PREVALENCE OF OBESITY IN ADULT PATIENTS WITH DIABETES MELLITUS TYPE 2 AND AUTOIMMUNE CHRONIC THYROIDITIS

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Abstract

Background & Aims: The higher prevalence of obesity is associated with a number of cardiovascular risk factors. The purpose of this study is to assess the prevalence of obesity in adult patients with diabetes mellitus (DM) type 2 and autoimmune chronic thyroiditis (ACT). Methods: The studied group was represented by 78 adult patients with DM type 2 and ACT (70 women and 8 men). Were used clinical, biochemical and imaging parameters. Results: 53 (67.94%) (45 women and 8 men) had different types of obesity. The obesity was more frequent in men than in women (100% vs. 64.28%, p = 0.04, X² = 4.2). In function of obesity type, android obesity was prevailed (94.34 % of cases), following by gynoid obesity type (5.66 %). Also, 26.92 % were overweight (all women). Regarding the type of android obesity, 39.62 % had type I, 37.73 % type II and 22.64 % type III. Also, 64.15 % had hypertension and dyslipidemia 79.24 %. Conclusions: In patients with DM type 2 and ACT the obesity prevailed in men. It was android type, represented an increased risk of cardiovascular morbidity-mortality, particularly for atherosclerotic cardiovascular disease. The association of thyroid disease, which over time can evolve with hypothyroidism, is an additional risk factor for atherosclerotic cardiovascular disease.

Keywords: Prevalence, obesity, adults, autoimmune chronic thyroiditis, diabetes mellitus type 2

Introduction

Obesity is a disease characterized by weight gain due to the body fat and currently defined by a body mass index value (BMI) ≥ 30 kg/m².

Obesity is a major public health problem in both developed countries and the developing ones, with a higher frequency, reaching affect all age groups and all social categories. In recent decades, obesity has reached
epidemic proportions, becoming the major cause of morbidity and premature mortality worldwide. According to WHO, worldwide, approximately 1 billion adults are overweight and over 300 million are obese (Şerban et al, 1999).

Significant progress in the epidemiology of adult obesity was its standardization by the WHO in 1988. According to this classification, are considered obese the people with BMI ≥ 30 kg/m² and those with BMI between 25 and 30 kg/m², overweight (Şerban et al, 1999).

In most EU countries, the number of new cases of obesity has increased rapidly in recent decades, more pronounced in males. In Central and Eastern Europe (Russia, Czech Republic, countries of the Former Yugoslavia) it was observed a much higher frequency in women than in men (Şerban et al, 1999).

Age is the most important factor influencing the prevalence of obesity. Its frequency increases parallel with age, at least up to 50-60 years and over 70 years it is recording a decrease, in both men and women (Şerban et al, 1999).

In developing countries, the peak prevalence is recorded at 0-45 years, while in economically developed countries; it is recorded usually after the age of 60 years (Şerban et al, 1999).

Regarding gender, there is a tendency of higher rates of obesity in women (with obvious differences in Arab countries, African continent, South America, Mexico and Central Europe), but also in other countries such as Malta, Cyprus, Greece, Austria, Ireland, its frequency is higher in men (Şerban et al, 1999).

Overweight is generally more common in men (Şerban et al, 1999).

WHO recognizes obesity as a disease of epidemic proportions in many countries. Its prevalence is increasing. Obesity has also become a problem in children and teenagers, recent data suggest that 8% are obese (Bundred et al, 2001). It seems that it occurs as a consequence of the decrease in daily physical activity and increased caloric intake, especially intake of fast food products.

WHO MONICA study conducted in Europe in 39 countries on subjects aged 35-64 years reported a prevalence of obesity of 10-20% for men and 15-20% for women. Overweight were more common among men, obesity and overweight frequency was over 50% in Europe (Uwaifo et al, 2002).

In our country, the prevalence of obesity is 17% in rural and 20% in urban, being more common in women; in children ranges between 5-10% (Pencea et al, 2004).
Uziceni study showed that at adult population overweight met in 22.8% of cases, and obesity in 25.2%, totaling 48% of cases (Pencea et al, 2004).

The increased prevalence of obesity is found in USA: 67% of men are obese and 27.5% overweight, while 62% of women are obese and 27.5% overweight (Pencea et al, 2004).

Obesity is also responsible for the increase of type 2 diabetes, 90% of patients with type 2 diabetes are obese. The risk of developing diabetes increases with increasing BMI (risk is 40-80 times higher at a BMI > 40 kg/m² than to a BMI < 21 kg/m²). Furthermore, overweight (BMI > 25 kg/m²) occurs in 64% of cases in men and in 74% of cases in women (Wilding, 2003).

Although obesity is a risk factor for developing diabetes, only 50% of obese develop diabetes (Wilding, 2003).

In the case of thyroid disease, obesity is secondary to those who evolve with hypothyroidism due to the decrease of the basal metabolic rate.

Hashimoto thyroiditis is a chronic autoimmune disease which in time can evolve with hypothyroidism. Weight gain due to the hypothyroidism is around 10% by weight from euthyroid stage and it is attributed to accumulation of the fluid in the interstitial tissue.

Obesity is associated with an increased risk of diabetes, dyslipidemia, kidney disease, cardiovascular disease, all-cause mortality, and cancer (Golden et al, 2009). Thus, severe obesity is an important cause of premature mortality among middle-aged adults (Mehta et al, 2009). Moreover, obesity, especially central obesity, is linked to many endocrine abnormalities (Kokkoris et al, 2003), including thyroid dysfunction (Reinehr, 2010). This is not surprising because T₃ regulates energy metabolism and thermogenesis and plays a critical role in glucose and lipid metabolism, food intake, and the oxidation of fatty acids (Reinehr, 2010).

Material And Method

Method

Investigated Population

78 patients with DM type 2 (70 F and 8 M), aged between 18 and 79 years represented the studied group.

Methods Of Investigation

The methods of investigation were represented by clinical data - case history, current status, anthropometric measurements: waist circumference and body mass index (BMI), determination of systolic and diastolic blood pressure, imagistic- thyroid ultrasound, biochemical - for glycemic
Investigation of glycemic balance

**Determination of plasma glucose** was performed by enzyme technique with glucosooxidasis. Normal values were taken between 70 - 110 mg%; diabetes mellitus - values equal or over 126 mg%, impaired glucose tolerance - values between 110 - 125 mg% and the OGTT at 2 h between 140 - 200 mg% and impaired fasting glucose - values between 110 - 125 mg% and OGTT at 2 h under 140 mg%.

**Determination of HbA1c** was achieved through the DiaStat for measuring HbA1c reported to the total Hb.

Investigation of lipid metabolism

**The "fasting" lipid profile** in the peripheral blood was appreciated by determining the total cholesterol (TC), triglyceride (TG), HDL-cholesterol (HDL-C), LDL-cholesterol (LDL-C) and the ratio TC / HDL-C. We used laboratory methods based on the enzyme principle, both for TC (Dimension AR, Dade Behring Inc., USA) and TG and HDL-C (REflectron IV, Roche, Switzerland). The level of LDL-C was calculated according to the Friedwald's formula: LDL = TC - (HDL + TG / 5). Were considered normal: TC < 200 mg%, TG < 150 mg%, HDL-C > 45 mg%, LDL-C < 115 mg%, TC / HDL-C between 2-3.5.

Investigation of the thyroid gland

To determine the **TSH level in plasma, the free fraction of triiodotironin (FT₃), and the plasma free fraction of thyroxin (FT₄)** were performed a quantitative method ARCHITECT; witch is an immunological method, Chemilumnescent Microparticle Immunoassay (CMIA). Normal values were following: TSH = 0.465-4.68 Miu/ml, FT₃ = 3.69 -10.4 pmol/l, FT₄ = 10-28.2 pmol/l.

The immunological parameters were represented by autoimmune thyroid markers - antibodies (antiTPO and antiTg antibodies).

To determine **serum levels of antiTPO antibodies** it was used the kit AxSYM antiTPO, an immunological method (Microparticle Enzyme Immunoassay) (MEIA). Normal values: antiTPO antibodies <35 IU/ml.

To determine **serum levels of antiTg antibodies** it was used the kit AxSYM antiTg, a MEIA method as well (Microparticle Enzyme Immunoassay). Normal values: antiTg antibodies <55 IU/ml.


**Thyroid ultrasound** was performed in all cases and allowed us to measure thyroid volume, thyroid study and the changes in parenchyma’s density. An increased density, uniform, characterizes normal thyroid parenchyma easily distinguished from the neck muscles that are hypo dens. Inflammatory processes and autoimmune pathology appears hypo dens. The scale was assessed as being discreet +, moderate ++ and marked +++.

In the autoimmune thyroid disease the parenchyma of the gland appears hypo dens. Chronic autoimmune thyroid disorder appears with a hypoecogenity of the parenchyma and normal or increased thyroid volume.

**Determination of blood pressure (BP)**

Blood pressure was measured using conventional sphygmomanometers (Didytest, Germany), respecting following conditions: "fasting", subject seated with left arm raised to the heart, physical rest for at least 5-10 min without the subjects smoke or drink coffee before the determination. The studied values were arithmetic mean of BP values obtained by three successive determinations.

**Determination of body mass index (BMI) and waist circumference (WC)**

We determined the subjects body weight (kg) and height (m) and we calculate BMI according to the formula: BMI (kg/m²) = body weight/height². The results were interpreted as follows: normal (18.5 to 24.9 kg/m²), overweight (25 to 29.9 kg/m²), obesity type I (30 to 34.9 kg/m²), obesity type II (35 to 39.9 kg/m²), obesity type III (> 40 kg/m²), underweight (<18.5 kg/m²) (De Backer, 2003, MacLean, 2000).

Waist circumference was determined with a centimeter by measuring the waist at the half distance between the umbilicus and xiphoid appendix (Șerban et al, 1999).

**Statistical Analysis**

For statistical analysis we used Microsoft Excel and POP Tools from Microsoft Office 2003 and EPI 2000 program. To measure the quantitative variables were determined average (A) and standard deviation (SD), and to assess the gender differences we used the unpaired t test and ANOVA test, considering statistically significant a p < 0.05.
Results And Discussion

From a group of 78 patients with DM type 2 and ACT (70 women and 8 men), 53 (67.94%) (45 women and 8 men) had different types of obesity. The medium age was 54.45 ± 9.57 years.

The obesity was more frequent in men than in women (100% vs. 64.28%, p = 0.04, X² = 4.2). In function of obesity type, android obesity was prevailed (94.34 % of cases), following by gynoid obesity type (5.66 %). Also, 26.92 % were overweight (all women).

![Fig. 1. Prevalence of obesity by gender at patients with DM type 2 and ACT](image)

![Fig. 2. Prevalence of obesity type at patients with DM type 2 and ACT](image)

Thyroid dysfunction is associated with changes in body weight and composition, body temperature, and total and resting energy expenditure independently of physical activity. Moreover, weight gain often develops after treatment of thyroid dysfunction (Kaptein et al, 2009). Both subclinical and overt hypothyroidism is frequently associated with weight gain, decreased thermogenesis, and metabolic rate (Hoogwerf et al, 1984, Asvold et al, 2009). In a recent cross-sectional, population-based study of 27,097 individuals above 40 yr of age with body mass index (BMI) of at least 30.0
kg/m², subclinical and overt hypothyroidism correlated with a higher BMI and a higher prevalence of obesity in both smokers and nonsmokers (Asvold et al, 2009). It has been noted that small variations in serum TSH caused by minimal changes in l-T₄ dosage during replacement therapy are associated with significantly altered resting energy expenditure in hypothyroid patients (Al-Adsani et al, 1997). These studies support the clinical evidence that mild thyroid dysfunction is linked to significant changes in body weight and likely represents a risk factor for overweight and obesity.

The role of obesity as a risk factor for type 2 diabetes has been demonstrated by numerous prospective studies that included Caucasian populations in Norway, Sweden, Israel and the U.S., Mexicans from Texas, USA, and Pima Indians (Pencea et al, 2004).

In other 2 population-based studies conducted in Israel and in the Pima Indians, it was found that the duration and types of obesity are risk factors for type 2 diabetes. In the group of Pima Indians, the risk of type 2 diabetes is twice at people with 10 years obesity history or over this period compared with those with a less than 5 years obesity history (Pencea et al, 2004).

Central distribution of body adiposity is a major risk factor for type 2 diabetes, independent of the type of obesity, hypothesis demonstrated by the prospective studies conducted on populations from Sweden, Japan and Pima Indians.

In the group of Pima Indians, 5-year longitudinal studies have shown the association of impaired glucose tolerance with weight gain, decreased insulin secretion and action. No changes were observed in hepatic glucose production. The higher weight and the defect of synthesis / action of insulin, and increased hepatic glucose production characterize abnormal glucose tolerance progression to diabetes (Pencea et al, 2004).

Obesity, especially abdominal (android type), with hip/waist ratio increased, contributing to the occurrence of hyperglycemia, probably by reducing the number of insulin receptors (Wilding, 2003).

Epidemiological studies show that over 80% of patients with type 2 diabetes are or were obese and 40% from obese are diabetics, if they are active detected (OGTT) (Katsilambros, 2000, Katsilambros et al, 2003).

Regarding the types of android obesity, 39.62 % had type I, 37.73 % type II and 22.64 % type III.

**Table 1.** Prevalence of obesity type by gender at patients with DM type 2 and ACT

<table>
<thead>
<tr>
<th>Obesity type</th>
<th>F</th>
<th>M</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>17</td>
<td>4</td>
<td>&lt;0.001, X² = 24.9</td>
</tr>
<tr>
<td>II</td>
<td>16</td>
<td>4</td>
<td>0.00014, X² = 14.4</td>
</tr>
<tr>
<td>III</td>
<td>12</td>
<td>0</td>
<td>&lt;0.001, X² = 24</td>
</tr>
</tbody>
</table>
**Fig. 3.** Prevalence of obesity type at patients with DM type 2 and ACT

In function of TSH level, 62.26% were euthyroid, and 38.74% hypothyroid \( (p = 0.01, \chi^2 = 6.38) \).

TSH seems to be positively related to the type of obesity (Iacobellis, 2005). Thyroid hormone levels have been reported to be normal, increased, and decreased in obese patients (Iacobellis, 2005); this discrepancy among studies probably reflects the fact that patients were examined at different times (during overeating or a hypocaloric diet) and may differ in type of obesity and in plasma insulin sensitivity.

There is some debate about the link between obesity and the risk of autoimmune thyroid dysfunction (AITD), which is the main cause of hypothyroidism in adults. The prevalence of AITD in obesity has been reported to be 12.4% in children and between 10 and 60% in adults (Marzullo et al, 2010, Rotondi et al, 2009). This discrepancy may be due to such factors as sex, age, menopausal status, smoking habit, environmental factors, iodine intake, and type of obesity.

Also, 64.15% had hypertension and dyslipidemia 79.24%. In function of dyslipidemia type, predominate mixed dyslipidemia (64.15%), followed by hypercholesterolemia (28.57%) and hypertrygliceridemia (9.52%).

**Fig. 4.** Prevalence of other cardiovascular risk factors at obese patients with DM type 2 and ACT
Marzullo et al. in their study show that 69% of their patients had severe obesity (BMI > 40 kg/m²), and the prevalence of hypothyroidism was higher in obese patients than in a control group of age- and sex-matched subjects with normal BMI (p < 0.05), as documented by lower FT₃ and FT₄ plasma levels (p < 0.01) and a deranged lipid profile.

The onset of thyroid hormone deficiency, especially the subclinical form, may go undiagnosed in obese patients. Consequently, these patients will continue to increase in weight and will develop a deranged lipid profile, thereby bringing the thyroid/obesity association to a full circle.

Recent studies suggest that a higher BMI is associated with an increased risk of thyroid cancer (Paes et al, 2010). Moreover, a serum TSH in the upper half of the normal range is considered as an independent predictor for the presence of thyroid cancer in thyroid nodules (Boelaert, 2006, Fiore et al, 2009). Both of these findings together suggest that the higher serum TSH levels could be responsible for the development of thyroid malignancy in obese patients.

Obesity and thyroid dysfunction are common diseases, and consequently clinicians should be particularly alert to the possibility of thyroid dysfunction in obese patients. On the other hand, although thyroid hormones have been inappropriately and frequently used in attempts to induce weight loss in obese euthyroid subjects, there is no indication for their administration to control body weight except in obese hypothyroid subjects. In fact, long-term treatment with thyroid hormones does not significantly improve weight loss in obese subjects without thyroid dysfunction and, on the contrary, will entail a risk of adverse effects (Kaptein et al, 2009). It is conceivable that selected thyroid analogs might be a means by which to improve weight loss by increasing energy expenditure (as well as improving lipid profiles) in obese patients with low T₃ during continued caloric deprivation (Ladenson et al, 2010).

Conclusion

In patients with DM type 2 and ACT the obesity prevailed in men. It was android type, represented an increased risk of cardiovascular morbidity-mortality, particularly for atherosclerotic cardiovascular disease.

Regarding the type of android obesity, prevailed type I, followed by type II and III.

Were also associated another cardiovascular risk factors such as hypertension and dyslipidemia. Regarding dyslipidemia type, prevailed mixed dyslipidemia, followed by hypercholesterolemia and hypertryglyceridemia.

Most of the patients were euthyroid and the remaining hypothyroid.
The association of thyroid disease, which over time can evolve with hypothyroidism, is an additional risk factor for atherosclerotic cardiovascular disease.

It is disputable to administrate thyroid hormones at obese patients with normal thyroid function because they don’t improve weight, but increase the risk of adverse effects. Some thyroid analogs can be administrating to these patients because they improve lipid profile and determinate weight loss.

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