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ORIGINAL ARTICLE

High Thyroid-stimulating Hormone Levels Increase Proinflammatory and Cardiovascular Markers in Patients with Extreme Obesity

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Background and Aims. Obesity is an important health problem worldwide and many studies have suggested a relationship between obesity and thyroid function, with controversial results. Interestingly, high TSH levels have been involved with the presence of inflammatory state and risk for developing cardiovascular diseases in hypothyroid and obese patients. The aim in this work was to determine the prevalence of hypothyroidism in patients with extreme obesity and to determine whether their TSH levels were related to increased serum levels of inflammatory and cardiovascular markers.

Methods. A cross-sectional study in 101 patients with extreme obesity (BMI ≥40) was performed. Anthropometric (weight, height and waist circumference) and biochemical (fasting glucose, glycosylated hemoglobin, triglycerides, total cholesterol, LDL-C, HDL-C and insulin) parameters were measured. TSH and FT4 levels as well as clinical exploration for diagnosis of hypothyroidism were carried out. Serum concentration of IL-10, IL-6, adiponectin, resistin, leptin, ICAM-1, VCAM-1 and E-selectin were determined.

Results. A high prevalence for diabetes (37.6%), prediabetes (50.5%), dyslipidemia (74.3%), hypertension (61.4%) and hypothyroidism (48.5%) was observed in patients with extreme obesity. The presence of hypothyroidism increased serum concentration of proinflammatory cytokines IL-6 and leptin and decreased the antiinflammatory cytokine adiponectin. In addition, serum TSH levels showed a correlation for waist circumference, weight, BMI, A1c, insulin, IL-6, leptin, ICAM-1 and E-selectin.

Conclusion. There is a high prevalence for hypothyroidism in patients with extreme obesity. High levels of TSH contribute to elevate proinflammatory and cardiovascular risk markers, increasing the risk for development of cardiovascular diseases.

Key Words: Extreme obesity, Hypothyroidism, TSH, Cardiovascular markers.

Introduction

Obesity has become one of the most important problems in public health worldwide and is considered a risk factor for the development of several diseases such as type 2 diabetes (T2D), cardiovascular disease (CVD), insulin resistance, hypertension, asthma, dyslipidemia, among others (1). In Mexico, obesity has increased at an alarming rate affecting

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up to 32.4% of the adult population. Interestingly, the prevalence of extreme obesity (obesity class III), a type of severe obesity that can be disabling, has increased from 1.7% in 2000 to 3.4% in 2012 (2). The pathophysiology of obesity is complex and genetic, environmental, behavioral, psychological and hormonal factors have been described to influence the development of obesity (3,4).

Thyroid hormones are involved in the modulation of metabolic processes such as appetite and rest energy expenditure (REE), involving thyroid dysfunction with the pathophysiology of obesity (5). Hypothyroidism is characterized by high levels of thyroid stimulating hormone (TSH) and low (overt hypothyroidism) or normal (subclinical hypothyroidism) levels of free thyroxine (FT4) (6). Hypothyroidism has been associated with weight gain, increasing body fat mass by reduction of REE and water retention (7). In severe obesity, a high prevalence of overt and subclinical hypothyroidism has been reported (19.5%) (4,8); however, the association between thyroid function and the pathophysiology of obesity has controversial results (9,10).

It is known that some of the comorbidities observed in obesity are related to the presence of an inflammatory state produced by abnormal accumulation of body fat, which is an important source of cytokines (11−13). This inflammatory state is augmented in patients with extreme obesity and contributes to the risk for cardiovascular disease development (14). Additionally, an inflammatory process was observed in patients with hypothyroidism, which has been associated with endothelial dysfunction and atherosclerosis development (15−18), suggesting a possible role of hypothyroidism for development of cardiovascular diseases (19,20). At this point, previous studies proposed that high serum levels of thyroid stimulating hormone (TSH) observed in hypothyroidism could be a possible predictive factor for coronary heart disease (CHD) and mortality associated with CHD (21,22).

Hypothyroidism and extreme obesity contribute to the establishment of an inflammatory state that is an important risk factor for cardiovascular disease. We developed a clinical study to determine the prevalence of hypothyroidism in patients with severe obesity and whether their TSH values contribute to elevate proinflammatory and cardiovascular risk markers, increasing the risk for development of cardiovascular diseases.

Materials and Methods

Subjects

We performed a cross-sectional study with 101 (21 males and 80 females) evaluated before bariatric surgery at the Obesity Clinic in the Hospital de Especialidades, Centro Medico Nacional Siglo XXI, IMSS in Mexico City. All the patients were >18 years of age and had extreme or grade III obesity defined by body mass index (BMI) ≥40 kg/m^2 in agreement with World Health Organization criteria. A multidisciplinary team composed of experts in endocrinology, clinical nutrition, psychiatry and internal medicine completed the evaluation. Patients with previous cardiovascular events were excluded from the study. The Institutional Research Scientific and Ethics Committee (IMSS 2014-785-005) approved this study and all participants signed informed consent.

Anthropometric and Clinical Evaluation

Weight was taken with a digital scale (Seca, Hamburg, Germany) and height was measured with a stadiometer (Seca 225). Waist circumference (WC) was measured at the midpoint between the lowest rib and the iliac crest in standing position. BMI was calculated as the weight divided by height squared (kg/m^2). Blood pressure was taken three times in the forearm with a mercury sphygmomanometer. We searched for comorbidities such as T2D and prediabetes in agreement with the American Diabetes Association guidelines for diabetes. Hypertension was established with blood pressure ≥140/90 mmHg in agreement with the American Heart Association's recommendations. Dyslipidemia was defined as triglycerides concentration >150 mg/dL or HDL-cholesterol (HDL-C) ≤40 mg/dL or any diseases under current medical treatment.

Table 1. General anthropometric and metabolic characteristics in the morbid obese population

Factor	*n* = 101
Age (years)	45 ± 0.4
Gender *n* (%)	
Male	21 (20.8)
Female	80 (79.2)
WC (cm)	130 ± 15.3
Weight (kg)	116 (104−135)
BMI (kg/m^2)	46 ± 8.5
Blood pressure (mmHg)	
Systolic	120 (110−120)
Diastolic	80 (70−80)
T2D *n* (%)	
No	12 (11.9)
Yes	38 (37.6)
Prediabetes	51 (50.5)
Dyslipidemia *n* (%)	
No	26 (25.7)
Yes	75 (74.3)
Hypertension *n* (%)	
No	39 (38.6)
Yes	62 (61.4)
Thyroid illness *n* (%)	
No	49 (48.5)
Hypothyroidism	49 (48.5)
Hyperthyroidism	3 (2.9)

WC, waist circumference; BMI, body mass index; T2D, type 2 diabetes. Note: Values represent the mean ± SD or median (p25−p75) for the continuous variables and frequency (%) for categorical variables.