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Relationship between thyrotropin and BMI in patients with subclinical hypothyroidism

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Abstract
Subclinical hypothyroidism is an asymptomatic illness characterized by elevated serum thyrotropin and normal values of thyroid hormones. Currently, epidemiological studies have suggested a positive relationship between serum thyrotropin and body mass index, although the primary source of this relationship is unknown. The aim of this study was to determine whether serum thyrotropin concentrations are associated with body mass index in patients with subclinical hypothyroidism. This is an observational, cross-sectional and analytical study, carried out in the Mexican Social Security Institute's General Hospital No. 1 in Chihuahua. Weight, height, concentrations of serum thyrotropin, age, sex and smoking status data were collected from the clinical records of 128 patients diagnosed with subclinical hypothyroidism. We found that in higher categories of BMI we found higher means of serum thyrotropin: 5.92 µIU/mL for normal BMIs, 6.14 µIU/mL for overweight, 6.41 µIU/mL for obesity class I, and 7.03 µIU/mL for obesity classes II and II, *P* for trend <0.001. In the multiple linear regression model, which adjusted for age, sex and smoking status, it was found that an increase of one percent in serum thyrotropin resulted in a body mass index increase of 0.08 units, *P* <0.001. In conclusion, serum thyrotropin and BMI are positively related in patients with subclinical hypothyroidism. It is recommended to take this into account in the comprehensive care of these patients.

Keywords: Thyrotropin, TSH, BMI, subclinical hypothyroidism

Introduction

Body weight has been considered as the main result of entering energy extracted from food consumed less energy expenditure, which it is divided into basal metabolism, the thermic effect of food, and physical activity [1]. However, recent research suggests that genetic and environmental factors may modify body weight [2]. The study of factors associated with excess weight has become a crucial objective for public health. According to the World Health Organization, obesity has doubled over the world since 1980. In 2014, about one in four people over 18 was overweight [3].

Thyrotropin, better known as the thyroid stimulating hormone (TSH), is produced by the pituitary gland and functions to notify the thyroid to produce and release blood thyroid hormones. Studies have suggested that high concentrations of serum TSH was positively related to body mass index (BMI) [4-7]. This relationship has been observed in subjects with thyroid disease, as hypothyroidism and hyperthyroidism, and those with normal function [5,8]. A high concentration of TSH has been linked, by itself, to an increased risk of cancer, dyslipidemia, ischemic heart disease and all-cause mortality [9-11].

The aim of this study was to determine whether serum TSH concentrations are associated with BMI in patients diagnosed with subclinical hypothyroidism.

Materials and methods

Design and study population

Between January and December 2014, clinical records of patients from the Mexican Social Security Institute's (IMSS) General Hospital No. 1 in Chihuahua City were selected. Men and women diagnosed with subclinical hypothyroidism over the age of 18 were included. Those who had had treatment with thyroid function modifiers, e.g. Amiodarone, Lithium or Interferon, were excluded.

Determination of serum TSH

Serum TSH concentrations were determined using the chemiluminescence technique with support of Architect i2000SR equipment (Abott Diagnostics®) in the hospital laboratory. The complete thyroid profile was determined with a TSH level greater than 4.5 µIU/mL, and serum free T_4 levels in the normal range (0.8-1.2 ng/dL).

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Somatometric measurements

The evaluation of the weight and height were carried out by nursing staff assigned to the endocrinology division. A scale with a stadiometer (Clinic 220, Nuevo León®) was used. BMI was determined by dividing weight in kilograms over height in meters squared (kg/m^2). In addition, data were obtained regarding age in completed years, sex (male/female) and consumption of tobacco (no/yes). This study was approved by the 801st Local Committee for Research and Ethics in Health Research of the IMSS.

Statistical analysis

Bivariate and multivariate analyses were carried out using simple and multiple linear regression models, respectively. Serum TSH was logarithmically transformed to meet the assumptions of the models. The beta coefficients and confidence intervals of the regressions were interpreted as follows: an increase of one percent in the independent variable increases (or decreases) the dependent variable by (coefficient/100) units [12]. *P* values <0.05 were considered statistically significant. Analyses were carried out with STATA 11.2.

Results

Clinical characteristics of patients are presented in Table 1. The study population was formed mainly by women (85.2%). Mean age was higher in women, 44.6 versus 44.2 years. Men had higher average concentrations of TSH and BMI, with 6.82 µIU/mL and 31.1 kg/m2 respectively. A higher proportion of men reported to smoke compared with women, 47.4% versus 39.5%.

TSH serum levels categorized by nutritional status are presented in Table 2, mean and median increase in the higher BMI categories, *P* for trend <0.001.

Table 1. Clinical Characteristics of Patients with Subclinical Hypothyroidism by Sex

Sex	Patients n (%)	Age Years	TSH µIU/mL	BMI kg/m^2	Smoking status n (%)
Men	19 (14.8%)	42.2 (21 - 61)	6.82 (5.18 – 9.50)	31.1 (20.3 – 43.5)	9 (47.4%)
Women	109 (85.2%)	44.6 (18 - 65)	6.24 (5.09 – 10.55)	29.9 (19.1 – 43.1)	43 (39.5%)

Sample size (n) and smoking status are presented in proportions. Age, TSH and BMI are presented in means over their ranges.

Table 2. Serum levels of TSH classified by categories of nutritional status n Media and middle ranges and interquartile ranges

	n	Ranges	Mean & SD	Median & Interquartile ranges
Normal	21 (16.4%)	5.18 – 9.15	5.92 (0.88)	5.80 (5.36 – 6.10)
Overweight	37 (28.9%)	5.09 – 10.55	6.14 (1.21)	5.90 (5.38 – 6.20)
Obesity class I	54 (42.2%)	5.19 – 9.94	6.41 (1.06)	6.26 (5.44 – 7.08)
Obesity classes II and III	16 (12.5%)	5.23 – 10.20	7.03 (1.34)	6.66 (6.22 – 7.82)

Nutritional status is presented as the World Health Organization classification; Normal 18.5 to 24.9, Overweight 25 to 29.9, Obesity Class I 30 to 34.9, Obesity Class II 35 to 39.9 Obesity Class III 40.0 to 44.9. [13] *P* for trend <0.001.

In Table 3, bivariate analysis showed shows that, when serum TSH increased by one percent, BMI increased by 0.09 units, *P* <0.001. In multivariate analysis, after adjusting for other variables such as age, sex and smoking status, it was found that, with an increase of one percent in serum TSH, BMI increased by 0.08 units, *P* <0.001.

Table 3. Beta Coefficients of Regression Models that Analyze the Relation Between the Natural Logarithm of Serum TSH and Body Mass Index

	Coefficient	Confidence Intervals 95%	*P*-value
Bivariate analysis			
Log Serum TSH	9.08	4.23 – 13.93	<0.001
Multivariate analysis			
Log Serum TSH	8.58	3.87 – 13.30	<0.001

In bivariate analysis, BMI was the dependent variable and natural logarithm of serum TSH the independent variable, a simple linear regression model was used. In multivariate analysis, BMI was the dependent variable and the logarithm of serum TSH the independent variable, a model of multiple linear regression adjusted for age, sex and smoking status was used. The interpretation of the coefficients corresponding to an increase of one percent in the independent variable increases (or decreases) to the variable dependent on (□1 / 100) units

Discussion

In these study carried out with 128 patients from General Hospital No. 1 of Chihuahua City, it was found that there is a positive and statistically significant association between the variables of interest. Patients with higher serum TSH concentrations showed on average a higher BMI; these results are similar to those reported by other research studies [4-7].

The study by Solanki A. et al [5] found that individuals with higher BMI had higher levels of serum TSH and that this trend continued from the underweight to the obese group (p <0.001). Research conducted by Milions et al [7] reported that, in euthyroid subjects, variations of normal thyroid function was associated with changes in body weight. Milions et al. reported a significant positive correlation between BMI and thyroid function in women; however, the correlation in males was not statistically significant. The authors suggest that the thyroid function has a primary source, while the changes in body weight are secondary to the thyroid function, and that the reason may be single or multifactorial, although the biological mechanism is not fully known [7].

On the other hand, in the study conducted by Nyrnes A. et al., [6] which was one of the first studies to analyze the data by smoking status, non-smoking men in the highest quartile of TSH had, on average, a BMI 0.4 kg/m^2 higher than those in the lowest quartile, whereas this difference in non-smoking women was 1.4 kg/m^2. In this study no relationship between the variables of interest was found among smokers [6]. In the research carried out by Gupta et al., a statistically significant correlation between serum TSH and BMI in both women with subclinical hypothyroidism and euthyroid women was found, although this study did not conduct more complex analyses to include other variables [14].

Other investigations have failed to establish the relationship between serum TSH and BMI. For example, Montoya-Morales et al. mentioned that it was not possible to establish this relationship in a group of patients with morbid obesity. Authors attribute it the use of metformin by patients, although it could also be because most patients were classified with class III obesity and a minority with classes IV and V (38, 9 and 5 subjects respectively), which could cause lack of variability in BMI. However, it is difficult to know because the authors did not report the types of statistical analyses performed [15].

Age is a factor of confusion because a gradual increase in serum TSH has been associated with age in both men and women. [16] Likewise, age has been associated with BMI [17]. The positive relationship between TSH and BMI could be due to the fact that the TSH stimulates differentiation of preadipocytes, which stimulate adipogenesis. [18] Leptin, a hormone that regulates the consumption and storage of energy, is another possible explanation for this association because it could partially control the thyroid function by maintaining the expression of thyrotropin releasing hormone (TRH) in the paraventricular nucleus [19].

In this context, it is important to determine if slightly elevated TSH concentrations can cause obesity or if the opposite occurs—that is, if the states of overweight and obesity can promote thyroid dysfunction, causing an increased risk of subclinical hypothyroidism [20]. The results of studies and longitudinal data show a positive association between the values of serum TSH and BMI [6]. However, in this relationship it is controversial what constitutes the cause and the effect; [21] hypothyroidism is associated with a moderate increase in weight gain, and it has recently been described that changes in TSH could be result of excess weight [22].

In the literature review, few studies were found that examined the relationship between serum TSH and BMI in Latino populations [15,23]. One of the study's limitations might be that clinical records of patients were used, which means that the data may present measurement errors. Due to its design, the study cannot determine causality, so it is recommended to carry out further research.

Conclusions

The study of patients of endocrinology at General Hospital No. 1 in Chihuahua City found a positive relationship between serum TSH and BMI; an increase by one percent of TSH matches a BMI increase of 0.08 units after adjusting for potential confounders. It is recommended to take this into account in the comprehensive treatment of these patients.

Declaration of interest

The authors declare that there is no conflict of interests regarding the publication of this article.

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