Association of Subclinical Hypothyroidism with Metaboic Syndrome and its Parameters

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Abstract

Metabolic Syndrome (MetS) (also known as syndrome X) is a cluster of cardiovascular risk factors, where the primary etiology is suggested to be related to Insulin Resistance (IR). The components of MetS include dyslipidemia, hypertension, abdominal obesity & hyperglycemia. Thyroid hormones also influence the parameters of MetS such as high density lipoprotein (HDL), Triglycerides (TGL) & Blood pressure (BP). Subclinical Hypothyroidism (SCH) defined as an asymptomatic condition with high thyroid stimulating hormone (TSH) has been suggested as a risk factor for cardiovascular disorders. The aim of the present study was to determine the association of SCH with metabolic syndrome . For the study 30 patients fulfilling 3 or more American National Cholesterol Education Program Adult III Treatment Panel (NCEP ATP III) criteria were diagnosed with MetS and considered as case group and 30 controls were included in the study, each group consisted of both sexes and the participants were between age of 27-73 years. Various parameters such as waist circumference, TGL, HDL, blood pressure and fasting glucose along with TSH was measured. A significant increase was seen in the mean TSH of patients with MetS when compared to control group (p=0.000) was found. 96.66% of the case group had SCH when compared with 60% of individuals from the control group. It may be concluded that SCH is significantly associated with metabolic syndrome.

Key words: metabolic syndrome (MetS), thyroid stimulating hormone (TSH), subclinical hypothyroidism (SCH), Obesity

Introduction

Metabolic syndrome (MetS) or insulin resistance syndrome [1], a cluster of metabolic abnormalitites which include hypertension, central obesity, dyslipidemia and glucose intolerance is being used to identify the risk of developing cardiovascular disease (CVD)[2]. Obesity, insulin resistance, hormonal imbalance physical inactivity and advanced age have been suggested as risk factors for this syndrome[3].Thyroid dysfunction is also considered as a risk factor for CVD as it is known to lipid profile and blood pressure [4].

Subclinical hypothyroidism (SCH) is an asymptomatic condition characterized with normal thyroid hormone levels accompanied with high levels of thyroid-stimulating hormone (TSH)[5]. Similar to MetS, SCH is also being considered as a risk factor for CVD and metabolic disorders such as hypertension and deranged lipid profile [6].

It was recommended by the national academy of clinical biochemistry (NCAB) to lower the upper reference limit of TSH to 2.5µIU/L for establishing SCH. This was based on a study which was conducted that showed more than 95% normal individuals had TSH levels <2.5 µIU/L and those with a higher value were likely to have underlying thyroid disorders [2].

Obesity, which is considered as a key component of MetS is known to occur due to increased energy intake or decreased expenditure of energy, or also due to a combination of both, thus leading to a positive energy balance. Thyroid hormones are known to up-regulate metabolic pathways concerned with resting energy expenditure. This

shows that obesity and thus MetS are related to thyroid hormones. It is still unclear if the alteration in thyroid hormones is a cause or due to the effect of obesity [7].

The present study was performed with the hypothesis that SCH may have an impact on the parameters of of MetS. Thus the aim of this study was to identify the association of SCH with MetS.

Materials and Methods

A total of 60 patients were included in the study. 30 participants (21 male and 9 female) between the ages of 32-71 with metabolic syndrome fulfilling 3 or more American National Cholesterol Education Program Adult III Treatment Panel (NCEP ATP III) criteria (namely waist circumference >40 inches in men and > 35 inches in women, blood pressure $\geq$ 130/85 mmHg, triglycerides $\geq$ 150 mg/dl, HDL cholesterol < 40mg/dl in men and <50mg/dl in women, and fasting plasma glucose > 110mg/dl). 30 normal individuals (15 males and 15 females) between age 27-73 were considered as controls. All the participants were randomly selected from the master health check up at Sri Ramachandra Medical College and Research Institute. Patients with known diabetes or other endocrine disorders, patients receiving any medication that may alter thyroid functions or lipid levels, pregnant women and patients with any known systemic illness were excluded. Study protocol was accepted by institutional ethics committee and all the participants gave written consent before performing the study.

The waist circumference was measured during mid respiration on bare skin at the narrowest indentation between 10th rib and the iliac crest. Blood pressure was recorded twice in the sitting position after a resting period of 5 minutes and the mean of two measurements was used for systolic and diastolic pressure. Fasting plasma glucose (FPG), serum triglycerides (TGL) and High density lipoprotein (HDL) were measured enzymatically using automated analyzer. Serum TSH was measured by ELISA.

Statistical analysis was done using SPSS 15.0 for windows evaluation version. Inter group comparisons of quantitative variables were made by using independent sample t test. A p value of <0.05 was considered significant.

Results

After statistical analysis it was found that both the groups were similar in age (p>0.05). Mean values for waist circumference, blood pressure, fasting plasma glucose, triglycerides and TSH was higher (p<0.05), whereas the levels of HDL were lower (p=0.000) in the case group when compared to the controls [table1].

Subclinical hypothyroidism (SCH) was found in 29 (96.66%) of patients in the case group and in 18 (60%) of those in the control group, the difference between them was found to be statistically significant (p=0.001) on using the chi square test [fig1].

Discussion

MetS is a cluster of cardiometabolic risk factors characterized by inflammation [8]. The cardiovascular system (CVS) is known to be sensitive to thyroid hormones [3]. Also, a lesser degree of thyroid deficiency is seen to affect the CVS [9]. The present study showed a significant increase (p=0.000) in TSH levels in patients with MetS when compared with the controls and also a higher percentage of patients (96.66%) had SCH when compared to the control (60%).

Thyroid hormones have been associated with the parameters used to diagnose metabolic syndrome in many studies. Firstly, obesity and weight gain: Pathways of resting energy expenditure are mediated by thyroid hormones and hypothyroidism is almost always associated with weight gain and obesity [10, 11]. Similarly, many studies have

demonstrated an increased TSH (but within normal limits) and also a positive correlation between TSH, BMI and obesity [12, 13]. Possible causes for this increase in obesity is due to neuro-endocrine dysfunction, alteration in the hypothalamic-pituitary axis that is leptin induced and also could be due to a consequence of throid receptor resistance [7,10, 13 -15]. Thus leptin may play a major role in linking increased TSH and obesity via insulin resistance (IR).

Lipoprotein production in the liveris also known to be regulated by thyroid hormones explaining why altered TSH is associated with dyslipidemia even when the elevated TSH was within normal levels, a finding which further supports this study. This may result from reduced lipoprotein lipase activity or also due decreased receptor dependant clearance of lipoproteins in hypothyroid patients [16, 17]. In addition to this increasing affect SCH is also known to decrease HDL levels [18]. Elevated TSH levels have also been reported to be associated with hyperglycemia or impaired fasting glucose [2]. As to the effect on blood pressure thyroid hormones have been shown to effect it in several studies and SCH in particular has been demonstrated to increase blood [9].

Since thyroid hormones and also SCH is thus associated with the parameters of MetS it is no surprise that it is seen to be associated with the condition as such. Also the presence of SCH in 60% of the control group is a concern as this suggests derangement of metabolic function even though MetS has not yet been established. This study is limited because of the small sample size and also that free thyroid hormones and thyroid antibodies were not measured ..

To conclude, this study showed a significant association between SCH and metabolic syndrome. It is thus suggested that apparently normal individuals with presence of SCH (TSH>2.5µIU/L) be assessed to detect MetS.

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Figures and Tables:

Table 1: patient characteristics

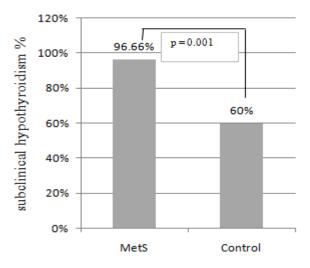|	Case (MetS)	Control	p value
Age (in years)	50.06±11.74	49.83±11.55	0.938
Waist circumference (inches)	40.83±3.40	38.13±4.78	0.015
Systolic blood pressure (mmHg)	131.26±17.05	111.93±12.16	0.000
Diastolic blood pressure(mmHg)	82.8±8.90	75.8±8.09	0.002
Fasting plasma glucose (mg/dl)	124.93±47.28	96.83±10.07	0.002
Triglycerides (mg/dl)	144.1±38.91	98.14±35.20	0.000
HDL cholesterol (mg/dl)	38.8±7.66	47.16±9.38	0.000
TSH (μIU/ml)	4.22±1.18	3±1.33	0.000

Fig 1: comparison of groups according to presence of SCH