

Thyroid stimulating hormone and leptin levels and severe growth retardation among β -thalassemic patients

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ABSTRACT

Objective: It has been proposed that Thyroid Stimulating Hormone (TSH) influences leptin secretion from adipocytes. We evaluated the association between TSH and leptin levels in thalassemic patients with growth retardation.

Methodology: Blood samples were collected from 30 major thalassemic patients and 24 normal subjects (range: 12 - 20 y). Both Leptin and TSH were measured by Enzyme-Linked Immunosorbent Assay (ELISA) method. The anthropometric data were collected based on standard methods. Independent sample t-test and Pearson's correlation were used to analyze data.

Results: Patients had severe growth retardation. Mean concentration of leptin in thalassemic patients was significantly lower than normal subjects (2.26 ± 2.61 vs 13.14 ± 15.95 ng/ml). The mean value of serum TSH concentration in β -thalassemic patients was higher than normal subjects. But the difference was not statistically significant ($P = 0.146$). There was no marked relationships between TSH and leptin concentrations in thalassemic patients ($r = -0.022$, $P = 0.909$) and in control group ($r = 0.289$, $P = 0.214$).

Conclusion: In both β -thalassemic patients and normal group leptin secretion is not affected by TSH concentration.

KEY WORDS: β -Thalassemia, Leptin, TSH.

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INTRODUCTION

Leptin is a protein secreted by adipose tissue which has important effects in regulating body weight, metabolism and reproductive functions.¹⁻³ Human adipose tissue also secretes interleukin-6 (IL-6)⁴, which can improve the natural response to infection and disease.⁵

Recently it has been showed that (TSH) induces interleukin-6 secretion by adipocytes.⁶ In regard to interleukin-6 role in regulating leptin secretion⁵, TSH can be considered as the indirect regulator of leptin secretion from adipose tissue.⁷ β -Thalassemia is an inherited autosomal recessive blood disorder.⁸ The prevalence of thalassemia is influenced geographically.⁹ About 150 million people worldwide carry β -thalassemia genes. The genes are particularly prevalent in Italy and Greece. Other regions with the high gene frequency are

Sardinia (11-34%), Sicily (10%), Greece (5-15%), and Iran (4-10%).⁹ β -Thalassemia is the most common subdivision of thalassemia in this country.¹⁰ Patients with β -Thalassemia major often present with endocrine abnormalities too.¹¹ There are few studies about TSH or Leptin (but not their association) in Iran among β -Thalassemic patients: one study in Yazd city showed that 7.5% of 52 β -Thalassemic patients with mean value of age of 10.8 year had hypothyroidism.¹²

Another study on 58 patients revealed the high incidence of hypothyroidism in poor control subjects.¹³ Thus because of abnormalities in both serum TSH and leptin concentrations, it has been hypothesized that β -Thalassemic patient's leptin deficiency may be the result of abnormal TSH concentration. Some studies about the relation between TSH and leptin in different groups of patients in different countries are available.¹⁴⁻¹⁷ To the best of our knowledge and updated literature review about studies on association between TSH and leptin concentration, it has been found that none of them were performed among β -Thalassemic patients.¹⁴⁻¹⁷

METHODOLOGY

The study was conducted in accordance with ethical procedures and policies approved by the Ethical Committee of Ahwaz Jondishapour University of Medical Sciences, Ahwaz, Iran. Informed consent of all patients and normal subjects was taken. The study group consisted of 30 β -Thalassemic major patients who were referred to Thalassemia Research Center of Ahwaz Jundishapour University of Medical Sciences, and 24 normal subjects as a control group. All β -Thalassemic patients and normal subjects were at the same range of age (12-20y). Five ml blood was obtained from each person. Serums were separated and stored at -20 °C. Leptin and TSH concentrations were determined by EnzymeLinkedImmunosorbent Assay (ELISA) method. Biovendor kit was used to measure leptin concentration and Monobind kit was used to determine TSH concentration. The normal range of serum leptin was 8-23 (ng/ml) in males and 12-23 (ng/ml) in females.¹⁸ The normal range of serum TSH concentration was defined as 0.4-6.2 (mu/l) both in males and females.¹⁹ Weight was determined to the nearest 0.01 kg.

Growth of the pediatric subjects was compared with World Health Organization (WHO) Child Growth Standards 2007 reference data. Weight for age, height for age and BMI for age were calculated using AnthroPlus software released by Department

of Nutrition, WHO, Switzerland. These analyses provided percentile (length-for-age, and Body Mass Index (BMI)-for-age).

All data were analyzed using the Statistical Package for the Social Sciences (SPSS) software (version 17.0, Nie, Bent & Hull, USA). The means of continuous variables were compared by Independent Sample t-test. Correlations were analyzed by use of Pearson's Correlation.

RESULTS

Mean of age was 14.1 year in case group and 17.04 year in control group. Although the mean value of serum TSH concentration in β -thalassemic patients was higher than normal subjects, but the difference was not statistically significant ($P=0.146$) (Table-I). TSH concentration was seen higher than normal in 16% of β -thalassemic patients. Mean concentration of leptin in β -thalassemic patients was significantly lower than normal subjects ($P=0.005$) (Table-I). All of 30 β -Thalassemic patients had leptin deficiency (in comparison with normal range). No significant correlation was found between leptin and TSH in patients ($r=-0.022$, $P=0.909$) and control group ($r=0.289$, $P=0.214$). The anthropometric analysis showed that all the subjects had short stature. The positive relationship between BMI and leptin concentration in normal subjects ($P=0.009$) was not found among thalassemic patients ($P=0.35$).

DISCUSSION

The present study was aimed to investigate the possible association between TSH and leptin secretion in β -Thalassemic major patients. Our investigation about decreased leptin levels is in agreement with the Karachaliou et al findings on 33 β -Thalassemic patients with the mean age of 19.3 years.¹¹ Another study on 219 adults with β -Thalassemic patients reported that adipocytes were unable to maintain adequate leptin production.¹⁴ However, these two studies^{11,14} did not evaluate the association between TSH and leptin concentrations. The observed short stature, low weight and delayed puberty in our study might be due to leptin deficiency.^{11,18}

Table-I: Mean values of BMI, leptin and TSH

	Case <i>n</i> =30	Control <i>n</i> =24
BMI(m/kg ²)	19.10± 4.01	21.21± 6.48
Leptin(ng/ml)	2.26±2.61	13.14±15.95
TSH(mu/l)	4.06±3.35	2.58±0.51

However, toxic effects of iron on adipocytes of β -thalassemic patients may influence leptin secretion.¹¹ Determination of main cause of leptin deficiency is needed in order to decrease β -Thalassemic patient's problems in growth and puberty. Because of TSH regulating role of T3 and T4 (two main body metabolism regulating hormones) and in regard to effects of leptin on metabolism, it has been proposed that leptin secretion from adipose tissue may be affected by TSH concentration (like Thyroid hormones).⁷ Furthermore, it has been demonstrated that TSH regulates interleukin-6 secretion from adipose tissue⁴ and interleukin-6 regulates leptin secretion.⁵ Hence in this study, we hypothesized that TSH concentration is one main regulator of leptin secretion. But in this study the correlation was not statistically significant ($P=0.146$). Soheilikhah et al showed 7.5% hypothyroidism in 53 β -Thalassemic patients.¹² The abnormalities in both leptin and TSH secretion in β -thalassemic patients supports the idea about the correlation between TSH and leptin. Botella demonstrated that in women with differentiated thyroid carcinoma, TSH withdrawal results in an increase in leptin concentration.¹⁹ However, Cecoli studies on level of leptin at 20 hours after the last rhTSH administration on 15 thyroidectomized patients, showed no regulating role of TSH on leptin concentration.⁶ The relationship between TSH and leptin levels in different patients has been widely studied, but the results are still controversial.¹⁴⁻¹⁷ Among our subjects there was no statistically significant relation between TSH and leptin concentrations (both in patients and normal subjects).

CONCLUSION

The β -Thalassemic patients who had severe growth retardation, showed abnormal TSH concentrations and abnormal leptin concentrations. But TSH concentrations under normal range were not the cause of leptin deficiency in β -Thalassemic patients. More investigation is recommended in order to determine the main cause of leptin deficiency in β -Thalassemic patients.

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