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A Study of Thyroid Function Tests and Different Parameters of Metabolic Syndrome

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ABSTRACT

Background: Metabolic syndrome also called Syndrome-X and Insulin resistance syndrome. It Consists of a constellation of metabolic abnormalities that confers increased risk of Cardiovascular disease & Diabetes mellitus. Thyroid hormones are known to affect energy metabolism. Thyroid dysfunction, prominently subclinical hypothyroidism has been observed more frequently in metabolic syndrome patients than general population.

Material and Methods: The present study is hospital based cross sectional case and control study being carried out in age group 30-60 years, 50 were cases of Metabolic syndrome and 50 were normal healthy controls of same age and sex. A study of Thyroid function (TSH, FT3, FT4) and Metabolic syndrome parameters (IDF-2005) were done.

Results: In the Case group (Metabolic Syndrome) 28% have Thyroid dysfunction and 72% have Euthyroidism. In Control group, 90% have Euthyroidism and 10% have Thyroid dysfunction (X^2= 5.263, p-value=0.0217), it shows significant correlation.

Conclusion: Increased prevalence of hypothyroidism and subclinical hypothyroidism in patients of metabolic syndrome, which might have an ill effect on cardiovascular health.

Keywords: TSH, FT3, FT4, Metabolic syndrome (MS)

INTRODUCTION

Thyroid hormones are known to affect the energy metabolism, hence it is very likely to have a deranged thyroid profile in patients with metabolic syndrome [MS]. Obesity plays a central role in the causation of metabolic syndrome and associated changes. On the other hand, obesity itself causes changes in thyroid functions such as increased thyroid hormone levels [1], increased TSH (Thyroid-stimulating hormone) with no effect on T3 (Triiodothyronine) and T4 (thyroxine)[2] or increase in TSH and T3 with no effect on T4. Similarly, subclinical hypothyroidism itself can lead to the obesity[3]. Insulin resistance, an integral component of MS, has a close association with both hyper and hypothyroidism [4]. Insulin resistance and thyroid dysfunction probably share a mutual cause and effect relationship. The combination of insulin resistance and compensatory hyperinsulinemia, not only leads to deranged lipid profile and blood glucose but ultimately leads to increased risk of cardiovascular disease and many other clinical syndromes. On the other hand, Clinical Hypothyroidism has been considered a risk factor for insulin resistance [5, 6, 7]. Subclinical Hypothyroidism which is defined as elevated TSH levels in blood along with normal levels of thyroid hormones (FT3 and FT4) and clinical hypothyroidism have been linked to lower sensitivity to insulin at the tissue level.

Thyroid function assessment in Metabolic Syndrome patients can prove very helpful in early detection and prevention of cardiovascular and other complications. Our intention in this study is to correlate thyroid dysfunction with the different parameters of Metabolic Syndrome. It will help us in evaluating the role of the different components of Metabolic syndrome so far as thyroid dysfunction is concerned.

MATERIAL AND METHODS

This study was conducted in the Department of Biochemistry, in a tertiary care health institute in western Uttar Pradesh. It is a cross sectional case-control study, with the intention to correlate the thyroid function tests with the different components of Metabolic Syndrome. The study was carried out in males and females of age groups 30 to 60 years, attending the Internal Medicine Out Patient Department (OPD), Male and females full-filling the criteria of Metabolic Syndrome (IDF-2005) were taken as cases and the individuals of same age and sex-matched were taken as controls.

Inclusion criteria

- Subjects who fulfilled the IDF (International Diabetic Federation) criteria for metabolic syndrome of the age group of 30 to 60 years were grouped under cases.
- Subjects who gave written informed consent.
- Persons who were free from other critical illnesses.

Exclusion criteria

- Subjects suffering from any major medical or surgical illness.
- Patients on medications affecting thyroid profile and serum lipids.

IDF criteria used in the study: (Table - 1)

The Cases fulfilling the criteria of Metabolic Syndrome based on the International Diabetes Federation (IDF-2005) were recruited in the study. IDF criteria were used as it takes into account the ethnic variations in contrast to NCEP (National Cholesterol Education Program) Adult Treatment Panel III [8].

Table – 1 IDF criteria

Waist circumference		
Men	Women	Ethnicity
≥94 cm	≥80 cm	Europid,Sub-Saharan African, Eastern and Middle Eastern
≥90 cm	≥80 cm	South Asian, Chinese and ethnic South and Central American
≥85 cm	≥90 cm	Japanese
Two or more of the following: **Fasting triglycerides** ≥150 mg/dL or on specific medication. **HDL cholesterol** <40 mg/dl and <50 mg/dl for men and women respectively or on specific medication. **Blood pressure** >130 mm Hg systolic or >85 mm Hg diastolic or previous diagnosis or on specific medication. **Fasting plasma glucose** ≥ 100 mg/dl or previously diagnosed Type 2 diabetes.		

Blood collection and measurement of the biochemical parameters:

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All the blood samples were collected after 8 -10 hours of overnight fasting in the morning. Serum HDL (High-Density Lipoprotein) - Cholesterol, Triglycerides, LDL (Low-Density Lipoprotein) - Cholesterol, Total Cholesterol were measured using the enzymatic method as instructed in information sheets. Plasma glucose were measured using the Enzymatic (GOD-POD) method. Free T4, free T3, TSH were measured by ARCHITECT Chemiluminescent Microparticle Immunoassay (CMIA).

Statistical analysis:

Statistical analyses were done using IBM SPSS statistics version 24. Continuous variables were presented as mean and standard deviation and categorical variables were presented as percentage or ratio. Unpaired t-test and the chi-squared test were used for comparison of continuous and categorical variables respectively. An analysis of variance (ANOVA) one-way used and 'p' value <0.05 were considered significant.

RESULTS

This study was intended to correlate the thyroid function tests with the different components of Metabolic Syndrome and to compare them with the healthy controls. After getting ethical permission for the study 50 cases and equal number of controls were taken from the Department of Internal Medicine during Feb 2019-June 2020.

Table -2 shows the demographic composition of the study population

	Case		Control	
Age(years)	Frequency(n=50)	%	Frequency(n=50)	%
30-40	17	34%	27	54%
40-50	13	26%	12	24%
50-60	20	40%	11	22%
Gender				
Male	18	36%	18	36%
Female	32	64%	32	64%

The participants included in the Case group were 50-60 years (40%) followed by 30-40 years (34%), 40-50 years (26%) and in the Control group were 30-40 years (54%) followed by 40-50 year (24%), 50-60 years (22%). In the Case group 64% female and 36% male and Control group 64% female and 36% male were included. The study being case-control study, an attempt was made to exclude any age or gender bias and the two groups were matched perfectly.

Table-3 shows distribution of participants according to gender in two groups and according to presence of different parameters of Metabolic Syndrome

	CASE					CONTROL				
	MALE (n=18)		FEMALE (n=32)		stat	MALE (n=18)		FEMALE (n=32)		Stat
	No.	%	No.	%		No.	%	No.	%	
Increase WC	16	88.8%	32	100%	X^2=3.70 p-v=0.05	11	61.1%	28	87.5%	X^2=4.67 p-v=.03

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Increase TG	14	77.7%	32	100%	X^2=7.72 p-v=.005	4	22.2%	3	9.3%	X^2=1.57 p-v<.20
Decrease HDL	16	88.8%	24	75.0%	X^2= 1.3 p-v=.23	9	50%	16	50%	X^2=0 p-v=1
Increase BP	11	61.1%	20	62.5%	X^2=.009 p-v=.92	4	22.2%	3	9.3%	X^2=1.57 p-v<.208
Increase FBS	9	50%	28	87.5%	X^2=8.42 p-v=.003	1	5.5%	2	6.2%	X^2=.009 p-v<.92

Table -3 shows that Central obesity (increased WC) in Case group 100% females and 88.8% males is significantly present (X^2=3.70, p-value=0.05) and in Control group 87.5% females and 61.1% males have increased WC (X^2=4.67, p-value= 0.03) which is significant.

Increased Triglyceride in females is 100% and in males is 77.7% of Cases (X^2=3.70, p-value=0.05) and in Controls 22.2% in males and only 9.3% in females (X^2=1.57, p-value=0.2) not significant. Decreased HDL-C in males is 88.8% and females 75.0% of Cases (X^2=1.38, p-value=0.23) not significant and in Control group 50% males and 50% females (X^2=0, p-value=1) which is not significant. Increased Blood Pressure in females is 62.5% and in males 61.1% of Cases (X^2=.009, p-value=0.92) not significant and in Control group 22.2% males and 9.3% females have raised BP (>130/85) (X^2=1.57, p-value = 0.208) not significant. Increased Fasting Blood Sugar (>100 mg/dl) in females is 87.5% and in males 50% of Cases (X^2=8.42, p-value= 0.003) significant, and in Control group 6.2% females and 5.5% males have increased FBS (X^2=.009, p-value = 0.92) not significant.

Table-4 shows Thyroid Dysfunction in Cases and Controls.

	Case		Control	
	Frequency (Male+Female)	%	Frequency (Male+Female)	%
Subclinical Hypothyroidism	2+8=10	20%	1+2=03	6%
Overt hypothyroidism	1+2=03	6%	0+1=01	2%
Hyperthyroidism	0+1=01	2%	0+1=01	2%
Euthyroidism	14+22=36	72%	18+27=45	90%
P Value	X^2=5.7692, p-value= 0.123 not significant			

20% of cases have been found with some or the other thyroid dysfunction on the other hand only 10% of controls have it.

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Table-5: Distribution of Thyroid Profile according to Gender in Case and Control:

GENDER	Reference value	CASE	CONTROL	STAT	
		Mean ± SD	Mean ± SD	p-v	f-v
Male	TSH (0.4-4.94 µIU/mL)	2.72±1.81	2.38± 1.91	0.58	0.30
	FT3 (1.71-3.7µIU /ml)	2.01 ± 0.85	1. 96 ± 0.74	0.85	0.03
	FT4 (0.89-2.76 ng/dL)	1.88 ±1.67	1.31 ± 0.58	0.18	1.87
Female	TSH (0.4-4.94 µIU/mL)	2.97 ± 2.11	2.68 ± 1.33	0.51	0.433
	FT3 (1.71-3.7 µIU/mL)	1.90 ± 0.66	2.16 ± 0.68	0.12	2.40
	FT4 (0.89-2.76 ng/dL)	1.30 ± 0.60	1.26 ± 1.32	0.87	0.02

In the group of cases, 96% of subjects had central obesity, 62% had raised blood pressure and 76% had raised fasting plasma glucose, a total of 94% had raised triglycerides and 80% had reduced HDL cholesterol. In control group, a total of 84% subjects fulfilled the IDF criteria for central obesity (Males >90 cm, Females >80 cm), 14% had raised blood pressure [>130/85 systolic blood pressure (SBP)/ diastolic blood pressure (DBP) or known hypertensive] and only 6% had raised fasting plasma glucose (>100 mg/dL or known diabetic), a total of 16% had raised triglyceride levels (>150 mg/dL) and 50% had reduced HDL cholesterol (Males ≤ 40 mg/dL, Females ≤ 50 mg/dL). The above data clearly indicates that all the above factors contributing to metabolic syndrome were present in significantly higher proportion ($p < 0.05$) in cases than in controls.

In the Case group (Metabolic Syndrome) 28% have Thyroid dysfunction and 72% have Euthyroidism. In Control group 90% have Euthyroidism and 10% have Thyroid dysfunction (X^2= 5.263, p-value=0.0217), it shows significant correlation.

The distribution of different types of Thyroid dysfunction in Case and Control with male and female, in the Case group, 20% Subclinical Hypothyroid, 6% overt Hypothyroid, 2% Hyperthyroid and 72% Euthyroid were observed and in the Control group, 6% Subclinical Hypothyroid, 2% overt Hypothyroid, 2% Hyperthyroid and 90 % Euthyroid were obsered.

The Hypertension [B.P.(SBP/DBP) >130/85 mmHg] in Cases group is found 62% with mean 137.9 ± 18.5 / 87.5 ± 9 mmHg and in Control group is 38% with mean 124 ± 8.1/ 81.7 ± 4.7 mmHg (p-value <0.001).

DISCUSSION

Population in Indian continent is more prone to metabolic syndrome and diabetes mellitus and subsequent development of cardiovascular and cerebrovascular complications [9]. Although many studies have been conducted on thyroid dysfunction and MS both in India and elsewhere but still data available is insufficient to establish a correlation between these two entities. Very limited data is available on the rural population of north India.

Thyroid dysfunction is common among patients with metabolic syndrome. In the present study, the prevalence of thyroid dysfunction in metabolic syndrome patients is 28 %, which correlates to similar studies conducted in places as Nepal, Middle

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East and some African countries, where it was found to be between 21-51 %. [10, 11, 12]

The prevalence of subclinical hypothyroidism was reported in various studies conducted in India by Saluja et al. [13] (37%), Shantha et al. [11] (21.9%), Khatiwada et al. [14] (26.6%), Kota et al. [15] (22%), Gyawadi et al. [16] (29.22%). Similar results were observed in the present study, as the prevalence of subclinical hypothyroidism is 20%.

Our study suggests that female with metabolic syndrome has the higher risk for subclinical hypothyroidism along with cardiovascular manifestation, although not statistically significant it correlates with other studies like Uzunlulu et al. [12] (16.5%) and Kota et al. [15] (22%).

In the present study group, the prevalence of thyroid dysfunction in females with metabolic syndrome was 78.6% and in males with metabolic syndrome was 21.4% and this data is compared with other study groups like Saluja et al. [13] and Vaishali et al.,[17].

In the present study, the mean waist circumference of the participants with MS with thyroid dysfunction was 106.46 ± 11.2 cm which correlates to the work of Saluja et al. [13], Deshmukh et al. [17] and Ogbera et al. [18]

The coexistence of thyroid dysfunction and insulin resistance of MS may be due to similarity of dysfunction at the receptor level [19]. This explains the relationship between hyperglycemia, obesity and thyroid dysfunction.

Presence of subclinical or clinical hypothyroidism alters the endothelial functions [20] leading to increased arterial stiffness [21], systemic vascular resistance [22] and diastolic dysfunction [23]. The prevalence of M.S. was found to be 10 times higher among the hypertensive participants than normotensives in our study. Thus patients of MS and thyroid dysfunction should be screened for cardiovascular dysfunctions.

Central abdominal obesity (WC) and insulin resistance lead to deranged lipid profile characterized by elevated triglyceride, very low density lipoprotein (VLDL) and intermediate density lipoprotein (IDL) levels apart from a decrease in high density lipoprotein (HDL) levels. These abnormalities are hallmark of metabolic syndrome. In the present study, 87.7% of cases had high levels of Triglycerides (>150 mg/dL), and 80.0% had low levels of HDL cholesterol. Elevated triglycerides are explained by the reduced removal from plasma due to decreased activity of hepatic Triglyceride lipases. The reason for decreased HDL cholesterol may be due to increased Cholesterol Ester Transfer Protein (CETP)[24, 16]. These abnormalities of lipid profile are known predictors of cardiovascular and cerebrovascular complications [25].

These findings reflect the influence of genetic, environmental factors and intake of iodine, which may vary between different geographical areas of the patients' inhabitancy.

CONCLUSION

The present study showed an increased prevalence of hypothyroidism and subclinical hypothyroidism in patients of metabolic syndrome, which might have an ill effect on cardiovascular health. Hypothyroidism causes an increase in lipids levels and hypertension leads to cardiovascular risk. Increased risk of cardiovascular and cerebrovascular events may be seen in patients with metabolic syndrome and dysfunction of the thyroid gland. Evaluating the thyroid function in patients with metabolic syndrome may help to identify and prevent the risk of cardiovascular and cerebrovascular events in the patients. The small sample size is a limitation of this study.

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