



METABOLIC SYNDROME AND HYPOTHYROIDISM

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Abstract:

Metabolic syndrome (MetS) and hypothyroidism are well known atherogenic cardiovascular disease. Considerable overlap occurs in the pathogenic mechanisms of atherosclerotic cardiovascular disease by metabolic syndrome and hypothyroidism. This cross sectional study assesses thyroid function in patients with metabolic syndrome and to investigate the association between hypothyroidism and metabolic syndrome.

MATERIAL AND METHODS: We included the patients who fulfilled the National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP) III criteria [three out of five criteria positive, namely, blood pressure $\geq 130/85$ mm Hg or on antihypertensive medications, fasting plasma glucose >100 mg/dl or on anti-diabetic medications, fasting triglycerides >150 mg/dl, high density lipoprotein cholesterol (HDL-C) <40 mg/dl in males and <50 mg/dl in females, waist circumference >102 cm in men and 88 cm in women] were included in the study group¹. We exclude the patients receiving medication that may alter thyroid functions or lipid levels, pregnant women, patients with liver or kidney disorder and patients with a cardiovascular disease, corticosteroid use, active liver disease, and renal dysfunction. Patients on weight loss therapies or steatogenic drugs, and known HIV-positive cases were excluded from the study.

RESULTS: A total of 200 patients were included in the study of which 100 were patients with MetS and 100 were control. Statistically significant difference was observed in all the characteristics except FT4 levels of metabolic syndrome patients and control group. BMI, waist circumference, mean systolic and diastolic blood pressure, fasting blood sugar, total cholesterol, LDL, triglycerides, and TSH were significantly higher in the study group compared to the control group. HDL was significantly lower in the study group. Of the 100 MetS patients, overt hypothyroidism was reported in 18 (18%) patients and overt hyperthyroidism in 2 (2%) patients. Subclinical hypothyroidism, overt hypothyroidism, and subclinical hyperthyroidism were reported in 7%, 2%, and 1 % patients with newly diagnosed TD, respectively. Total number of TD patients was 28(28%).

CONCLUSION: There was a high prevalence of TD in patients with MetS, so there is a positive relation between thyroid hormone status and MetS. Hypothyroidism was the most common TD in patients with MetS. It is advisable to assess the thyroid function in all patients with MetS.

KEY WORDS: Mets, TD, Cholesterol, TG, LDL, HDL, FT3, FT4, TSH and Hormone.

Introduction

Metabolic syndrome (MetS) is a combination of risk factors such as hypertension, dyslipidemia, hyperglycemia, truncal obesity, and prothrombotic and proinflammatory conditions, that could increase the risk of cardiovascular diseases, diabetes, and also death. According to an estimate by the International

Diabetes Foundation, nearly one-fourth of the world's population has MetSⁱⁱ. Metabolic Syndrome can also be defined as a cardiometabolic risk factors which increase the risk of suffering cardiovascular diseases and type 2 diabetes mellitusⁱⁱⁱ. The prevalence of metabolic syndrome has started increasing all over the world with evidence of high prevalence in India and other South Asian countries^{iv}.

It has been observed that thyroid dysfunction, prominently subclinical hypothyroidism is more frequent in metabolic syndrome patients than general population[3]. From various studies it has been projected that about 42 million people in India suffer from thyroid diseases^v. Due to impact of thyroid hormones on lipid metabolism, glucose, blood pressure, and cardiovascular dysfunction metabolic syndrome is closely associated with thyroid dysfunction^{vi}. Also there is a considerable overlap in the pathogenic mechanisms of atherosclerotic cardiovascular disease by MetS and hypothyroidism. Insulin resistance has been studied as the basic pathogenic mechanism in MetS^{vii}. Role of insulin resistance in development of dyslipidemia in hypothyroidism has been suggested in recent studies^{viii}.

Some physiological or pathological functional changes in the thyroid gland have shown an association with MetS and its related components which includes obesity, insulin resistance, abnormal lipid and glucose metabolism, hypertension, and cardiovascular dysfunction. MetS and thyroid dysfunction are both characterized by a group of common abnormalities like abdominal obesity, hyperglycemia, hypertension, reduced high-density lipoprotein cholesterol (HDL-C), and elevated triglycerides (TG). Moreover insulin resistance has been identified as a basic mechanism for MetS, also plays a role in hypothyroidism^{ix}.

In the present study we examined the thyroid function and also examined the association between components of metabolic syndrome and thyroid function

MATERIAL AND METHODS

This cross-sectional study was conducted in Dept. of General Medicine Darbhanga Medical College and Hospital Laheriasarai Darbhanga, Bihar. We included the patients who fulfilled the National Cholesterol Education Program-Adult Treatment Panel (NCEP-ATP) III criteria [three out of five criteria positive, namely, blood pressure $\geq 130/85$ mm Hg or on antihypertensive medications, fasting plasma glucose >100 mg/dl or on anti-diabetic medications, fasting triglycerides >150 mg/dl, high density lipoprotein cholesterol (HDL-C) <40 mg/dl in males and <50 mg/dl in females, waist circumference >102 cm in men and 88 cm in women] were included in the study group^x. We exclude the patients receiving medication that may alter thyroid functions or lipid levels, pregnant women, patients with liver or kidney

disorder and patients with a cardiovascular disease, corticosteroid use, active liver disease, and renal dysfunction. Patients on weight loss therapies or steatogenic drugs, and known HIV-positive cases were excluded from the study.

After obtaining an informed signed consent to participate in the study. Three blood pressure readings were taken in the supine position and a mean value of the readings was taken as the final recording. Waist circumference was measured at the plane between anterior superior iliac spines and lower costal margin at the narrowest part of the waistline while the patient was standing and during expiration. Blood samples were collected for assessment of hemogram, plasma glucose, lipid profile (TG, total cholesterol (TC), HDL-C, and low-density lipoprotein cholesterol (LDL-C)), and thyroid function (free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH)). Normal range for TSH was $0.27-4.2$ μ IU/ml, FT3 was $1.4-4.2$ pg/ml, and for FT4 was $0.93-1.7$ ng/dl. A high serum TSH level ($4.2-10$ μ IU/ml) and normal FT3 and FT4 levels were required for the diagnosis of subclinical hypothyroidism. Patients with high TSH (>10 μ IU/ml) and low FT3 and FT4 levels were classified as being overt hypothyroid. Patients with normal TSH, FT3, and FT4 were considered euthyroid. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared.

Body mass index (BMI) was calculated. The BMI cut-off limits for overweight and obesity were as follows: overweight (BMI > 23 and <25), class I obesity (BMI >25 and <30), and class II obesity (BMI > 30)^{xi}.

Baseline characteristics of the study participants were expressed in mean \pm SD and percentage. Linear regression model was created to know any significant relationship between the components of MetS and TSH levels. Associations between patient characteristics such as age, sex, mean systolic and diastolic blood pressure, waist circumference, total cholesterol, HDL-C, LDL-C, triglycerides, fasting blood sugar and subclinical hypothyroidism in the study group were analyzed using multiple logistic regression. *P* value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS windows version 17.0 software

OBSERVATIONS AND RESULTS

A total of 200 patients were included in the study of which 100 were patients with MetS and 100 were control.

Table 1: Characteristics of MetS and Control group.

Characteristics	MetS group (n=100)	Control (n= 100)	P value
Age in years	42.8±9.25	46.9±7.24	0.0006
BMI (Kg/m ²)	27.52±2.97	21.45±3.11	< 0.0001
Waist circumference (cm)	91.22±7.5	82.49±5.4	< 0.0001
Systolic BP	139.77±15.87	118.78±12.44	< 0.0001
Diastolic BP	89.88±5.48	72.45±8.41	< 0.0001
Fasting blood sugar	124.21±20.87	88.45±9.54	< 0.0001
Total cholesterol(mg/dl)	220.11±25.44	186.46±11.54	< 0.0001
LDL (mg/dl)	118.5±29.08	89.21±18.54	< 0.0001
HDL (mg/dl)	46.58±4.87	51.44±5.11	< 0.0001
Triglycerides (mg/dl)	178.09±21.44	129.54±15.82	< 0.0001
TSH (µIU/ml)	4.57±3.54	2.27±2.11	< 0.0001
FT3 (pg/ml)	2.59±0.84	3.45±0.81	< 0.0001
FT4 (ng/ml)±	1.34±0.29	1.38±0.28	0.3223

Statistically significant difference was observed in all the characteristics except FT4 levels of metabolic syndrome patients and control group. BMI, waist circumference, mean systolic and diastolic blood pressure, fasting blood sugar, total cholesterol, LDL, triglycerides, and TSH were significantly higher in the study group compared to the control group. HDL was significantly lower in the study group.

Values in the table 2 were taken for grading the thyroid dysfunction

Table 2: Definitions for different grades of thyroid dysfunction.

Parameters	Hyperthyroidism		Hypothyroidism	
	Overt	Subclinical	Overt	Subclinical
TSH (µIU/mL)	<0.45	<0.45	>4.50	>4.50
FT4 (ng/dL)	>1.8	0.8-1.8	<0.8	0.8-1.8
FT3 (pg/mL)	>4.4	1.4-4.4	<1.4	1.4-4.4

Of the 100 MetS patients, overt hypothyroidism was reported in 18 (18%) patients and overt hyperthyroidism in 2 (2%) patients. Subclinical hypothyroidism, overt hypothyroidism, and subclinical hyperthyroidism were reported in 7%, 2%, and 1 % patients with newly diagnosed TD, respectively. Total number of TD patients were 28(28%)

Table 3: prevalence of different grades of thyroid dysfunction.

Thyroid dysfunction	MetS patients (n=100) %
Hypothyroidism	18 (18%)
New overt hypothyroidism	2(2%)
New subclinical hypothyroidism	7(7%)
Hyperthyroidism	1(1%)
New overt hyperthyroidism	0(0%)
New subclinical hyperthyroidism	0(0%)
Total TD patients	28(28%)

DISCUSSION AND CONCLUSION

In human being thyroid hormones has an essential role in regulating energy balance and metabolism of glucose and lipids, hence these hormones affects the MetS parameters, which includes HDL-C, TG, blood pressure, and plasma glucose. Hypothyroidism is also found to be associated with obesity, dyslipidemia, and increased risk of atherogenic CVD^{xii}.

Pathophysiological basis for glucose intolerance in patients with hypothyroidism is thought to be insulin resistance^{xiii}.

In our study The MetS group included 100 cases and 100 controls. The two groups were not similar in their distribution of age (*P* = 0.0006). In this study, the mean systolic and diastolic pressure, fasting blood sugar level, total cholesterol, LDL-C, triglycerides,

waist circumference, and BMI were significantly higher and HDL-C levels were significantly lower in the MetS group than in the control group. These results were in accordance with the study by Garcia *et al*^{xiv}, and Shantha *et al*^{xv}.

Our study showed a prevalence of 18% of hypothyroidism and overt hypothyroidism was 2%. In a study in adult population in India, the prevalence of hypothyroidism was 3.9% while that of subclinical hypothyroidism was 9.4%^{xvi}. In a study by Uzunzulu *et al*, there was significant association of subclinical hypothyroidism and MetS^{xvii}. The predominance of hypothyroidism (overt and subclinical: 20%) suggests that MetS could also be a consequence or sequel of various grades of hypothyroidism during the natural course of the disease. In other studies predominance of subclinical hypothyroidism (14.6% to 53%) was reported followed by overt hypothyroidism (3.5% to 7.4%)^{xviii, xix, xx}. It has also been proposed that the increase levels of TSH in obesity is a parphenomenon similar to insulin resistance, in which leptin is the responsible for rising levels of thyrotropin, being the resistance in TSH receptors a consequence of this process^{xxi, xxii}.

To conclude there was a high prevalence of TD in patients with MetS, so there is a positive relation between thyroid hormone status and MetS. Hypothyroidism was the most common TD in patients with MetS. It is advisable to assess the thyroid function in all patients with MetS.

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