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Original Article

The Evaluation of Metabolic Syndrome Parameters of Patients with Hashimoto's Thyroiditis

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Abstract

Objective: In this study, we aimed to investigate the relationship between the prevalence of metabolic syndrome (MS) and the relationship between MS parameters in patients diagnosed with Hashimoto's thyroiditis (HT).

Methods: A total of 100 patients admitted to the internal medicine clinic between July and March 2013 and diagnosed with HT were included in this study. Age, gender, height, weight, waist circumference, arterial blood pressure, fasting blood glucose, HDL cholesterol, and triglyceride levels were recorded. Patients were evaluated according to the diagnostic criteria of the MS in the National Cholesterol Education Program - Adult Treatment Panel III (NCEP- ATP III) - 2001.

Results: The ages of HT patients included in the study ranged from 19 to 67 years, with an average of 45.00±12.20 years; 90% of patients were females. According to the NCEP-ATP III diagnostic criteria, MS was observed in 30% of patients (n=30). We observed abdominal obesity in 73.3% of the patients (n=22), hyperglycemia in 73.3% (n=22), hypertriglyceridemia in 60% (n=18), hypertension in 46.7% (n=14), and low high-density lipoprotein cholesterol (HDL-K) in 86.7% of the patients diagnosed with MS (n=26). We also noted a statistically significant difference between thyroid stimulating hormone (TSH) levels of patients and the presence of MS ($p<0.01$). TSH levels were higher than normal levels in patients with MS.

Conclusion: Various parameters of MS are frequent among patients with HT, and ideal level of MS parameters should be aimed during the treatment.

Keywords: Hashimoto's thyroiditis, metabolic syndrome, thyroid stimulating hormone

Introduction

Hashimoto's thyroiditis (HT) is one of the most common causes of hypothyroidism along with goiter. HT is defined by diffuse mononuclear cell infiltration, decreased thyroid follicles with fibrosis, large thyrocytes called Hurthle cells that have a granular pink cytoplasm, and the presence of anti-thyroid peroxidase antibody (anti-TPO) and anti-thyroglobulin antibody (anti-TG) in the circulation (1). The incidence of HT is 0.3–1.5 per 1000 individuals per year (2). The disease is often encountered at ages ranging from 30 years to 50 years, and approximately 95% of patients are females (3). It can present with various clinical pictures. These include euthyroidism or subclinical hypothyroidism with goiter, overt hypothyroidism, and changing hypo-hyperthyroidism (4).

The characteristic features of metabolic syndrome (MS) are central obesity, hypertension, dyslipidemia, glucose intolerance, vascular inflammation, and prothrombotic state (5). According to the data of Turkish Adult Heart Diseases and Risk Factor Study 2000, MS was detected in 28% of Turkish males and in 45% of Turkish females at the age of 30 years and above. It is estimated that approximately 9.1 million people at the age of 30 years and above have MS in Turkey (6). In this study, it was aimed to investigate the relationship between the frequency of MS and MS parameters in patients with HT.

Methods

Data of 100 patients who were admitted to the Outpatient Clinic of Internal Diseases in İstanbul Haydarpasa Numune Training and Research Hospital and who were diagnosed with HT between March 2013 and July 2013 were retrospectively examined. The ages of patients with HT who were included in the study varied between 19 years and 67 years, and the mean age was 45.00±12.20 years. In total, 90% of the patients (n=90) were females and 10% (n=10) were males. Based on the results of laboratory examinations, HT diagnosis was established in patients who had anti-TPO against thyroid antigen or increased anti-TG levels in the serum with normal or high levels of thyroid-stimulating hormone (TSH). In our hospital, TSH levels were evaluated using the Roche Elecsys Modular Analytics E170 Immunoassay method after 8 h of fasting in the morning. The normal reference intervals of thyroid function tests in our center are 0.7–1.48 ng/dL for free TF and 0.35–4.94 µIU/mL for TSH. The levels of sT4 and TSH in overt hypothyroidism were <0.7 ng/dL and >4.94 µIU/mL, respectively. In subclinical hypothyroidism, free hormone levels were normal but TSH levels were >4.94 µIU/mL. The measurement of waist circumference was performed

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from the umbilicus region when patients were in the standing position. Body weight and height were measured in kilogram and centimeter, respectively. Body mass index (BMI) was obtained by dividing the body weight in kilogram by the square of the height in centimeter (kg/m^2).

Patients with coronary artery disease, a history of thyroidectomy, chronic renal failure, pregnancy, malignancy, and chronic liver and lung diseases were excluded from the study.

The diagnostic criteria of NCEP ATP-III were used for the diagnosis of MT (waist circumference>88 cm in females and >102 cm in males; triglyceride level≥150 mg/dL; high-density lipoprotein cholesterol (HDL-C) level<50 mg/dL in females and <40 mg/dL in males, blood pressure ≥130/85 mmHg; and impaired fasting glucose or impaired glucose tolerance or overt diabetes). Patients in whom at least 3 of the 5 criteria were positive were diagnosed with MS.

All patients were examined in terms of age; gender; body mass index (BMI); and fasting blood glucose (FBG) (mg/dL), blood urea nitrogen (BUN) (mg/dL), creatinine (mg/dL), alanine aminotransferase (U/L), aspartate aminotransferase (U/L), hemoglobin A1C (%), total cholesterol (mg/dL), low-density lipoprotein cholesterol (LDL-C) (mg/dL), HDL-C (mg/dL), triglyceride (mg/dL), free T4 (fT4), TSH, anti-TG (IU/mL), and anti-TPO (IU/mL) levels; the dose and duration of levotiron use; and the use of antihypertensive drugs. Data were evaluated considering patients' backgrounds and the drugs they used.

Statistical analysis

For statistical analysis, the Number Cruncher Statistical System 2007 and Power Analysis and Sample Size 2008 (Utah, USA) statistical softwares were used. While evaluating the data, Student's t-test was employed for comparing quantitative data and normally distributed parameters in addition to descriptive statistical methods (mean, standard deviation, median, frequency, and ratio). Mann–Whitney U test was used in the comparisons of non-normally distributed parameters between two groups. For comparing qualitative data, Yates' continuity correction test was used. Statistical significance was evaluated at the values of $p<0.01$ and $p<0.05$.

Results

The ages of patients with HT who were included in the study ranged between 19 and 67 years, and the mean age was 45.00±12.20 years. In total, 90% of the patients were females (n=90) and 10% (n=10) were males. The patients' heights varied between 1.44 and 1.90 m, and the mean height 1.58±0.08 m. Their waist circumferences were between 65 and 120 cm, and the mean waist circumference was 92.14±14.86 cm. The BMIs ranged from 18.36 to 53.33 kg/m^2, and the mean BMI was 31.44±7.50 kg/m^2. The distribution of patients' laboratory findings is presented in Table 1. MS was observed in 30% of the patients (n=30) in accordance with the NCEP-ATP III diagnostic criteria. Of the patients diagnosed with MS, 73.3% had abdominal obesity (n=22), 73.3% had hyperglycemia (n=22), 60% had hypertriglyceridemia (n=18), 46.7% had hypertension (n=14), and 86.7% had low HDL-C levels (n=26). A statistically significant difference was detected between the TSH levels of patients considering the presence of MS ($p<0.01$) (Table 2). In patients with MS, TSH levels were observed to be higher than normal. According to the presence of MS, no statistically significant difference was found between sT4 levels ($p>0.05$). On the other hand, there was a statistically significant difference in terms of the incidence of hypertension ($p<0.01$).

Table 1. Laboratory findings of patients

	Min–max	Mean±SD
Fasting blood glucose (mg/dL)	84-186	106.70±23.25
BUN (mg/dL)	14-28	20.46±3.00
Creatinine (mg/dL)	0.59-1.19	18.68±4.59
ALT (U/L)	10-28	18.68±4.59
AST (U/L)	10-30	20.20±4.76
HBA1C (%)	5-8	5.93±0.62
T chol (mg/dL)	140-299	205.04±37.02
LDL-C (mg/dL)	73-250	131.72±35.19
HDL-C (mg/dL)	29-65	41.90±9.13
Triglyceride (mg/dL)	55-281	142.76±47.37
TSH (µIU/mL)	0.36-18.00	6.05±3.97
fT4 (ng/d L)	0.50-3.50	1.16±0.41
Anti-TPO (IU/mL)	0.50-1000	329.98±401.48
Anti-TG (IU/ mL)	0.50-1000	163.72±284.09
Levothyroxine dose (µg/day)	25.00-125.00	59.24±27.91
Treatment duration (year)	0.25-5.00	2.15±1.33

ALT: alanine aminotransferase; TSH: thyroid-stimulating hormone; AST: Aspartate aminotransferase; fT4: free T4; HBA1C: hemoglobin A1 C; anti-TPO: Anti-thyroid peroxidase antibody; T chol: total cholesterol; Anti-TG: anti-thyroglobulin antibody; LDL-C: low-density lipoprotein cholesterol

Table 2. Evaluation according to metabolic syndrome

	Metabolic syndrome		
	Yes (n=30) Mean±SD	None (n=70) Mean±SD	p
fT4 (ng/dL)	1.07±0.25	1.19±0.46	a0.174
HBA1C (%)	6.43±0.75	5.71±0.40	a0.001**
BMI (kg/m^2)	34.44±9.38	30.16±6.17	a0.027*
TSH (µIU/mL); (Median)	9.29±4.18 (10.00)	4.65±2.96 (4.03)	b0.001**
	n (%)	n (%)	
There is no hypertension	16 (%53.3)	66 (%94.3)	c0.001**
There is hypertension	14 (%46.7)	4 (%5.7)	c0.001**
a.Student's t-test	b.Mann-Whitney U Test	c.Yates Continuity Correction	
*p<0.05	**p<0.01		

sT4: free T4; HBA1C: hemoglobin A1C; BMI: body mass index; TSH: thyroid-stimulating hormone; SD: standard deviation

Discussion

Metabolic syndrome is characterized by hypertension, low HDL-C and increased triglyceride levels, and visceral obesity. It is associated with insulin resistance and increases the risk of diabetes, cardiovascular diseases, and microalbuminuria (7, 8). According to the results of Turkish Metabolic Syndrome Survey, the incidence rate of MS was found to be 35% among adults at the age of 20 years and above. In this research, the frequency of MS was calculated to

be 41.1% in females and 28.8% in males (9). In our study, 30% of the patients with HT (n=30) had MS according to the NCEP-ATP III diagnostic criteria.

Hashimoto's thyroiditis is mostly a thyroid disease and the most common cause of hypothyroidism in regions with iodine deficiency. HT, which is seen in more than 2% of the general population, is more frequently encountered among females than males (10). In our study, 90% of the patients with HT were females and 10% were males. In the laboratory findings of patients with HT, thyroid hormone levels can be normal, low, or normal. The levels of serum anti-TPO and anti-TG are positive at the rate of 95–100% in HT, which helps to establish diagnosis. HT can clinically present as subclinical hypothyroidism (SCH), overt hypothyroidism, or euthyroidism. The indications for thyroid replacement treatment in HT include patients with TSH level of 4–10 mIU/L and normal T3 and T4 levels, and patients with TSH levels above 10 mIU/L. It is recommended that thyroid replacement treatment should be initiated with a low dose at 25–75 µg/day of levothyroxine, that serum TSH levels should be followed-up at 6–8-week periods, and that dose titration should be done when necessary (11). For our patients, levothyroxine replacement dose per day was 25–125 µg/day, and the mean dose was 59.24±27.91 µg/day. In the study by Al Adsani et al. (12), it was reported that slight changes in levothyroxine replacement doses significantly affected energy expenditure at rest. On the other hand, in the study conducted by Fox et al. (13), it was stated that slight changes in the normal reference intervals of TSH contributed to weight gain and regional obesity development.

Thyroid hormones play an important role in the synthesis, metabolism, and mobilization of lipids. The effect of thyroid hormones has great importance in lipoprotein metabolism that controls cholesterol synthesis. On the other hand, the effect of thyroid hormones on insulin and glucose is controversial (14). One of the significant symptoms of hypothyroidism is weight gain (15). Hypothyroidism does not affect leptin levels in the short term (16).

In the study performed by Erdogan et al. (17), MS prevalence was found to be higher in patients with overt hypothyroidism than in the subclinical and control group patients (44%, 35%, and 33%, respectively). This demonstrates that the presence or degree of hypothyroidism will have a role in the development of MS.

The risk of cardiovascular diseases and mortality is associated with increased waist circumferences (18). When the distribution rates of MS components in our patients were examined, abdominal obesity was found in 73.3% of the patients (n=22), which was in parallel to increased FBG levels. Moreover, the waist circumferences varied between 65 and 120 cm, and the mean waist circumference was 92.14±14.86 cm. BMIs ranged between 18.36 and 53.33 kg/m^2, and the mean BMI was calculated to be 31.44±7.50 kg/m^2. In a study, the rate of abdominal obesity was found to be higher in the subclinical and overt hypothyroidism group than in the control group (17). In our study, the rate of hypertension was detected to be 46.7% (n=14). Some studies showed that SCH negatively affected total cholesterol, low-density lipoprotein cholesterol (LDL-C), ApoA1, Apo B, and lipoprotein (a) levels, but it did not affect triglyceride and HDL-C levels (19). McDermott et al. (20) revealed in their study that total cholesterol, LDL-C, triglyceride values and blood pressure increased and HDL-C decreased in patients with SCH. In our study, 60% (n=18) of HT patients had hypertriglyceridemia, and 86.7% (n=26) had low HDL-C levels. Caron et al. (21) demonstrated that the atherogenic effect increased with high TSH levels. In the study by Erdoğan et al. (17), no difference was found among the overt hypothyroidism, SCH, and control groups in terms of elevated triglyceride levels. Hypothyroidism increases LDL-C level and blood pressure and causes hypercoagulability and obesity, thereby negatively affecting the cardiovascular system (22). There are some studies suggesting that SCH is associated with cardiovascular diseases, although it is clinically asymptomatic (23, 24). In the Turkish population, the level of HDL-C is lower than that in other countries (25). In our study, the low level of HDL was found in 86.7% (n=26) of the patients with HT.

The effect of hypothyroidism on glucose metabolism and insulin resistance is controversial. In a study, it was reported that hypothyroidism did not affect insulin resistance measured with HOMA-IR (26). However, in another study, it was demonstrated that hypothyroidism could contribute to insulin resistance by reducing glucose consumption in fat cells (27).

Subclinic hypothyroidism is defined as increased serum TSH level and a normal free T4 level (28). In vitro studies showed that SCH can lead to energy expenditure and affect cell functions (29). Thyroid functions are determined through metabolic parameters. Moreover, they are risk factors for both SCH and MS cardiovascular events (30). In the study conducted by Uzunlulu et al. (31), it was reported that MS prevalence was high among SCH patients in the Turkish population. However, it was stated in a recent study that MS prevalence was equal in patients with SCH and euthyroidism and that there was a positive correlation between TSH levels and cholesterol and triglyceride levels (32).

In our study, the TSH level was found to be higher than normal in patients with MS ($p<0.01$). In our patients with HT, the mean TSH level was 9.29±4.18 µIU/mL in patients with MS and 4.65±2.96 µIU/ml in patients without MS ($p<0.01$).

Uzunlulu et al. (31) reported an MS prevalence of 53.6% (40.7% in females and 12.9% in males) and SCH prevalence of 11.5% (1% in females and 15% in males). SCH was found to be present at a rate of 16.4% in MS patients and at a rate of 5.8% in the control group. These findings demonstrated that SCH should be investigated during the treatment of patients with MS. SCH prevalence was found to be higher in female patients with MS than in those without MS. However, there was no significant difference between male patients with and without MS.

Subclinical hypothyroidism treatment provides three main benefits. Its effects improve the lipid profile and some symptoms of mild hypothyroidism, and they prevent the progress of overt hypothyroidism (33). In some studies, a decrease was observed in the levels of total cholesterol and LDL-C after levothyroxine replacement treatment (34). SCH was found to be associated with multiple mechanisms such as hyperhomocysteinemia, changes in coagulation parameters, chronic inflammation, and atherosclerotic cardiovascular diseases (20).

Conclusion

Various parameters of MS are frequently encountered in patients with HT, and it should be aimed to keep MS parameters at ideal

levels in treatment. Levothyroxine replacement treatment can prevent the deterioration of overt hypothyroidism, improve the quality of life, and reduce cardiovascular risks in patients with mild thyroid dysfunction.

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