



A Comparative Study of Thyroid Profile in Individuals with and Without Metabolic Syndrome

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Abstract

Metabolic syndrome is increasingly recognised as emerging threats to health of human race. Thyroid hormones up regulate metabolic pathways relevant to resting energy expenditure. Obesity causes alteration in thyroid function tests. We compared the thyroid profiles of individuals with and without Metabolic Syndrome and assessed the possibility of obesity influencing the results. This is a cross sectional study which includes 200 patients above the age of 18 years attending the outpatient department of our institution from January 2015 to August 2016. They were divided into four groups where group 1 consists of patients with Metabolic syndrome and obesity, group 2 with Metabolic Syndrome without obesity, group 3 without Metabolic syndrome but obese and group 4 without Metabolic syndrome and non obese. The NCEP ATP III criteria was used for assessing Metabolic syndrome and revised consensus guidelines for Asian Indians was chosen to determine the Body Mass Index (BMI) for obesity. TSH, T4, T3 were measured as indicators of thyroid function. The difference in mean TSH levels between individuals with Metabolic Syndrome (3.84 ± 2.44 uIU/L) and without Metabolic Syndrome (2.10 ± 1.70 uIU/L) was statistically significant ($p = \leq 0.05$) while the mean T4 and T3 levels were comparable. Amongst individuals with metabolic syndrome, difference of mean TSH between obese and non-obese group was not significant ($p=0.984$). Individuals with Metabolic syndrome have a higher TSH level but normal T3 and T4 levels. This rise in TSH is independent of obesity.

Keywords: Metabolic syndrome, Thyroid profile.

Introduction

Metabolic syndrome is now being increasingly recognised as an emerging threat which will invade desktops of public health policy planners in the decades to come. Metabolic syndrome is a constellation of many abnormalities or disease. The major features of metabolic syndrome include central obesity,

hypertriglyceridemia, low high density lipoprotein cholesterol, hyperglycemia and hypertension¹. The prevalence of metabolic syndrome in western world is about 20-30%^{2,3,4}. By National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) criterion, 41.1% of Asian Indian were suffering from metabolic syndrome, whereas the

prevalence of metabolic syndrome was 11.2% in Chennai urban population^{5,6}. The Jaipur heart study have reported that prevalence of metabolic syndrome in urban Indian population was 18.4% in men , 30.9% in women and 24.9% overall⁷. Obesity, a main component of metabolic syndrome occurs due to increased energy intake , decreased energy expenditure or a combination of both , thus leading to positive energy balance . Thyroid hormones up regulate metabolic pathways relevant to resting energy expenditure . Obesity causes alteration in thyroid function tests. There are studies which showed subclinical thyroid dysfunction and even thyroid stimulating hormone within high normal range can be related to metabolic syndrome and its components^{8,9}. This study is intended to compare thyroid function in patients with and without metabolic syndrome and asses the possibility of obesity influencing the results.

Materials and Method

Study area and period: This cross-sectional study was conducted at our institution from January 2015 to August 2016. This institution is tertiary referral centre for patients of neighbouring seven districts and part of neighbouring State . All participants were provided with written informed consent and the study protocol was approved by the Ethical Committee of the institution .

Study population : The study subjects included 200 patients with 100 having metabolic syndrome and 50 patients out of these 100 patients were obese. The remaining 100 patients did not have metabolic syndrome and this group was further subdivided into groups of 50 patients with or without obesity each. All subjects were divided into four groups for statistical comparison – 1. Metabolic syndrome with obesity (Mets Obese); 2. Metabolic syndrome without obesity (Mets non-Obese); 3. Non-metabolic syndrome with obesity (Non- mets

Obese); 4.Non- metabolic syndrome without obesity (Non- Mets non -Obese)

People above the age of 18 years attending General Medicine outpatient department of our institution were included in this study. The National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) criteria was used for identifying individuals with metabolic syndrome. Three or more out of five criterion was taken to define metabolic syndrome: 1. Waist circumference- Men >40 inches, women >35 inches; 2. Triglyceride- ≥ 150 mg/dl or on treatment for hypertriglyceridemia; 3. HDL Cholesterol- men <40mg/dl, women <50mg/dl or on treatment for low HDL Cholesterol ; 4. Blood pressure >130/85 mm of Hg or on treatment for hypertension and 5. Fasting glucose ≥ 100 mg/dl or on treatment for diabetes mellitus¹⁰. The criteria for obesity was taken as per revised consensus guidelines for Asian Indians with Body Mass Index (BMI) ≥ 25 kg/m²¹¹. Those excluded consisted of participants having a personal history of thyroid disease and have been taking thyroxin, antithyroid drugs or radioiodine for treatment ; taking medication affecting thyroid function such as glucocorticoids , antiepileptics and contraceptive drugs ; pregnant woman or within first year of post partum ; renal and liver disorders.

Data Collection: Consecutive samples taken till desired sample size reached. All subjects underwent careful interview with questionnaire using a structured Performa. We abstracted general information such as name, age, gender, educational qualification, profession, history of smoking and drinking , personal and family history of thyroid disease , diabetes, hypertension and dyslipidaemia. The relevant clinical and investigative data were recorded. Patient particulars including height, weight, body mass index and waist circumference were recorded. All the patients were asked to rest at least 30 minutes and then blood pressure of their right arm was measured twice with a sphygmomanometer with the participants in a sitting position. There

was a 5-min interval between the two measurements for each participant, and the mean value of the two measurements was used. All blood samples were taken in empty stomach. Blood glucose was measured by glucose oxidase method. Lipids were measured by Hitachi 704 analyser. Acuu Lite VAST CLIA Kits was used for TSH (Thyroid stimulating hormone), T3 (Triiodothyronine) and T4 (Thyroxin) measurements.

Statistical Analysis: The analysis was performed using SPSS 20 software. The unpaired student t test was used to find a relation between mean TSH levels in those with and without metabolic syndrome and amongst four groups with each other.

Result

On comparison of different clinical data amongst patients of metabolic and non-

metabolic syndrome BMI, waist circumferences and systolic blood pressure were significantly different. But diastolic blood pressure was comparable (Table 1). The mean blood fasting and post prandial sugar, triglyceride, HDL cholesterol were significantly different amongst individuals with metabolic and non-metabolic syndrome. The difference in mean TSH levels in individuals with Metabolic Syndrome (3.84 ± 2.44 μ IU/L) and without Metabolic Syndrome (2.10 ± 1.76 μ IU/L) was statistically significant ($p = \leq 0.05$) while the mean T4 and T3 levels were comparable (Table 2). Difference of mean TSH in groups Mets obese (3.86 ± 2.62) and Mets non-obese (3.87 ± 2.27) was not significant ($p = 0.984$). Similar results ($p = 0.791$) was found in mean TSH in groups Non-mets obese (2.14 ± 1.94) and Non-mets non-obese (2.04 ± 1.43) was (Table 3).

Table 1: Comparison of different demographic, physical and clinical data in subjects with and without metabolic syndrome.

Variables	With Metabolic syndrome	Without Metabolic syndrome	p-value
Age(years)(mean \pm SD)	56.83 \pm 12.42	52.99 \pm 14.60	0.047
Sex(number- %) male	51	57	
	Female	43	
BMI (Kg/m ²)(mean \pm SD)	24.11 \pm 4.41	22.35 \pm 4.73	0.007
Waist circumference (cm) (mean \pm SD)	87.74 \pm 11.77	84.52 \pm 9.88	0.037
Systolic BP(mm of Hg) (mean \pm SD)	125.80 \pm 19.99	120.54 \pm 16.17	0.043
Diastolic BP(mm of Hg) (mean \pm SD)	77.86 \pm 9.73	77.20 \pm 6.60	0.575

Table 2 Comparison of different investigative data in subjects with and without metabolic syndrome

Variables	With Metabolic Syndrome	Without Metabolic syndrome	p-value
F Sugar(mg/dl) (mean \pm SD)	120.47 \pm 41.54	98.41 \pm 16.70	≤ 0.05
PP Sugar(mg/dl) (mean \pm SD)	190.80 \pm 61.48	146.50 \pm 51.76	≤ 0.05
Triglyceride(mg/dl) (mean \pm SD)	135.97 \pm 27.26	117.15 \pm 21.07	≤ 0.05
HDL-Cholesterol (mg/dl) (mean \pm SD)	44.66 \pm 7.22	50.81 \pm 8.50	≤ 0.05
T3(mean \pm SD) (ng/ml)	1.28 \pm 0.65	1.41 \pm 0.64	0.156
T4(mean \pm SD) (μ g/dl)	7.99 \pm 3.11	8.01 \pm 3.54	0.966
TSH(mean \pm SD) (μ IU/ml)	3.84 \pm 2.44	2.10 \pm 1.76	≤ 0.05

Table 3 Comparison of mean TSH level among each other of different study group

	TSH level (μ IU/ml)		TSH level (μ IU/ml)	p-value
Mets obes	3.86 \pm 2.62	Mets non-obes	3.87 \pm 2.27	0.984
		Non-mets obes	2.14 \pm 1.94	\leq 0.05
		Non-mets non-obes	2.04 \pm 1.43	\leq 0.05
Mets non-obes	3.87 \pm 2.27	Mets obes	3.86 \pm 2.62	0.984
		Non-mets obes	2.14 \pm 1.94	\leq 0.05
		Non-mets non-obes	2.04 \pm 1.43	\leq 0.05
Non-mets obes	2.14 \pm 1.94	Mets obes	3.86 \pm 2.62	\leq 0.05
		Mets non-obes	3.87 \pm 2.27	\leq 0.05
		Non-mets non-obes	2.04 \pm 1.43	0.791
Non-mets non-obes	2.04 \pm 1.43	Mets obes	3.86 \pm 2.62	\leq 0.05
		Mets non-obes	3.87 \pm 2.27	\leq 0.05
		Non-mets obes	2.14 \pm 1.94	0.791

Mets obes = Metabolic syndrome with obesity , Mets non-obes = Metabolic syndrome with no obesity ,
Non-mets obes = No metabolic syndrome with obesity, Non-mets non – obes = No metabolic syndrome with no obesity .

Discussion

There is an inconsistency in thyroid function in metabolic syndrome. The rise of TSH with normal T3 and T4 are mostly reported,^{8,9} but the rise in TSH with alteration of T3 without any effect on T4 or increased thyroid hormone levels have also been described in obesity.^{12,13} Ruhla S et al found that euthyroid subjects with a TSH in the upper normal range (2.5-4.5uIU/L) were more obese, had higher triglycerides and had an increased likeliness of metabolic syndrome.¹⁴ Lee YK et al found that high normal TSH levels were significantly associated with metabolic syndrome.¹⁵

These studies have similar findings with that of ours. We found that the mean TSH was a significantly higher in individuals with metabolic syndrome (3.84 \pm 2.44) compared to those without (2.10 \pm 1.76) but T3 and T4 levels were comparable. We further found that this rise in TSH levels among individuals with metabolic syndrome was independent of them being obese as mean TSH of met obese (3.86 \pm 2.62) and met non-obese (3.87 \pm 2.27) were comparable (p=0.984), so was the mean TSH of non-mets-obese (2.14 \pm 1.94) and non-mets non-obese (2.04 \pm 1.43) with p=0.791.

The metabolic syndrome is associated with insulin resistance and a hyperinsulinemia is a metabolic consequence. These patients with metabolic

syndrome may have a thyroid receptor resistance, similar to insulin resistance resulting in persistent elevated TSH levels.

Studies showed that adipocytes and preadipocytes expressed TSH receptors. TSH binds with this TSH receptors and induces preadipocytes to produce and release adipokines . One of them is leptin which plays a very important role in the onset of metabolic syndrome and cardiovascular disease.¹⁶

Recently, an experimental study in an animal model has demonstrated that the mutation of alpha isoform of the thyroid hormone receptor caused insulin resistance and thyroid hormone resistance.¹⁷ In addition, studies investigating thyroid hormone receptors in metabolic syndrome subjects demonstrated a decrease of TSH-R density.^{18,19}

Our findings in this study suggests that raised TSH levels in those with metabolic syndrome could be due to associated thyroid receptor resistance similar to insulin resistance. This is supported by the normal T3 and T4 levels . Insulin resistance in hypothyroidism is usually thought to be due to decreased intracellular glucose utilisation and reduced glucose transporter (GLUT 4) translocation. It is also due to decreased glycogen synthesis and reduced glucose oxidation²⁰. Administration of TSH to euthyroid patients caused endothelial dysfunction and increased serum level of C-

reactive protein, TNF- α , several indices of oxidative stress and IL -6, which leads to an increase in the components of metabolic syndrome, thus explaining the relation between increased TSH and metabolic syndrome^{21,22}. The raised TSH could be due to hormones secreted by adipose tissue but our study have shown that this rise in TSH is independent of obesity. Whether metabolic syndrome and thyroid dysfunction is related to common biochemical markers or risk factors are still not known. More studies are needed to determine whether TSH should be routinely done in patients with metabolic syndrome.

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