Metabolic Syndrome in Overt and Subclinical Hypothyroidism Syrian Patients

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Abstract- Thyroid hormones have important functions in many metabolic pathways, including glucose and lipid metabolism, and may cause metabolic syndrome. Both hypothyroidism and metabolic syndrome are common in the Syrian population. This research was carried out to evaluate the incidence of the metabolic syndrome in two types of hypothyroidism and the effect of TSH levels on its occurrence. A retrospective cross-sectional study was performed of 91 overt hypothyroidism patients, 31 subclinical hypothyroidism patients without clinical symptoms, and 53 controls without thyroid disorders. We used the criteria for metabolic syndrome as per International Diabetes Federation (IDF) which are defined as central obesity depending on race- and gender-specific WC cutoffs(Waist circumference (WC)≥94 cm for male, WC≥80 cm for female) in addition to any two of the following four parameters: (Triglycerides level: ≥150 mg/dl (1.7 mmol/l) or history of treatment for TG abnormality, HDL cholesterol level: <40 mg/dl (1.03 mmol/l) in males and <50 mg/dl (1.29 mmol/l) in females or history of treatment for HDL cholesterol abnormality, high blood pressure: systolic BP ≥130 mm Hg or diastolic BP≥85mm Hg or on treatment for previously diagnosed hypertension and high FPG: ≥100 mg/dl or previously diagnosed type 2 Diabetes mellitus. In conclusion, our study showed a significant correlation between overt hypothyroidism and metabolic syndrome. It also revealed that a TSH level over 2.5 uIU/ml significantly increases the risk of metabolic syndrome.

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Keywords: Overt hypothyroidism; Subclinical hypothyroidism; Metabolic syndrome; Thyroid-stimulating hormone; Obesity

Introduction

Thyroid hormones control thermogenesis and play an important role in gene expression, lipid, and glucose metabolism, food intake and fat oxidation (1), and basal metabolism, which includes catabolic and anabolic reactions (2). Thyroid impairment, which appears as either overt or subclinical hypothyroidism, negatively influences lipid metabolism and can lead to hypercholesterolemia which progressively increases the risk for cardiovascular disease and, potentially, mortality (3). There is a strong link between diabetes mellitus and thyroid dysfunction (4). Metabolic syndrome is a state of chronic low-grade inflammation as a consequence of a complex interplay between genetic and environmental factors. It is generally considered to be the concurrence of abdominal obesity, high blood pressure, insulin resistance/glucose intolerance, and dyslipidemia (5), and it consults with a 5-fold increase in the risk of type 2 diabetes mellitus and 2-fold the risk of developing cardiovascular diseases (6). Metabolic syndrome increases the risk of stroke, myocardial infarction (MI), and dying from such an event compared with those without the syndrome (7).

Metabolic syndrome is defined as per IDF criteria. This definition identified central obesity as an essential component of metabolic syndrome and defined the metabolic syndrome as central obesity depending on

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race- and gender-specific WC cutoffs (WC≥94 cm for male, WC≥80 cm for female) in addition to any two of the following four parameters: (Triglycerides level: ≥150 mg/dl (1.7 mmol/l) or history of treatment for TG abnormality, HDL cholesterol level: <40 mg/dl (1.03 mmol/l) in males and <50 mg/dl (1.29 mmol/l) in females or history of treatment for HDL cholesterol abnormality, high blood pressure: systolic BP ≥130 mm Hg or diastolic BP ≥85 mm Hg or on treatment for previously diagnosed hypertension, high fasting plasma glucose ≥100 mg/dl or previously diagnosed type 2 Diabetes mellitus) (8).

Different normal TSH limits have been suggested by different studies in various (9).

The National Academy of Clinical Biochemistry has recommended reducing the upper limit of TSH to 2.5 μIU\L (10). There are not enough studies about subclinical definitions depending on TSH levels according to the Syrian population. In this study, we have tried to evaluate the effect of TSH levels on the incidence of Metabolic syndrome.

Materials and Methods

This retrospective cross-sectional study was performed from December 2017 to October 2018 at Al Assad University Hospital in Damascus-Syria. 175 Age-matched adult women and men have similar BMI were included in this study and were divided according to TSH levels: 91 patients with overt hypothyroidism (TSH>4.20 μIU/ml), 31 patients with subclinical hypothyroidism (TSH>2.5 μIU/ml) without clinical symptoms, and 53 controls without thyroid disorders with an average of TSH (1.49 μIU/ml).

Study groups were analyzed for many variables, including gender, age, lifestyle, doing sport, smoking status, and alcohol consumption. None of the cases had diabetes mellitus, polycystic ovary syndrome, familial hypercholesterolemia, familial hyperproteinemia. None of the participants had been treated with lipid-lowering agents, steroidal Drugs, radioiodine treatment, or external radiation therapy. Pregnant women were excluded.

Bodyweight (kg) and height (m) were assessed by using standardized techniques and equipment. The BMI was determined using the formula (BMI=kg/m^2) where Kg is a weight of the individual and m^2 is the height in meters squared.

The waist circumference was measured with a paper tape horizontally at the level of the umbilicus in the standing position. Blood pressure was measured from the left arm in the sitting position with apparatus at the level of the heart. Venous blood samples were taken after 12 h of fasting. The serum levels of TSH were measured to evaluate the thyroid function using the electrochemiluminescence immunoassay method by Elecsys 2010 apparatus. Blood sugar levels were analyzed using the UV-Hexokinase method by Cobas 6000 apparatus. Fasting serum concentrations of triglycerides and HDL were measured enzymatically by Cobas 6000 apparatus.

Statistical analysis

The data analysis was done using IBM SPSS software (version 23). The data do not follow the normal distribution, so nonparametric tests were used. Data were presented as mean±SD. The *P* was calculated for statistical significance. Logistic regression analysis was used to determine the risk factors of metabolic syndrome. Statistical significance was set at $P<0.05$.

Results

The age, weight, BMI, waist circumference and blood pressure of the study groups are shown in Table 1. The laboratory results of TSH, FPG, TG and HDL levels of the study individuals have been summarized in Table 2.

The prevalence of metabolic syndrome was found to be 13.2% in euthyroid participants, 79.1% in overt hypothyroid participants, and 71.0% in subclinical hypothyroid participants.

Table 1. General characteristics and a number of metabolic syndrome components of the Study groups

	Controls (Mean±Std)	Overt hypothyroidism patients (Mean±Std)	Subclinical hypothyroidism patients (Mean±Std)
Age in years	39.81±11.55	45.10±10.13	41.39±10.76
Weight in Kg	88.06±20.05	87.81±19.76	89.50±21.81
BMI for adults	33.05±7.90	33.80±6.79	33.80±7.22
Systolic blood pressure in mmHg	120.28±9.52	125.22±12.15	125.48±13.37
Diastolic blood pressure in mmHg	73.77±6.71	75.11±8.69	75.16±8.61
Waist circumference(cm)	101.04±15.65	106.50±17.01	102.80±18.39

Table 2. TSH levels and a number of metabolic syndrome components of the study groups

	Controls (Mean±Std)	Overt hypothyroidism patients (Mean±Std)	Subclinical hypothyroidism patients (Mean±Std)
TSH(uIU/ml)	1.49±0.50	12.24±27.50	4.90±2.26
Fasting glucose(mg/dl)	90.77±12.53	100.80±11.47	99.3±10.62
Triglycerides(mg/dl)	107.99±52.05	174.54±88.36	155.37±92.31
High density lipoprotein(mg\dl)	53.05±12.28	42.96±8.96	41.87±11.90

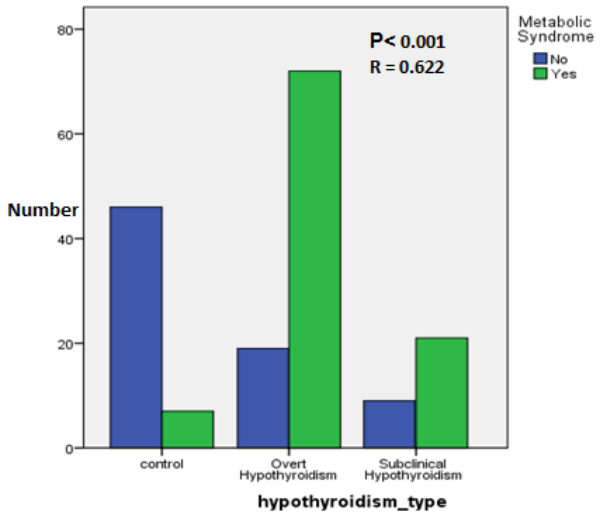

Figure 1. The correlation between Metabolic syndrome and thyroid function

The *Chi*-Square test showed evidence of the statistically significant difference between the Metabolic syndrome and the three study groups where the value *P*<0.001, R=0.622 (Figure 1).

Adjusted Bonferroni test was performed between the groups trying to determine the difference between them after calculating Adjusted standardized residuals and the value of a-error=0.05.

A statistically significant difference was found where there was no correlation between Metabolic syndrome and controls group *P*<0.001, the correlation between Metabolic syndrome and overt hypothyroidism group *P*<0.001, and no significant correlation between Metabolic syndrome and subclinical hypothyroidism group *P*=0.25 (1).

In logistic regression test between controls group, patients with TSH levels (2.5-4) µIU\L, patients with TSH levels more than 4 µIU\L and their correlation to Metabolic syndrome incidence, showed Metabolic syndrome occurs with a significant probability when TSH levels are (2.5-4) µIU\L (OR=4.36, *P*=0.001) and in more significant probability when TSH levels are more than 4 µIU\L (OR=11.05, *P*<0.001).

Metabolic syndrome occurs with a high probability of age (OR= 1.072، *P*=0.036) and with a higher probability of the value of TSH (OR=1.226, *P*=0.008). There was no statistically significant value for the effect of body mass index on the incidence of Metabolic syndrome in study groups *P*=0.396. There was no statistically significant value for the effect of gender on the incidence of Metabolic syndrome in study groups *P*=0.690. There was no statistically significant value for the effect of smoking on the incidence of Metabolic syndrome in study groups *P*=0.573.

There was no statistically significant value for the effect of sport on the incidence of Metabolic syndrome in study groups *P*=0.123. There was no statistically significant value for the effect of lifestyle on the incidence of Metabolic syndrome in study groups *P*=0.911.

Table 3. The odds ratio of study variables

Variable	*P*	Odds Ratio
BMI	0.396	
TSH	0.008	1.226
Age	0.036	1.072
Gender	0.690	
Smoking	0.573	
Sport	0.123	
Lifestyle	0.911	

Discussion

Metabolic syndrome in hypothyroidism patients may be due to deficiency of thyroid hormones which induces insulin resistance and disrupts glucose metabolism. Hypothyroidism also leads to dyslipidemia (11). The number of subclinical hypothyroidism patients was only 31 participants, and the distribution was homogeneous for the metabolic syndrome. Metabolic syndrome occurs with a high probability of aging, as it may be explained by decreasing metabolic rate with age. The occurrence of Metabolic syndrome with a high probability when TSH value (2.5-4) μIU\L and with more probability when TSH value is greater than 4 μIU\L. According to a study conducted in China in 2011, high levels of TSH were observed in patients with Metabolic syndrome, and it was suggested during this study that hypothyroidism may be a risk factor for metabolic syndrome (10).

According to population-based studies, people with high TSH levels (above 2 μIU\L or 2.5 μIU\L) have an increased risk of future hypothyroidism (12).

High glucose levels were noticed in both overt and subclinical hypothyroid participants. Several studies showed the association between overt hypothyroidism and type II diabetes mellitus.

In Chinese individuals, patients with metabolic syndrome have higher TSH levels than those without metabolic syndrome which suggested that subclinical hypothyroidism may be a risk factor for metabolic syndrome (13). Overt and subclinical hypothyroidism is related to decreased

glucose transport in myocytes. This is mediated by glucose transporters (GLUT) on the cell surface, which regulate intracellular glucose uptake. Basal expressions of GLUT are stimulated by thyroid hormones (14), so thyroid hormones deficiency reduces the GLUT transporters expression.

We have not been able to measure the average male values of HDL and compare them among study groups due to their few numbers, and it is explained by that all Metabolic syndrome of thyroid disorders are more prevalent in females than males (15).

Limitations

The sample size and we did not analyze Free thyroxine because of its cost.

Our findings confirm that overt hypothyroidism induces incidence of metabolic syndrome and metabolic syndrome may occur when TSH level [2.5-4] μIU\L and in more potential when TSH level >4 μIU\L or (high TSH levels of over 2.5 μIU\L is a risk factor for metabolic syndrome). More studies with a larger sample size of participants are needed to determine the upper limit of normal TSH.

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