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Research Article

Relation between Metabolic Syndrome & Its Components and Thyroid Dysfunction in an Urban Population in Ahvaz

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Abstract: Metabolic syndrome is a cluster of cardiovascular risk factors. A direct association of normal TSH with insulin sensitivity and abdominal obesity has been shown. The present study designed to assess the prevalence of thyroid dysfunction in patients with metabolic syndrome and its association with components of metabolic syndrome. In this cross-sectional study, the subjects were selected through randomized cluster sampling from the project of Ahvaz metabolic syndrome study included 77 patients with metabolic syndrome and 92 healthy people. Height, weight, waist circumference (WC), BP, and BMI were measured. Blood samples were collected after 12 hours of fasting for FBS, TG, total cholesterol, TSH, T4, T3RU and Anti TPO and Anti TG antibodies and HDL, and people with at least three ATP III criteria were considered as metabolic syndrome. The results in this study included 169 subjects (77 patients with metabolic syndrome in and 92 healthy subjects in control group). In the metabolic syndrome group 55.8% were female and 44.2% were male. There was 48.9% female and 51.1% male in the control group. The prevalence of thyroid dysfunction in patients with metabolic syndrome and normal subjects was 13% and 6.5%, respectively (P=0.24). The prevalence of positive level of thyroid auto antibodies were 48% and 20% in metabolic syndrome patients and control group respectively (P=0.0002). Serum TSH levels had direct and significant association with WC (P=0.01) and BMI (p=0.0001). This study shows that the conclusion was prevalence of thyroid dysfunctions in patients with metabolic syndrome was not significantly higher than normal people, while the prevalence of thyroid auto antibodies was higher in patients with metabolic syndrome. The serum levels of TSH had a significant relationship with some components of the metabolic syndrome, including abdominal obesity and obesity.
Keywords: Thyroid Dysfunction, Metabolic Syndrome, Thyroid Auto antibody, Abdominal Obesity

INTRODUCTION

Metabolic syndrome is a cluster of cardiovascular risk factors which may occur simultaneously in an individual, and increases mortality, cardiovascular disease, and type II diabetes [1].

Although an uncertainty exists regarding that whether the metabolic syndrome is a distinct feature or a set of several features, there is no much debate on this fact that the syndrome has detrimental effects on human health [1]. Most published data show an increase of 1.5 to 3 times in cardiovascular mortality and all-cause mortality in these patients [1].

Several definitions have been proposed of this syndrome. Regardless of these definitions, the prevalence of the syndrome is increasing throughout the world and has affected even young adults and children [1]. Although the pathogenesis of the syndrome is not well-known, several mechanisms are involved, including genetic predisposition, coping with stress, nutritional factors, lifestyle, and hormonal interactions. Several studies in recent years indicate multiple factors and these conditions increase the risk of cardiovascular diseases.

Hypothyroidism is the most common endocrine disorders and numerous studies have shown its association with atherosclerotic arterial diseases [1]. That affects an estimated 2.1% of the population [2].

Wickham's Survey, have been evaluated incidence of hypothyroidism over 20 years to be 3.5 per 1000 and 0.6 per 1000 in men and women respectively [3, 4].

Cols and Vzunlulu found three times higher prevalence of subclinical hypothyroidism in metabolic syndrome [5]. Another study into a large population of Taiwanese elderly did not show this relationship [6]. Cols and Roef showed a direct relationship of TSH levels with arterial blood pressure and serum lipid in euthyroid people [7].

A direct association of normal TSH with insulin sensitivity and abdominal obesity has been shown [8]. Thyroid hormones have strong effects on energy homeostasis, glucose and lipid metabolism, and blood pressure; therefore, it is hypothesized that changes in thyroid function may be related to metabolic syndrome and its components, including obesity, insulin resistance, impaired metabolism of glucose and lipid, and hypertension [9].

Objectives

In this study, the possible relationship between metabolic syndrome and thyroid dysfunction was investigated, given that a controversy exists regarding thyroid dysfunction, metabolic syndrome, and its components.

PATIENTS AND METHODS:

The subjects of this study were selected from the project of Ahvaz metabolic syndrome which was performed in 6 health centers on 912 participants (10). The study was approved by the ethics committee of Ahvaz University of Medical Sciences. A total of 77 patients with metabolic syndrome and 92 healthy subjects were included in the study. The control group was matched with the metabolic syndrome group for age and sex. The subjects were evaluated in terms of metabolic syndrome using ATP III criteria (update 2005) [11].

The NCEP-ATP III criteria are as follows:

1. Abdominal obesity (abdominal circumference of ≥102 cm for men and ≥88 cm for women)
2. TG ≥150 mg/dL or consumption of lipid-lowering drugs
3. HDL ≤40 mg/dL in men and women
4. BP ≥130/85 mmHg
5. History of diabetes, use of hypoglycemic agents, or FBS ≥100 mg/dL

Three of these 5 criteria are required for the diagnosis of metabolic syndrome. Measurement of the height (cm), weight (kg) and waist circumference (cm) was performed by trained personnel. BMI was calculated using the equation [weight (kg)/height (m) ^{2}].

Waist circumference (WC) was measured at the midway of the lower ribs and the upper surface of iliac crest (right) after a normal expiration. A standard sphygmomanometer was used to measure blood pressure with the right arm at the heart level after 15 minutes of resting in a chair.

Venous blood sample was collected for biochemical analysis from the antecubital vein after 12 hours of fasting, and was sent to the Diabetes Research Center laboratory of Ahwaz University of Medical Sciences observing the cold chain. The blood samples were subjected to FBS, TG, total cholesterol, LDL, HDL, TSH, T4, T3RU, anti-Tg Ab, and anti-Tpo Ab tests. FBS, TG, total cholesterol, LDL, HDL were measured through colorimetric method using the auto analyzer BT3000 and Pars Azmoon kits. TSH was analyzed through chemiluminescence method using the Liaison device, and the reference ranges of TSH were considered 0.3-4.5 mIU/L. In addition, T4, T3RU and antibodies were measured by ELISA.

Reference ranges of T4, T3RU, anti-Tg Ab, and anti-Tpo Ab are 5.4-12.6 mg/dL, 25-38%, >40 IU/mL, and >125 IU/mL, respectively [12,13].

In this study, high TSH was attributed to the values greater than 4.5 and low TSH to the values less than 0.1. In addition, TSH >4.5 and T4 <5.4 were defined as hypothyroidism, and TSH >4.5 and T4 ≥5.4 were defined as subclinical hypothyroidism. Moreover, TSH <0.1 and T4 >12.6 were defined as hyperthyroidism, and TSH <0.1 and T4 <12.6 were defined as subclinical hyperthyroidism [9, 10].

Statistical Analysis

Statistical variables were expressed as mean ± standard deviation, and independent t-test and chi-squared test were used to compare variables. Statistical analyses were performed using SPSS-21 and p-values less than 0.05 were assumed statistically significant. The sample size was 169 persons.

RESULTS

Study population characteristics are shown in Table 1. The study included 169 subjects (77 patients in metabolic syndrome group and 92 people in the control group). Among the 77 patients with metabolic syndrome, 43 were women (55.8%) and 34 were men (44.2%). Among the 92 control subjects, 45 were women (48.9%) and 47 were male (51.1%). Mean age, waist circumference, systolic and diastolic blood pressure, FBS and TG were significantly higher in the metabolic syndrome group than the controls.

The prevalence of thyroid dysfunction in patients with metabolic syndrome and the healthy subjects was 13% and 6.5%, respectively. Although

noticeable, the difference was not statistically significant (P=0.24).

In patients with metabolic syndrome, the prevalence of hypothyroidism, subclinical hypothyroidism, hyperthyroidism, and subclinical hyperthyroidism was 2.6%, 7.8%, 1.3%, and 1.3%, respectively.(Table 2)

Mean serum T4 level was significantly lower in patients with metabolic syndrome(Table3)

The prevalence of thyroid autoantibodies in the metabolic syndrome and control group was 48% and 19% respectively. The difference was statistically significant (P=0.0002).(Table 4)

Serum TSH levels were significantly associated with WC and BMI (P=0.01) and (P=0.0001) respectively. (Table 5)

There was no significant difference between mean TSH levels in hypertensive and normotensive subjects (P=0.26), patients with and without hyper triglyceridemia (P=0.2), and between patients with low HDL and those with normal HDL (P=0.77).

Table-1: Characteristics of the study population

	With metabolic syndrome (X±SD)	Without metabolic syndrome (X±SD)	p-value
Female/Male	43/34	45/47	
Age	50.7±12.82	36.72±12.59	0.0001
BMI	36.7±2.7	32.4±3.6	0.34
W.C(cm)	96.66±10.01	80.02±9.12	0.0001
FBS(mg/dl)	136.06±65.21	86.61±8.41	0.0001
TG(mg/dl)	229.66±13.12	101.78±4	0.0001
HDL-C(mg/dl)	49.9±10.64	64.13±13.83	0.0001
LDL-C(mg/dl)	112.5±32.62	109.6±33.01	0.58
SBP(mmHg)	129.35±20	107.73±26.66	0.0001
DBP(mmHg)	80.19±13.36	67.06±17.9	0.0001

Table 2: Prevalence of thyroid dysfunction in patients with and without metabolic syndrome

	Euthyroid (%)	Hypothyroidism (%)	Subclinical hypothyroidism (%)	Hyperthyroidism (%)	Subclinical hyperthyroidism (%)	Total
With metabolic syndrome	67(87%)	2(2.6%)	6(7.8%)	1(1.3%)	1(1.3%)	77(100%)
Without metabolic syndrome	86(93.5%)	0(0%)	5(5.4%)	0(0%)	1(1.1%)	92(100%)
Total	153(90.2%)	2(1.2%)	11(6.5%)	1(0.6%)	2(1.2%)	169(100%)

Table 3: Mean values of thyroid function tests in patients with and without metabolic syndrome

	With metabolic syndrome	Without metabolic syndrome	p-value
TSH(mIu/L)	1.84±1.19	2.06±1.49	0.27
T4(mg/dl)	7.3±1.25	8.1±1.29	0.0001
T3RU(%)	28.36±2.25	26.92±2.58	0.0001
Anti Tg Ab(IU/ml)	73.96±111.46	133.23±152.29	0.006
Anti Tpo Ab(IU/ml)	16.3±42.91	25.96±51.48	0. 19

Table 4: Prevalence of thyroid auto antibodies in patients with and without metabolic syndrome

	Anti Tpo Ab (%)	Anti Tg Ab (%)	Sum
With metabolic syndrome	9(11.7%)	28(36.4%)	37(48%)
Without metabolic syndrome	8(8.7%)	11(12%)	19(20%)
With metabolic syndrome	9(11.7%)	28(36.4%)	37(48%)

Table 5: Relationship between serum TSH concentration and BMI

	W.C	Number	Mean serum TSH(MIU/L)	p-value
TSH	Normal<102ccm in men , <88cm in women High	124 42	1.8 2.35	0.01

DISCUSSION

The results of this study showed that thyroid dysfunction was found in 13% of patients with metabolic syndrome and 6.5% of normal subjects, and this difference was not statistically significant (P=0.24). The prevalence of thyroid autoantibodies in the metabolic syndrome was 48% which was significantly higher than control (P=0.0002). The study found a significant association between serum levels of TSH with WC and BMI.

In a study by Jee-Youngoh *et al.;* the prevalence of metabolic syndrome in Korea in patients with TSH greater than 2.5 was higher than those with lower TSH levels[14]. In another study by Nathalie Heimo *et al.;* performed on a number of elderly, a positive association was found between serum TSH and metabolic syndrome, and the prevalence of metabolic syndrome was higher in people with TSH greater than 2.25 [15]. Alexander Shinkov *et al.;* demonstrated a significant association between normal TSH and metabolic syndrome. The prevalence of metabolic syndrome increases at the upper quarter of TSH [1]. In the study by Chih-Cheng Lai *et al.;* on Taiwanese elderly, the prevalence of subclinical disorders was about 8%, and one third of them were diagnosed with metabolic syndrome [16].

Since the prevalence of thyroid dysfunction is affected by the investigated population, race, and the amount of iodine intake in the diet, differences between this study and other studies may arise from analysis of a specific population, the study methodology, and inclusion criteria.

Numerous studies have shown that the prevalence of subclinical hypothyroidism in metabolic syndrome ranges from 16.4 to 26% [9]. The prevalence of thyroid autoantibodies has been reported 17% for anti-TP Ab and 5.1% for anti-Tg Ab [17].

In another study, the prevalence of hypothyroidism and subclinical hypothyroidism has been reported 4%-20% and 0.6%-9.8%, respectively. These numbers depend on gender, age, and level of iodine intake [18].

The prevalence of subclinical hypothyroidism is higher in iodine sufficient area, and iodine supplementation increases its incidence; in contrast, the prevalence of subclinical hyperthyroidism is higher in areas with iodine deficiency [18].

It was observed in this study that significant changes in serum TSH level had a significant association with some parameters of the metabolic syndrome. Similar too many other studies, a positive correlation between serum TSH and BMI and abdominal obesity was observed. Possible causes of increased TSH levels in obese subjects include neuroendocrine dysfunction, changes in hypothalamic-pituitary-adrenal axis (HPA) due to leptin, and resistance to thyroid hormone due to TSH protein which is biologically inactive [14].

Several cross-sectional and longitudinal studies indicated a relationship between TSH and leptin levels, and the association of circulating levels of leptin with body fat and insulin resistance. Therefore, leptin may play an important role through insulin resistance (IR) in the association between TSH and obesity [14].

Thyroid dysfunction affects the activities of cholesterol ester transfer protein (CETP) and hepatic lipase (HL). Hypothyroidism is associated with decreased activity of CETP and HL which alters HDL metabolism [15].

An alternative explanation for the relationship between elevated TSH and BMI is that TSH affects adipocyte and pre-adipocyte receptors of adipose tissue and induces the differentiation by which pre adipocytes become adipocytes, and lead to stimulation of adipogenesis [9].

Semra Ayturk *et al.;* reported a positive significant correlation between TSH levels and BMI and WC, indicating that hormonal or blood mediators from adipose tissue, stimulates the HPA axis to increase TSH secretion [9].

In this study, no difference was found in TSH levels in normal and hypertensive patients. Although, hypothyroidism may elevate blood pressure, many researchers have reported controversial results about their relationship, and in many studies, no significant correlation has been found [11]. Asvold *et al.;* found a significant association between serum TSH level and BP in men and women [19].

The relationship between elevated TSH level (especially higher than 10 mIU/L) and hyperlipidemia has been proven in many studies (mainly because the production of thyroid hormones regulates hepatic lipoprotein). But in the present study, unlike the study of Alexander Shinkov et al. who showed a positive correlation between TSH levels and hypertriglyceridemia and low HDL cholesterol [1], no significant relationship was found between TSH and levels of TG and HDL.

Michalo poulou *et al.;* reported that people with TSH levels at the upper normal range and positive thyroid antibodies had higher cholesterol levels than those without thyroid antibodies [20].

In this study, no significant relationship was found between FBS with TSH, anti-Tpo Ab and anti-Tg Ab. In the study of Jee-Youngoh *et al.;* in Korea the prevalence of IFG (impaired fasting glucose) was relatively low and no statistically significant difference was reported between groups with high and low TSH [11]. Many studies have shown that there is no correlation between TSH levels and FBS. Although IFG frequency is associated with increased TSH levels, a study conducted in Korea reported a remarkable relationship between 2 hours postprandial glucose and TSH, implying elevated TSH level is associated with impaired glucose tolerance [14].

There are some limitations in this study**.** This cross-sectional study did not allow a cause-effect conclusion, and thus similar longitudinal studies should be done for gaining better knowledge. Second, insulin sensitivity (IR) which is the main pathophysiologic component of metabolic syndrome is better to be determined.

CONCLUSION:

The results of this study indicate that the prevalence of thyroid dysfunction in patients with metabolic syndrome is not significantly higher than normal people, while the prevalence of thyroid autoantibodies is significantly higher in patients with metabolic syndrome. Serum TSH level was significantly related to abdominal obesity (WC) and obesity (BMI), while it had no significant relationship with other components of the metabolic syndrome.

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