Body mass analysis in patients with Hashimoto thyroiditis

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ABSTRACT

Introduction: Hashimoto thyroiditis (HT) is one of the most common autoimmune thyroid disorders and o the most common cause of hypothyroidism, but the relation between TSH and body mass is still unclear.
Material and methods: The group studied consisted of 53 patients with HT in euthyreosis and 28 healthy individuals. All the patients underwent thyroid ultrasonography and body mass analysis with the use of a medical analyzer INBODY 200. Blood samples were also analyzed for TSH and anti-thyroid antibodies.
Results: The patients with HT had higher body mass (p=0.008), body mass index (BMI) (p=0.02), Waist-Hip Ratio (WHR) (0.01) and fat mass (p=0.02) than had the controls. In HT group increased body mass was observed in 72% of the patients (overweight in 38% and obesity in 35% of them), as compared with 38% of overweight/obesity in the control group. Thyroid volume was significantly lower (p=0.01) and anti-peroxidase antibodies level was two times higher in the group with the treatment period > 2 years, but the patients with relatively short treatment period were 7 kg heavier and their fat mass was 6 kg higher than in the subjects treated longer than 2 years.
Conclusions: Our results suggest that the patients with HT, even in euthyreosis, have significantly higher body mass, BMI, WHR and fat mass than healthy individuals, which is probably associated with previous disturbances that led to the increase in fat mass at the stage of hypothyroidism. The observed changes tend to normalize during L-thyroxine replacement therapy.
Key words: Thyroid, thyroiditis, body mass index, thyrotropin.

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Received: 31.01.2014
Accepted: 03.03.2014
Progress in Health Sciences
Vol. 4(1) 2014 pp 18-23

INTRODUCTION

Hashimoto disease (HT) is the most common autoimmune thyroid disorder (AITD) and is now more easily detected by sensitive laboratory tests and more invasive procedures such as fine needle aspiration. According to various epidemiologic data its incidence ranges from 30 – 150 to even 500 new cases per 100,000 citizens per year. High titers of anti-thyroid antibodies are observed in 15-25% of adult women and in 5-10% of men with no symptoms of hypothyroidism [1, 2]. The incidence of subclinical hypothyroidism (SH) is estimated as 10-15%, but overt hypothyroidism (OH) caused by HT affects approximately 0.1 – 2% of the population only [3, 4].

An increase in the incidence of obesity in the last decade has led to numerous studies concerning thyroid function in obese patients. According to the National Health and Nutrition Examination Survey in 2003-2004 obesity was observed in 32.2% of adults, especially in the fifth decade of life [5]. Furthermore, according to these observations, subclinical hypothyroidism (SH) was diagnosed more frequently in obese patients in comparison with the general population [6]. Its occurrence was estimated as 4-10% in the general population and as 20% among obese individuals [7].

It is also known that obesity, in particular abdominal, is related with numerous endocrine disorders, including thyroid dysfunction and that triiodothyronine (T3) regulates energy metabolism and thermogenesis, as well as plays a key role in glucose and lipid metabolism, the regulation of food intake and fatty acids oxidation [8]. Thyroid hormones increase the demand for ATP due to the increase in metabolic cell activity and the decrease in ATP synthesis [9]. Thyroid hormone deficiency in the course of subclinical and overt hypothyroidism is frequently related to the increased body mass, reduced thermogenesis and metabolic rate [9].

It has been observed that even minor changes in thyrotropin (TSH) level caused by minimal changes in the dose of levothyroxine significantly change energy utilization in hypothyroidism. Clinical studies confirm that even a minor thyroid dysfunction is related to significant changes in body mass [10, 11]. However, the relation between TSH and body mass index (BMI) seems still controversial since some authors found a correlation between TSH levels and BMI [12-14] while others did not [15].

In subjects with marked hypothyroidism appetite is often suppressed offsetting the impact of a decreased metabolic rate. Moreover, severe hypothyroidism and myxedema may be connected with normal or even low weight and overt hypothyroidism does not appear to be more common in obese subjects than in the general population [16]. On the other hand, early observations of significant weight loss following the resolution of myxedema, an effect that was generally ascribed to fluid mobilization [17], was recently confirmed in a prospective study of newly diagnosed patients with overt hypothyroidism, whose mean TSH level at the onset of the study was 102μIU/ml [18].

Obesity may also have an impact on the hypothalamic–pituitary–thyroid axis, as evidenced by relatively elevated TSH levels in morbidly obese adults with ultrasound findings typical for chronic thyroiditis but without either elevated antithyroid antibodies or decreased T4 and T3 levels [19]. Caution must therefore be kept when diagnosing subclinical hypothyroidism in marked obesity [20]. Furthermore, BMI fails to give precise information on the body composition, as it does not provide any information about fat and fatless mass or regional fat distribution. So, the pathogenesis of improper body mass in HT patients is still an open question.

Therefore, in the present study we compared body mass and body composition between the patients with Hashimoto thyroiditis who were in clinical and hormonal euthyreosis and healthy individuals who had never been treated for autoimmune thyroid disorders.

MATERIALS AND METHODS

The group studied consisted of 81 patients, including 53 subjects with HT in clinical and hormonal euthyreosis (mean age 44.6±15.3 years, F/M 90.6%/ 9.4%) and 28 healthy individuals matched for gender, age, multivitamin preparation intake and the use of hormonal contraception (mean age 40.8±15.6 years, F/M 89.3%/10.7%). All the patients underwent thyroid ultrasonography to establish thyroid echogenicity, vascularity with Power Doppler method, the signs of fibrosis and calcification, as well as the presence of inflammatory foci. Body composition analysis was performed using medical body analyzer INBODY 220 (*Biospace, Korea*), which allows measurements of body mass, total body water (TBW), fat and free fat mass, skeletal muscle mass (SMM), BMI, the percent of body fat (PBF) and basic metabolic rate (BMR). Reliability of an estimated BMR was confirmed by calorimetric method performed in 5 patients with HT. Differences between these results were smaller than 5%. Waist to Hip Ratio (WHR) was calculated as waist circumference in centimeters divided by hip circumference in centimeters.

Blood samples were collected from antecubital vein, between 7:30 and 8:30 am, after an overnight fast. Serum TSH concentration was measured using an enzyme-linked immunoassay

(DiaSource, Louvain-la-Neuve, Belgium). Anti-peroxidase antibodies (TPOAb) and TNF-α levels were also determined by commercial immunoassays (Euroimmun, Lubeck, Germany and R&D Systems, Minneapolis, USA, respectively). The concentration of anti-TSH receptor antibodies (TRAb) was measured by a commercial radioimmunoassay (TRAK HUMAN, B-R-A-H-M-S Berlin, Germany).

All patients and controls gave their informed consent to participate in the study before enrolment. The protocol was approved by the local ethics committee (Medical University of Bialystok).

Statistical analysis

STATISTICA 10.0 for Windows (StatSoft.Inc, USA) and IBM SPSS Statistics 21.0 (Predictive Solutions, USA) Software were used for the statistical analysis. Before analysis data were tested for normality of distribution using Shapiro-Wilk test. Differences between the groups were compared by U Mann-Whitney test and relationships between variables were tested using Spearman's rank correlation test. P value lower than 0.05 was considered statistically significant.

RESULTS

The clinical and biochemical characteristics of the groups studied are summarized in Table 1. As expected, the patients with HT had significantly higher concentrations of TPOAb (p=0.00001) and TRAb (p=0.00001), and smaller thyroid volume (p=0.001) than had the controls. As it was shown in Table 2, the patients with HT had also significantly higher body mass (p=0.008), BMI (p=0.02), WHR (p=0.01, fat mass (p=0.02) and the percentage of body fat (p=0.005) in comparison with the healthy subjects.

In the whole group studied TRAb level correlated significantly with body mass (R=0.288, p=0.01), BMI (R=0.325, p=0.007), WHR (R=0.399, p=0.0007) and the percentage of body fat (R=0.316, p=0.009). In the same group and in the subgroup with HT there were also positive correlations between TSH concentration and WHR (R=0.271, p=0.04 and R=0.437, p=0.004, respectively), as well as between TSH and the percentage of body fat (R=0.296, p=0.03 and R=0.489, p=0.001, respectively).

Table 1 .Clinical characteristics of the studied groups.

	Control group n=28	**Hashimoto thyroiditis n=53**	**P value**
Thyroid volume (ml)	18.54 (12.52-19.47)	12.25 (7.93-15.32)	0.001
TSH (μIU/ml)	1.13 (0.92-1.37)	1.48 (1.0-1.86)	ns
TPOAb (IU/ml)	6.14 (4.91-10.17)	169.7 (27.23-413.27)	0.00001
TRAb (IU/l)	0.3 (0.3-0.53)	1.16 (0.82-1.35)	0.00001
Levothyroxin dose (ug/day)	-	50.0 (0.0-88.0)	

Data are shown as medians (interquartile range), differences between groups were tested by Mann-Whitney *U* test.

Table 2. Body composition analysis in patients with Hashimoto thyroiditis and control subjects.

	Control group n=28	**Hashimoto thyroiditis n=53**	**P value**
Body mass (kg)	65.0 (60.0-74.1)	74.1 (63.5-91.60)	0.008
Height (cm)	165.5 (16.5-170.0)	166.5 (162-170)	ns
BMI (kg/m^2)	22.12 (20.7-27,1)	27.2 (23.9-32.1)	0.02
WHR	0.84 (0.76-0.94)	0.94 (0.87-1.0)	0.01
TBW	33.0 (31.0-36.9)	34.4 (30.5-41.1)	ns
FFA (kg)	44.9 (41.1-49.0)	47.0 (42.2-56.0)	ns
Fat mass(kg)	21.0 (13.6-28.4)	26.8 (20.6-37.1)	0.02
PBF (%)	30.0 (22.5-38.3)	38.0 (31.8-41.5)	0.005
SMM (kg)	24.5 (22.8-27,9)	25.7 (22.7-31.1)	ns
BMR	1342.9 (1282.0-1455.0)	1383.5 (1278.5-1581.0_	ns

Data are shown as medians (interquartile range), WHR - waist/hip ratio, TBW - total body water, PBF - percentage of body fat, FFA - free fat mass, SMM -skeletal muscle mass, BMR - basic metabolic rate, differences between groups were tested by Mann-Whitney *U* test.

When the patients with HT were divided into two groups, dependent on the treatment period, we found that thyroid volume was significantly lower (p=0.01) and TPOAb titer was two times higher in the group with the treatment period > 2 years as compared with the patients with shorter treatment period (Table 3). On the other hand, median body mass, BMI and fat mass were higher in the patients treated with L-thyroxine < 2 years. Although these differences were not significant, the patients with relatively short treatment period were approximately 7 kg heavier and their fat mass was 6 kg higher in comparison with the subjects treated longer than 2 years (Table 3).

Table 3. Anthropometric and biochemical characteristics of patients with Hashimoto thyroiditis depending on the treatment period.

Parameter	**Group I, n=23 Treatment period < 2years**	**Group II, n=30 Treatment period > 2years**	**P value**
Age (years)	50.5 (33.5-55.0)	50.0 (34.0-59.0)	ns
Thyroid volume (ml)	14.4 (12.6-16.8)	10.7 (6.6-14.3)	0.01
TSH (IU/ml)	1.59 (1.17-1.89)	1.43 (1.0-1.86)	ns
TPOAb(IU/ml)	148.53 (26.95-396.27)	270.36 (45.19-453.88)	ns
TRAb (j/l)	1.18 (0.67-1.35)	1.12 (0.87-1.39)	ns
Body mass(kg)	77.2 (69.1-89.8)	70.2 (63.5-91.6)	ns
Height (cm)	167.0 (162.0-170.0)	166.0 (162.0 -172.0)	ns
BMI(kg/m^2)	29.1 (26.4-33.9)	26.2 (23.6-32.1)	ns
WHR	0.94 (0.87-1.10)	0.95 (0.87-1.00)	ns
TBW	34.6 (29.7-41.1)	34.3 (30.5-41.2)	ns
FFA (kg)	48.6 (42.2-56.0)	46.9 (42.0-56.0)	ns
Fat mass(kg)	32.0 (24.6-38.3)	26.3 (18.2-35.8)	ns
PBF (%)	38.6 (33.6-41.3)	37.1 (29.7-42.3)	ns
SMM (kg)	26.5 (21.7-31.0)	25.6 (22.7-32.0)	ns
BMR	1420.0 (1281.0-1581.0)	1377.0 (1273.5-1593.5)	ns

Data are shown as medians (interquartile range), WHR - waist/hip ratio, TBW - total body water, PBF - percentage of body fat, FFA - free fat mass, SMM -skeletal muscle mass, BMR - basic metabolic rate, differences between groups were tested by Mann-Whitney *U* test.

DISCUSSION

The present study revealed that the patients with HT had significantly higher body mass, BMI and WHR in comparison with the healthy individuals. There was also a trend towards higher body mass, BMI and fat mass in the HT patients treated with L-thyroxine < 2 years.

The relation between obesity and the risk of autoimmune thyroid disorders is still under discussion. The incidence of obesity in AITD has been estimated as 12.4% in children and 10-60% in adult population [21, 22]. These differences may result from such factors as age, gender, smoking, environmental factors, iodine intake, contraception or hormone replacement therapy and the degree of obesity. In our study increased body mass was observed in 72% of the HT patients, including overweight in 38% and obesity in 35% of them. In the control group overweight or obesity was observed in 38% of the subjects studied. These results indicate the overweight/obesity was twice more frequent in the patients with autoimmune thyroiditis, even when thyroid function was normal. However, the causes of increased BMI in HT patients and the relation between TSH and body mass, as well as body composition have not been fully elucidated so far. In the present study TSH concentration correlated significantly with WHR and the percentage of body fat. Moreover, positive correlations between serum TRAb level and body mass, BMI, WHR and the percentage of body fat were also noted. The obtained results seem consistent with the findings of Knudsen et al. [17], who showed a positive correlation between body mass and TSH concentration, even if TSH level was inside the normal range. The authors demonstrated that the difference in BMI between the female patients with the highest and the lowest TSH levels was 1.9 kg/m^2, which corresponds with 5.5 kg of body mass [12].

Diez et al. [23] also found a positive correlation between TSH and BMI in patients with both overt and subclinical hypothyroidism, but only in the group with the presence of antithyroid

antibodies, suggesting a contribution of AITD to the pathogenesis of obesity. Marzullo et al. [22] published an intriguing hypothesis on the relation between obesity, leptin, autoimmunity and hypothyroidism. In this study, conducted in obese men and obese pre-menopausal women, the authors demonstrated that leptin increases the risk of developing AITD by direct regulation of immune processes. A higher occurrence of AITD was observed in the patients with leptin concentration over 33.8 ug/l. On the basis of logistic regression the authors identified female gender and leptin level as significant predictors of autoimmune thyroiditis [24]. However, the following issues still remain unexplained: whether high TSH and leptin concentrations are responsible for obesity development or the increase in their levels is secondary to obesity? The next problem is that the majority of all studies concerning the relation between hypothyroidism and body mass is based on the analysis of simple indices such as BMI, which fail to give precise information of muscle or fat mass, as well as fat distribution . The present study showed that the patients with HT had not only higher .body mass and BMI, but also significantly higher fat mass in comparison with the healthy individuals, however free fat body mass, muscle mass, as well as estimated rate of basal metabolism were comparable in these two groups. Moreover, there was also a trend towards higher body mass, BMI and fat mass in the patients with relatively short treatment period as compared with the subjects treated with L-thyroxine > 2 years. On the basis of our results we may speculate that even subclinical hypothyroidism lasting several years, which frequently remains undiagnosed (in particular in obese persons) might cause a decrease in energy utilization. It is well known that thyroid hormones increase thermogenesis, so even subclinical hormone deficiency may lead to an increase in the amount of fat tissue and thus to an increase in leptin concentration. There is also good evidence that leptin stimulates autoimmune processes, decreases TRH gene expression in the hypothalamus and TRH synthesis, enhances the resistance to thyroid hormones and thus leads to hypothyroidism and starts the vicious circle of obesity and HT [24-26]. On the other hand, the results obtained by are, as well by other authors strongly suggest that the implementation of L-thyroxine could stop the effects caused by the activation of leptin synthesis [24-27]. We should also mention that the effect of L-thyroxine treatment on the changes in thyroid volume and anti-thyroid autoantibodies is still unclear. Available data suggest a gradual decrease in thyroid volume in the course of the therapy [28,29], which is consistent with our results, and no changes [28] or a decrease in circulating antibodies, but only in patients with overt not subclinical hypothyroidism [29]. There is also good evidence that BMR was regarded to be the "gold standard" for diagnosing hypothyroidism and that extremely low BMR values were noted in marked hypothyroidism [30, 31]. However, the values of estimated basal metabolism rate in the HT patients with normal thyroid function did not differ significantly from these found in the healthy individuals, strongly suggesting that the previously observed changes were related to low thyroid hormones, but not to autoimmune process.

In conclusion, the patients with HT, even in euthyreosis, have significantly higher body mass, BMI, WHR and fat mass than healthy individuals, which is probably associated with previous hormonal and autoimmune disturbances that led to the increase in fat mass at the stage of hypothyroidism. The observed changes tend to normalize during L-thyroxine replacement therapy. Therefore, an early L-thyroxine supplementation in HT seems reasonable for the prevention of overweight and high-fat mass in AITD patients.

Conflicts of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the review reported.

Disclosure information

All authors declare any financial or other potential conflict of interest. This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

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