



Patients of Metabolic Syndrome with Thyroid Disorder

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Submitted: 01-08-2022

Accepted: 07-08-2022

ABSTRACT

Introduction: Metabolic syndrome (MetS), also known as Syndrome X, Deadly quartet, Reaven's syndrome. Approximately 20-25% of the world population are suffering from MetS. It consists of a constellation of metabolic abnormalities which include central obesity, hyperglycemia plus insulin resistance, high triglycerides (TG) plus low HDL cholesterol and hypertension.

Aim: To correlate the finding of MetS patients with Thyroid dysfunction for early diagnosis of thyroid disorder in patients suffering from MetS which could help to evaluate appropriate management of TD in terms of reduction in MetS and its related component.

Materials and methods: A total 50 patients of metabolic syndrome with thyroid disorder and 50 healthy individuals aged between 17-80 years who were not having any liver disorders, renal insufficiency, congestive cardiac failure, pregnant women, acutely ill patients, patients on statins and other medications that alter thyroid function or lipid level visiting to medicine OPD were include in study. Parameter such as waist circumference (WC), blood pressure (BP), TG, HDL-C, T₃, T₄, and TSH were determined and compared with control subjects.

Result: WC, BP, TG, and serum TSH level were reported significantly higher in case whereas lower mean HDL-C and serum T₃ and T₄ in case as compared to control (p = 0.000) in both genders. **Conclusion:** Thyroid disorder is most common in middle aged subjects. So, clinicians should remain highly suspicious in middle aged subjects with thyroid disorder for increase in metabolic syndrome parameters which may enhance the risk for atherosclerosis leading to coronary artery disease.

Keywords: Metabolic syndrome, Thyroid disorder, Central obesity, Insulin resistance.

I. INTRODUCTION

Metabolic syndrome (MetS), also known as Syndrome X, Deadly quartet, Reaven's syndrome. It is disorder of energy use and storage and finding suggest that approximately 20-25% of the world population are suffering from MetS. Individual with metabolic syndrome are at higher risk to develop cardiovascular disease, stroke and disease related to fat deposition in artery walls. Finding suggest that, people with MetS has double the chance to develop heart disease or/and five times as likely to develop diabetes with people without the syndrome or/and three times as likely to have a heart attack or stroke. [1-4]

It consists of a constellation of metabolic abnormalities which include central obesity, hyperglycemia plus insulin resistance, high triglycerides plus low HDL cholesterol and hypertension. Several cardiovascular risk factors like hypertension, atherogenic dyslipidemia, and prothrombotic and proinflammatory condition cluster with metabolic syndrome. [5]

It was also referred to as insulin resistance syndrome till 1999, when WHO named it metabolic syndrome as there was insufficient evidence to show that all its component was caused by insulin resistance. [6]

Clinically MetS is diagnosed with on the following criteria and if the individual positive for three or more of the following measurements, is treated as positive syndrome patients. [7]

1. Waist circumference more than 40 inches in men and 35 inches in women
2. Elevated triglycerides 150 mg/dL of blood or greater
3. Reduced high-density lipoprotein cholesterol (HDL) less than 40 mg/dL in men or less than 50 mg/dL in women
4. Elevated fasting glucose of 100 mg/dL or greater
5. Blood pressure values of systolic 130 mm Hg or higher and/or diastolic 85 mm Hg or higher.

Thyroid gland is a butterfly shaped gland, located immediately below the larynx on each side



of and anterior to the trachea, is one of the largest of the endocrine glands, normally weighing 15 to 20 grams in adults.^[8]

The thyroid gland secretes two major hormones; thyroxine and triiodothyronine, commonly called T4 and T3, respectively. Both of these hormones profoundly increase the metabolic rate of the body. Complete lack of thyroid secretion usually causes the basal metabolic rate to fall 40 to 50 percent below normal, and extreme excesses of thyroid secretion can increase the basal metabolic rate to 60 to 100 per cent above normal. Thyroid secretion is controlled primarily by thyroid-stimulating hormone (TSH) secreted by the anterior pituitary gland.^[8]

Thyroxine and Triiodothyronine play an important role in maintaining thermogenesis and metabolic homeostasis. The set point in thyroid axis is established by thyroid stimulation hormone (TSH).^[6]

MetS and hypothyroidism are well established forerunners of atherogenic cardiovascular disease. Considerable overlap occurs in the pathogenic mechanisms of atherogenic cardiovascular disease by MetS and hypothyroidism.^[9] Various studies have been done on relation between MetS and thyroid function but there is paucity of data from Kanpur region. In my study I assist the association between MetS and the thyroid function so that it helps in management of patients with thyroid disorder.

II. MATERIALS AND METHODS

The present observational case control hospital based study was carried out after approval of Institutional Medical ethics committee conducted on 14/03/2020 at Rama Medical College, Hospital & Research Centre in Collaboration with Department of Biochemistry on "patients of metabolic syndrome (MetS) with thyroid disorder". The study population included 50 patients of metabolic syndrome with thyroid disorder 50 healthy individuals were enrolled in the study as per inclusion criteria who visited/referred to medicine OPD. Informed consent was duly taken from each subject prior to study.

Inclusion criteria:

Patients satisfying the International Diabetes Federation (IDF) consensus worldwide definition of the metabolic syndrome (2006):

1. Central obesity - defined as waist circumference with ethnicity specific values for south Asians: ≥ 90 cm for Men and ≥ 80 cm for women and any two of the following:

2. Raised triglycerides: > 150 mg/dL, or specific treatment for this lipid abnormality.

3. Reduced HDL cholesterol: < 40 mg/dL in males, < 50 mg/dL in females, or specific treatment for this lipid abnormality

4. Raised blood pressure: systolic BP > 130 or diastolic BP > 85 mm Hg, or treatment of previously diagnosed hypertension.

Exclusion criteria

1. Known hypothyroid or sub-clinical hypothyroid or hyperthyroid patients or on treatment. 2. Patients with liver disorders, renal insufficiency, congestive cardiac failure, pregnant women. 3. Also acutely ill patients, patients on statins and other medications that alter thyroid function or lipid levels.

Sample collection

5ml of fasting blood sample was collected from antecubital vein into each plain vial for Thyroid profile and for TG, HDL-C fresh serum/plasma EDTA, Citrate, heparinized or oxalate anticoagulated sample can be taken from each of the subjects under all aseptic conditions after explaining the procedure to the study subjects. The blood sample was allowed to clot at room temperature for 20 minutes and Serum was obtained by centrifugation at 3500 rpm (rotation per minute) for 15 minutes in the biochemistry laboratory and stored at -20° C until assayed. The supernatant serum will be used for the analysis of serum triacylglyceride, high density lipoprotein cholesterol, triiodothyronine, tetraiodothyronine, and thyroid stimulating hormone level.

Anthropometric indices

The anthropometric indices, waist circumference (WC) in centimeters, blood pressure (BP), age and sex were noted in pre-tested study proforma.

Measurement of waist circumference

Waist circumference was measured to nearest 0.1 cm at the midpoint between lowest costal margin and upper margin of iliac crest at full expiration in the standing position by measuring tape.

Blood pressure measurement

Blood pressure was measured by Auscultatory method.

TG estimation

Serum TG was estimated by GPO – Trinder method on Erba CHEM – 5 plus semi-auto analyzer.

High Density Lipoprotein-Cholesterol (HDL-C) estimation



Serum HDL-C was estimated on Erba CHEM-7 semi auto analyzer by Phosphotungstic method.

Serum T₃ estimation

Estimation of Serum T₃ was done on Tosoh AIA-360 auto analyzer by Competitive Fluorescence Enzyme Immunoassay method

Serum T₄ estimation

Estimation of Serum T₄ was also done on Tosoh AIA-360 auto analyzer by Competitive Fluorescence Enzyme Immunoassay method.

Estimation of Serum TSH

Estimation of Serum TSH was done on Tosoh AIA-360 auto analyzer by Sandwich Fluorescence Enzyme Immunoassay.

Statistical analysis

Collected Data were analysed using the Statistical Package of the Social Sciences (SPSS version 22.0). Data were presented as mean ± standard deviation. Independent sample t-test, Chi-square test, Pearson correlations were used to compare different parameters. The differences among the means (Mean ±SD) were considered significant if P < 0.01 & 0.05.

III. RESULT

The present research work include 50 healthy populations, 9 male and 41 female, while

out of 50 cases 19 were males and 31 were female in the age group of 0-80 years. The observations of the prevalence predominantly female population which comprises 62% in case and 82% in control and the ratio of male over female is 1:1.63 (1:2 approximately), and 1:4.5 respectively. There is a trend toward a higher prevalence of metabolic syndrome with thyroid disorder in the age group 21-40 years in case; majority (42%) of subjects in control are in 41-60 years age group.

In the study we found highly significant positive correlation between TSH and WC, systolic blood pressure in both case and control (p=.000) and (p=.000). A strong positive correlation was found between TSH and TG with statistically significant (P=0.000) in case while a significant negative correlation in control (p=.000). There is a strong significant negative correlation was found between TSH and HDL-C (p=.000) in both case and control.

The strength of correlation is not dependent on the direction or the sign. A positive correlation coefficient indicates that an increase in the first variable would correspond to an increase in the second variable. A negative correlation indicates that an inverse relationship whereas one variable increases, second variable decreases.

Table 3.1: The gender and age distribution of the total Subjects (metabolic syndrome with thyroid disorder and healthy individuals) included in the study.

Subject		Case		Control		Total	
		n	%	n	%		
Gender	Male	19	38	09	18	28	100
	Female	31	62	41	82	72	
Age (years)	0-20	06	12	05	10	11	100
	21-40	24	48	19	38	43	
	41-60	17	34	21	42	38	
	61-80	03	06	05	10	08	
Total		50		50			
		100					

n = frequency of subjects.

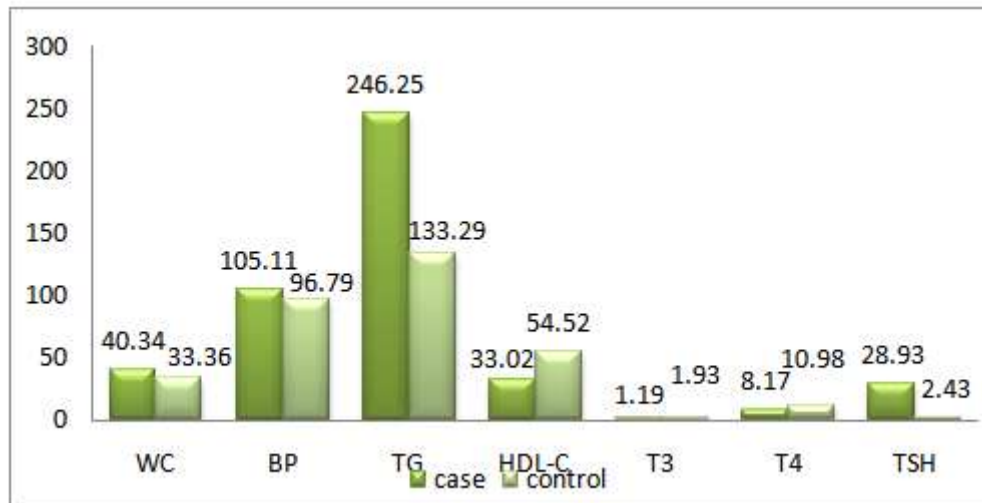


Table 3.2: Patients of MetS with TD with demographic, anthropometric & biochemical parameters of study subjects

Parameter	case	control	p value
WC	40.34±3.31	33.36±2.57	.000
Mean BP	105.11±4.02	96.79±5.85	.000
TG	246.25±67.02	133.29±32.63	.000
HDL-C	33.02±5.12	54.52±12.30	.000
T ₃	1.19±0.65	1.93±1.16	.000
T ₄	8.17±3.97	10.98±4.08	.000
TSH	28.93±27.37	2.43±1.32	.000

Table 3.2 shows higher mean WC [40.34±3.31] is recorded in case compared to control [33.36±2.52] with p value (0.000). Higher mean BP [105.11±4.02] is recorded in case compared to control [96.79±5.85]. The variance in mean BP among the case and control is found to be highly significant with p value (0.000). Mean serum TG level in case is higher [246.25±67.02] compared to control [133.29±32.63] and found to be highly significant with p value (0.000).

Lower mean HDL-C [33.02±5.12] is recorded in case compared to control [54.52±12.30] with p value (0.000). The mean serum T₃ level in case is lower [1.19±0.65] compared to control [1.93±1.16] with p value (0.000). Mean serum T₄ level in case is lower [8.17±3.97] compared to control [10.98±4.08] with p value (0.001). Higher mean TSH [28.93±27.37] is recorded in case compared to control [2.43±1.32] with p value (0.000).



Graph 3.1: Analysis of mean variance among case and control.

Table 5-3: Pearson correlation studied of TSH with MetS in cases and controls.

S.N.	Parameters	Cases		Controls	
		r -value	p -value	r -value	P -value
1.	WC	.516**	.000	.183	.000
2.	BP	.418**	.000	.003	.000



3.	HDL-C	.175	.000	.012	.000
4.	TG	.602**	.000	-.185	.000

IV. DISCUSSION

The concept of Metabolic syndrome was first described in 1923 by Kylin, a Swedish physician. Several other metabolic abnormalities have been associated with this syndrome, including obesity, Microalbuminuria and abnormalities in fibrinolysis and coagulation. There are various criteria based on certain clinical, anthropometric and biochemical parameters to define the metabolic syndrome. Commonly used is International Diabetes Federation (IDF). The prevalence of metabolic syndrome varies around the world, in part reflecting the age and ethnicity of the populations studied and the diagnostic criteria applied. In general, the prevalence of metabolic syndrome increases with age.^[10]

Hypothyroidism is associated with all parameters of metabolic syndrome.^[11] More than 60% of hypothyroid patients have obesity; there is decrease in basal metabolic rate and energy metabolism in hypothyroidism.^[12]

Rotterdam study suggested that there was a two fold increase in risk of atherosclerosis in hypothyroid patients.^[13] Both the synthesis and degradation of lipids are depressed in hypothyroidism, the latter especially so, the net effect being one of the lipid accumulation, especially of LDL cholesterol and triglycerides.^[14]

The activity of cholesterol ester transfer protein is decreased in hypothyroidism, thus HDL cholesterol level reduced in hypothyroidism. Aneemieke Ross et al. in 2007 found that free T4 was significantly associated with insulin resistance and with four of five components of the metabolic syndrome.^[15]

In our study mean systolic pressure, waist circumference, triglycerides and TSH values were significantly higher in the case compared to the control. These observations are similar to study by Uzunlulu et al.^[16]

Lai Y, Wang J, et al study of more than 1,500 subjects, found that those with metabolic syndrome had statistically significantly higher Thyroid Stimulating Hormone (TSH) levels than healthy control subjects. Slight increases in TSH may put people at higher risk for metabolic syndrome.^[17] These results are similar to our study (28.93±27.37) in case and (2.43±1.32) in control.

Research published in the February 2007 issue of the Journal of Clinical Endocrinology and Metabolism found a connection between thyroid function & metabolic syndrome. In those with

normal TSH levels, the thyroid hormone level of free T4 was important. Free T4 levels that were slightly low, but still within the normal range, significantly increased the risk of many risk factors for metabolic syndrome.^[18]

The Tromso study and the Basel thyroid study have shown that L-Thyroxine replacement in patients with sub-clinical hypothyroidism has a beneficial effect on low density lipoprotein cholesterol levels and clinical symptoms of hypothyroidism. An important risk reduction in cardiovascular mortality of 9–31% can be estimated from the observed improvement in low density lipoprotein cholesterol.^[19]

Elevated triglycerides, low HDL cholesterol and increased waist circumference were more common in women whereas increased triglycerides, low HDL cholesterol and hypertension were more common in men. Higher prevalence of metabolic syndrome in women is because of higher rate of obesity.

Our study shows that the prevalence of thyroid dysfunction in metabolic syndrome patients is higher than in normal subjects. This finding indicates a need for investigating the presence of Thyroid dysfunction during managing metabolic syndrome patients. As shown in previous evidences, managing these hypothyroid in metabolic syndrome patients are rewarding by improvement in the metabolic parameters and reducing cardiovascular risk.

In our study, we also evaluated the relationship between TSH levels and WC, BP, TG, HDL-C. To some extent, we have succeeded in correlating hypothyroidism with the altered above parameters.

V. CONCLUSION

Thyroid disorder is common in metabolic syndrome. Since the prevalence of thyroid disorder is more common in metabolic syndrome as evident from our study.

Biochemical screening for thyroid disorder is of paramount importance in all metabolic syndrome patients, as well as in all patients with unexpected worsening of their TG, HDL-C, obesity, or vice-versa because our data statistically suggest that the effect of thyroid hormone is associated with metabolic syndrome that are characterized by increased WC, BP, Triglycerides, and reduced HDL-C,



From this study, it can be concluded that thyroid disorder is most common in middle aged subjects. So, clinicians should remain highly suspicious in middle aged subjects with thyroid disorder for increase in metabolic syndrome parameters which may enhance the risk for atherosclerosis leading to coronary artery disease.

Prevalance of hypothyroidism is more common in metabolic syndrome as evident from our study.

Therefore, treatment and follow-up of thyroid disorder should include the monitoring of WC, BP, TG, HDL-C in order to decrease the possible effect of changing in the level of these parameters on the risk of cardiovascular diseases in the patients of MetS.

On the other hand, there is an absolute need for large studies designed to answer the questions to whether the metabolic syndrome is associated with increased risk for thyroid disorders.

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