BMI and are frequently higher in obese people than in people who are age, gender, and weight-matched to those of normal weight.[4]. Hypothyroidism is commonly associated with elevated blood levels of triglycerides, LDL-C, and total cholesterol. Thyroid hormone (TH) affects the production, elimination, and modification of cholesterol [7].

Adipokines are a class of biological agents and cytokines that are mostly released by adipocytes. They are essential for controlling immunological responses, inflammation, and glucose and energy balance [8]. Adipose tissue secretes more than 600 distinct forms of adipokines. Adipokines are a group of chemicals that have a range of activities, including crucial signal molecules, and include hormones, cytokines, growth factors, and vasodilators [9] .These processes are carried out via paracrine, autocrine, and endocrine systems [10]. When a person is obese, their adipokine expression patterns change, expressing more pro-inflammatory adipokines and less anti-inflammatory adipokines. This leads to the development of metabolic disorders associated with obesity, including insulin resistance (IR), dyslipidemia, weight gain, and vascular dysfunction [11].

Ghrelin is a powerful circulating stimulates appetite hormone that regulates food intake, energy expenditure, obesity, and the release of growth hormone (GH). It is a 28-amino acid peptide that is mostly generated by X/A-like enteroendocrine cells in the gastrointestinal tract [12].Before meals, the entero endocrine cells in the gastrointestinal system, particularly the stomach, release ghrelin, or the "hunger hormone," which stimulates the intake of food and the secretion of gastric acid. It performs a variety of physiological tasks, including as promoting hunger, causing fat to accumulate, and releasing growth hormone [13]. There are two types of ghrelin in the blood. The first is desacyl-ghrelin, which is present at higher and more stable quantities than other forms. The second is the acylated form (acyl-ghrelin AG), which is produced when ghrelin-oacyltransferase (GOAT) catalyzes the post-translational acylation of the hydroxyl group of the ser3 residue of the developing ghrelin. The acylated form of ghrelin is what gives it its biological action and accounts for around 20% of the total amount circulating in the body[14] .Obestatin is a peptide that results from different splicing of the same basic molecule, known as pre-proghrelin, and is broadly linked to ghrelin. It promotes anorexia. When it comes to humans, obestatin is mostly found in the stomach and upper gastrointestinal tract. Although this chemical may reduce food intake and stomach emptying, these effects have not yet been thoroughly shown [15]. The pancreas, the gut, and the thyroid gland all express it [16] To present, the changes in obestatin associated with thyroid dysfunction have only been studied in one study. [17].The study aims to determine the relationship between adipokines with hypothyroidism.

**Patient and Methods**

The case-control study was conducted in the consulting department at Al-Hilla Teaching Hospital for the period from October to December, it included total 90 samples

**Inclusion criteria**

All 60 patient were subjected clinical history and pertinent laboratory testing were performed on each patient in order to determine any clinical cases of thyroid problems. The most recent WHO clinical standards were also applied to them, and the kind of condition was identified using laboratory results which shows a high concentration of TSH and low concentration of T3,T4 and clinical evaluation measurements

**Exclusion criteria**

A group of volunteers consisting of 30 healthy women with no family history of thyroid disorders was selected by drawing blood samples from the participants, and their ages were similar in the entire study group. Demographic information was also collected for the participants through a questionnaire

all individuals had their venous blood collected was put in a gel tube and allowed to centerfusion for 10 minutes at a weight of around 4000xg. Put the serum in an Eppendorf tubes once it has been separated. For a lipid panel analysis and hormone analysis

The patients' medical history was taken via a questionnaire that included height, weight, chronic diseases, and treatments ,The samples FT4, FT3, and TSH were determined using the immunoassay for electrochemiluminescence method (GmbH, Mannheim, Germany).

Lipid profile were measured for both groups included TG, TC, LDL-C and HDL-C , The body mass index was then calculated for each patient measured by using Eq **BMI=Weight(kg)/Height2(meter)**

Serum ghrelin and obestatin levels were determined using ELISA methods (enzyme linked immunosorbent assay) we use human GhRE and OB Eliza kit of Elabscience Company in USA (for reseach use only. Not for use in diagnostic or therapeutic procedures).

***Ethical approval:*** The ethical standards for human experimentation outlined by pertinent national and institutional organizations were met by this study in accordance with the 2008 Helsinki Declaration Amendment. The University of Kerbala's College of Medicine granted clearance for all procedures involving patients or people (code: 155 on June 8, 2023). All participants were also fully informed about the goals and methods of the study. Informed permission was given by research participants prior to their enrollment.

**Statistical analysis:** The data analysis for this work was generated using the graphical Pad Prism. For normal data, scale variables were shown as mean ± 2 standard deviation; for non-normal data, continuous variables were shown as the median and interquartile range. The Shapiro-Wilk test was used to examine the data distribution and determine normality numerically. Analytical statistical analyses revealed significant variations in categorical variables across the parameters. Any outcome of a hypothesis test that had a two-sided p-value of less than 0.01 was taken to be statistically significant.

**Results**

Patients with hypothyroidism had higher mean levels of Thyroid Stimulating Hormone (TSH) (8.37±3.6 mU/L) than the control group (1.17±1.004 mU/L). The pituitary gland secretes TSH, a hormone that causes the thyroid to generate thyroid hormones. When a person has hypothyroidism, their body tries to make up for low thyroid hormone levels by producing more TSH. The main active thyroid hormone, free triiodothyronine (FT3), was found to be lower in the hypothyroid group (60.98±17.01 ng/mL) than in the control group (80.55±14.76 ng/mL) in this investigation. This may be because, as Table 1 shows, fewer patients in this group convert FT4 (thyroxine) to FT3.As with FT3, the

hypothyroid group had lower levels of free thyroid hormone (FT4) (1.22±0.45 mcg/dL) than the control group(1.57±0.26 mcg/dL). Thyroid hormone is mostly stored in FT4 form, which the body converts to FT3

| Table (1) Mean level± SD of the thyroid function test in patients group of hypothyroidism compared to control group | | | | |
|---|---|---|---|---|
| Variable | | Patients Group | Control group | P value |
| Hormones | TSH mU/L | 8.37±3.6 | 1.17±1.004 | 0.006 |
| | FT3 ng/mL | 60.98±17.01 | 80.55±14.76 | 0.003 |
| | FT4 mcg/dL | 1.22±0.45 | 1.57±0.26 | <0.001 |

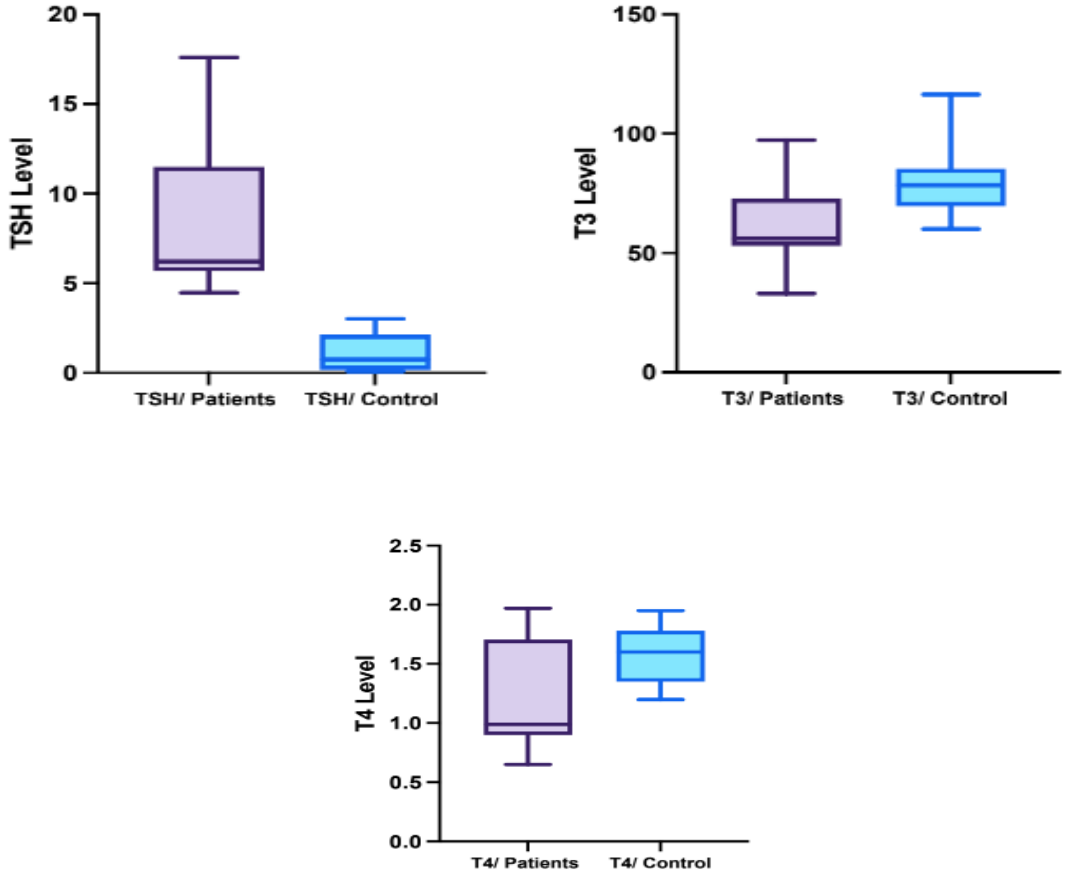


Figure (1) Thyroid function Hormones in patients group of hypothyroidism compared to control group

According to the results, patients with hypothyroidism had significantly higher levels of triglycerides (199.55±83.3 mg/dL) than those in the control group (86.6±33.39 mg/dL). As with TG, Table2& Figure 2 reveal that the hypothyroidism group had higher Total Cholesterol TC values (186.91±40.88 mg/dL) than the control group (132.15±26.48 mg/dL). The

hypothyroid group had lower levels of HDL cholesterol (37.57±8.25 mg/dL) than the control group (56.44±7.49 mg/dL). HDL cholesterol is considered the "good" cholesterol. In contrast to the control group

(37±16.34 mg/dL), the hypothyroid group had greater levels of LDL cholesterol, or the "bad" cholesterol (108.12±29.66 mg/dL). Moreover, the hypothyroid group had higher VLDL (40.57±16.63 mg/dL) than the control group (17.71±6.98 mg/dL).

Table (2): Comparison of the mean level± 2SD of the lipid profile panel between the hypothyroidism patient group and the control group

| Variable | | Patients group | Control group | P value |
|---|---|---|---|---|
| Lipid Profile | TG mg/dL | 199.55±83.3 | 86.6±33.39 | 0.003 |
| | TC mg/dL | 186.91±40.88 | 132.15±26.48 | 0.02 |
| | HDL mg/dL | 37.57±8.25 | 56.44±7.49 | >0.001 |
| | LDL mg/dL | 108.12±29.66 | 37±16.34 | >0.001 |
| | VLDL mg/dL | 40.57±16.63 | 17.71±6.98 | <0.001 |

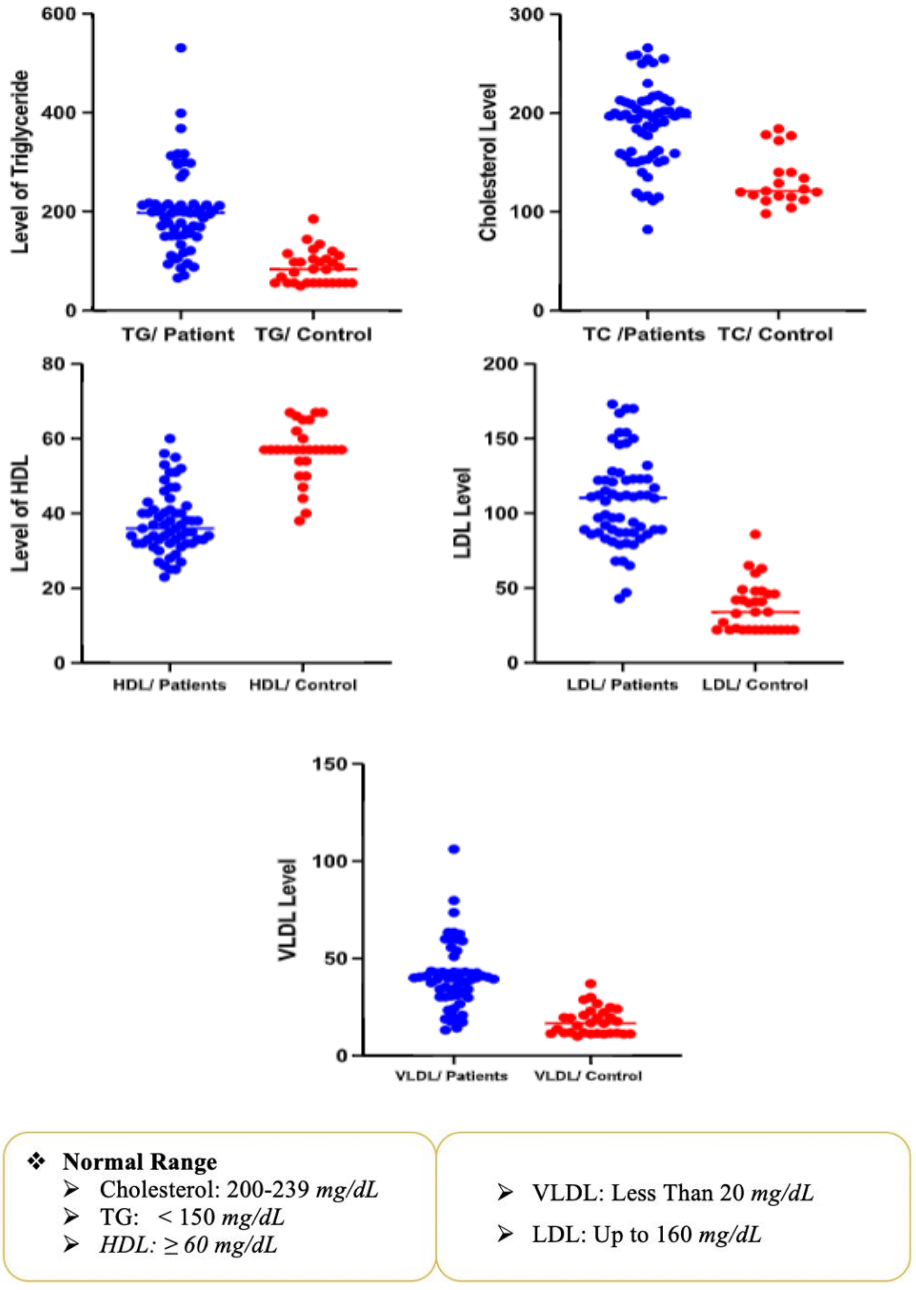


Figure (2) Lipid profile Level in patients group of hypothyroidism compared to control group

The findings showed that the hypothyroid patients' blood ghrelin concentrations were higher—35.26±12.10 ng/ml—than those of the control group, which had values of 26.92±7.58 ng/ml. Similarly, as Table 3 shows, patients with hypothyroidism had greater obestatin levels (10.99 ±4.23 ng/mL) than the control group (7.22 ± 1.32 ng/mL) as presented in Table (3)

Table (3) Mean level± SD of the Adipokines in patients group of hypothyroidism compared to control group

| Variable | | Patients group | Control group | P value |
|---|---|---|---|---|
| Adipokines | Obestatin ng/mL | 10.99 ±4.23 | 7.22± 1.32 | <0.001 |
| | Ghrelin ng/mL | 35.26±12.10 | 26.92±7.58 | <0.001 |

The concentrations of two adipokines, ghrelin and obestatin, in the control and hypothyroid groups are displayed in the above table. It is well known that ghrelin stimulates appetite whereas obestatin suppresses it ,the table demonstrates that the hypothyroid group had greater levels of ghrelin and obestatin than the control group. Nonetheless, for both obestatin and ghrelin, There are significant differences when comparing hormone values in patients compared to healthy people

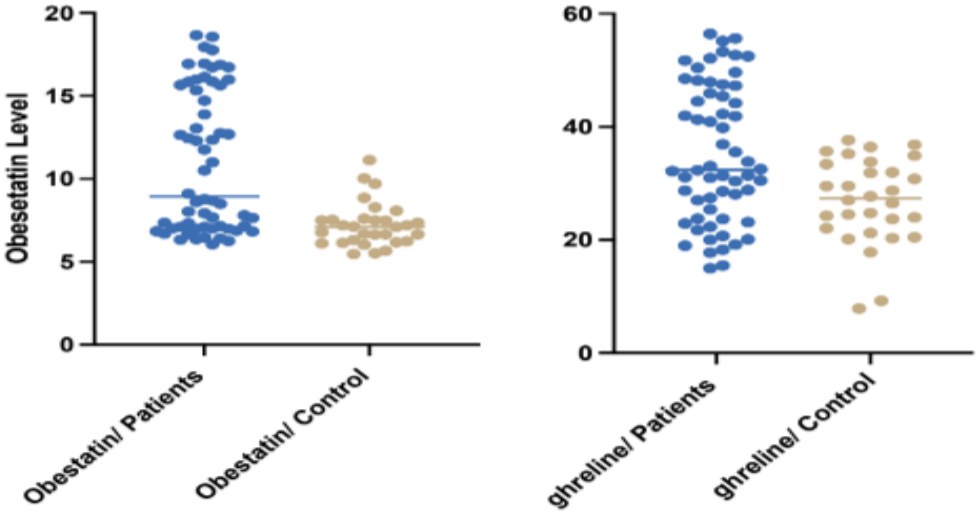


Figure (3) Adipokines Level in patients group of hypothyroidism compared to control group

The findings of a research comparing the levels of obestatin and ghrelin in patients and control people are displayed in the figures. The y-axis displays the obestatin level, ghrelin level while the x-axis displays the two groups. The obestatin level of each individual and ghrelin are shown by a dots .According to the figures, patients' obestatin ,ghrelin levels are noticeably greater than those of the control group. While the dots for controls are generally in the lower range, most of the dots for patients are concentrated in the higher range of obestatin and ghrelin. The median obestatin ,ghrlin level for each group is probably represented by the horizontal line in that group.

As seen in Figure (4), there are modest to moderate relationships between obestatin and

ghrelin and a variety of biomarkers. Ghrelin has a negative link with FT3, FT4, and the amount of HDL, while obestatin has a positive correlation with TSH, TG, TC, LDL, and VLDL. The results point to potential connections between these hormones and the metabolism of cholesterol in hypothyroidism. As shown in Figure, there was a substantial association between adipokines and cholesterol as well as between obestatin and FT3.

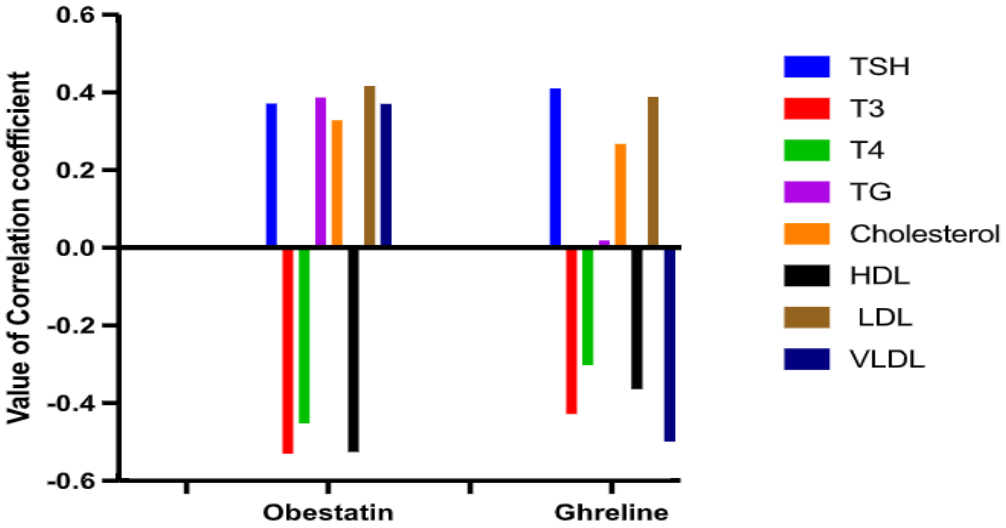


Figure (4) The correlation coefficient ( r ) between obestatin, ghreline and the studied biomarkers among patients group of hypothyroidism

## Discussion

Ghrelin, obestatin, and thyroid function are related, and it is important to take this into account as the thyroid gland's function is linked to the maintenance of energy balance. Adipokines are hormones generated by adipose tissue that control hunger, metabolism, and inflammation. Both biomarkers in this study may differ from one another and show how they affect cases of hypothyroidism .

The most crucial metric for assessing thyroid function is thought to be TSH. As the biological state that is active in plasma, FT3 and FT4 are regarded as significant and sensitive markers for thyroid illness diagnosis [18]

The hypothyroid group had greater levels of LDL, VLDL, triglycerides, and cholesterol than the control group, according to the research findings. Nonetheless, the HDL values of the control group were greater than those of the hypothyroid individuals [19].Investigations on hypothyroid individuals have revealed contradictory results, with serum ghrelin levels being higher, normal, or even lower [20]

Rising ghrelin levels are linked to falling thyroid hormone levels and vice versa. [21]. and increased amounts in individuals with hypothyroidism [22]. To encourage food intake and gastric acid secretion, the enteroendocrine cells in the gastrointestinal tract, primarily the stomach, produce the hunger hormone ghrelin prior to meals. It promotes appetite, causes fat to accumulate, and releases growth hormone [23]. The positive correlation between obestatin and TSH is in line with the elevated TSH hormone levels observed in hypothyroidism. This suggests a possible relationship between obestatin and the thyroid hormone axis. [24]. It is well known that obesity decreases appetite. It decreases hunger by acting on the

hypothalamus, a part of the central nervous system. In hypothyroidism, a condition where there is already a lowered metabolic rate and the possibility of impaired appetite control, elevated obestatin levels may potentially have an impact on appetite control. While too much obestatin may offset some of the effects of excessive ghrelin on appetite, the total effect depends on the balance between these hormones [25]. The present study was restricted in its capacity to elucidate the mechanism or processes by which gastrointestinal peptides are influenced by thyroid hormones and TSH, and vice versa. The bioactivity, synthesis, and/or metabolism of obestatin and ghrelin hormone are now believed to be modulated by thyroid hormone. Moreover, metabolic hormones originating in the stomach may regulate pituitary, thyroid, and brain function. However, it is yet unknown how obestatin affects the thyroid axis, thus further research is required [26]

## Conclusion

According to the study, hypothyroidism is linked to high serum levels of obestatin and ghrelin as well as a dysfunctional lipid profile, which suggests serious metabolic consequences for those who have this illness. These results highlight the need for more research into the metabolic and hormonal abnormalities associated with hypothyroidism.

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