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Study of Thyroid Hormones in Patients with Metabolic Syndrome

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Abstract: Metabolic syndrome constitutes a cluster of risk factors characterized by hypertension, atherogenic dyslipidemia, hyperglycemia, prothrombotic and proinflammatory conditions. This cluster of metabolic abnormalities is associated with increased risk for atherosclerotic cardiovascular disease and type 2 diabetes mellitus. Thyroid hormone plays an important role on various aspects of metabolism, development and differentiation of the cells. Metabolic syndrome and thyroid dysfunction are independent risk factors for cardiovascular disease risk and mortality associated with it, it is possible that patients suffering from both these disease may have a compounded risk. The present study was a cross-sectional study design carried out at the Outpatient Department of Maheshwara Medical College & Hospital, Sangareddy, Telangana from January 2017 to August 2018. Subjects were selected and the data was collected using a structured questionnaire. A total of 154 people have given their consent for participating in the present study. Out of these, 112 were eligible after consideration of the inclusion and exclusion criteria. 100 age and sex matched subjects are selected as control group after considering the inclusion and exclusion criteria. The Ethics Committee of the Maheshwara Medical College & Hospital, Sangareddy, and Telangana has approved the study. Written informed consent in the language understandable to the subjects has been obtained from all the participants of the study. Among 100 subjects of Metabolic Syndrome and 100 subjects of control group, in our present study, there was a significant change in the levels of BMI, SBP, DBP, WC, Serum Glucose, Total Cholesterol, LDL-Cholesterol, Triglycerides, TSH, FT4 & FT3 among the Metabolic Syndrome Group when compared to Control Group. But, the levels of HDL-Cholesterol among Metabolic Syndrome and Control Group was found to be non-significant. Metabolic Syndrome is related to increased BMI, SBP, DBP, WC, Serum Glucose, Total Cholesterol, LDL-C, Tg and TSH. This confirms that the persons with Metabolic syndrome are more prone to diseases related to Cardio-vascular System. Hence, an early detection of altered Cardio-vascular functioning followed by early intervention may either decrease or may even postpone the severity of the Cardio-vascular complications. Decreased levels of FT3 and FT4, suggesting hypothyroidism in the persons with metabolic syndrome suggest an early detection in the complications.

Keywords: Metabolic Syndrome, Hormones, BMI, SBP, DBP, WC, Serum Glucose, Cholesterol, Thyroid.

INTRODUCTION

Metabolic syndrome constitutes a cluster of risk factors characterized by hypertension, atherogenic dyslipidemia, hyperglycemia, prothrombotic and proinflammatory conditions [1]. This cluster of metabolic abnormalities is associated with increased risk for atherosclerotic cardiovascular disease and type 2 diabetes mellitus [2]. The prevalence of metabolic syndrome is increasing all over the world with distinct evidence of high prevalence in India and other South Asian countries [3]. Metabolic syndrome is not only risk factor for diabetes but also for cardiovascular diseases [4]. Recent research studies shows that the deficiency of vitamin D causes metabolic syndrome, diabetes mellitus, heart failure, stroke, cancer, polycystic ovary syndrome, gout, and asthma and coronary artery disorders [5].

The Metabolic syndrome identifies a cluster of metabolic disorders that place affected individuals at increased risk for developing cardiovascular disease, as well as increased mortality from all causes[6-9]. The

third report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III) provides a clinically useful working definition of the metabolic syndrome that includes the presence of at least 3 of the following characteristics: abdominal obesity, increased triglycerides, reduced levels of high–density lipoprotein (HDL) cholesterol, high blood pressure, and increased fasting glucose [10].

Thyroid hormone plays an important role on various aspects of metabolism, development and differentiation of the cell [11]. Thyroid disease constitutes the most common endocrine abnormality in the recent years, diagnosed either in subclinical or clinical form in patients with metabolic syndrome[12] Thyroid dysfunction is defined as the alteration in serum TSH level with normal or altered thyroid hormones (T3, T4). About 300 million people in the world are affected from thyroid dysfunction and over half are presumed to be unaware of their condition. It has been estimated that about 42 million of people in India suffer from thyroid disease [13]. Thyroid function affects the parameters causing metabolic syndrome including low density lipoproteins, triglycerides, blood pressure and plasma glucose. The prevalence of thyroid dysfunction was reportedly more among women with metabolic syndrome[14,15] Metabolic syndrome and thyroid dysfunction are independent risk factors for cardiovascular disease risk and mortality associated with it, it is possible that patients suffering from both these disease may have a compounded risk[16,17].

MATERIALS & METHODS

The present study was a cross-sectional study design carried out at the Outpatient Department of Maheshwara Medical College & Hospital, Sangareddy, Telangana from January 2017 to August 2018 were selected and the data was collected using a structured questionnaire. A total of 154 people have given their consent for participating in the present study. Out of these, 112 were eligible after consideration of the inclusion and exclusion criteria. 100 age and sex matched subjects are selected as control group after considering the inclusion and exclusion criteria. The inclusion criteria were as follows: age range of 25 to 50 years, with metabolic syndrome are diagnosed based on the criteria by the joint statement committee [International Diabetes Federation (IDF) task force on Epidemiology and Prevention, National Heart, Lung and Blood Institute (NHLBI), the American Heart Association, the World Heart Federation, the International Atherosclerosis Society, and the International Association for the Study of Obesity].

The patients having at least three components of joint statement definition of metabolic syndrome are included in the study - Waist circumference >90 cm for men and >80 cm for women; Raised triglyceride level ≥150 mg/dl or any specific treatment; HDL cholesterol levels <40 mg/dl in males, <50 mg/dl in females or any specific treatment; Raised blood pressure ≥130/85 mm of Hg or any medication; Raised fasting glucose ≥100 mg/dl or previously diagnosed type 2 diabetes mellitus.

The patients with known thyroid dysfunction; any medications that alter or modify thyroid profile like estrogen, corticosteroids, iodine containing drugs; Severely ill patients; Pregnant women are also excluded from the study. The Ethics Committee of the Maheshwara Medical College & Hospital, Sangareddy, Telangana has approved the study. Written informed consent in the language understandable to the subjects has been obtained from all the participants of the study.

A detailed history including physical examination was done in all patients diagnosed of metabolic syndrome. Fasting blood samples were obtained (venous blood samples taken after overnight fast of a minimum of 8 h); glucose, total cholesterol, low density lipoprotein cholesterol (LDL-C), HDL-C, and triglyceride levels were determined. Serum thyroid stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) measurements were made using electrochemiluminescence immunoassay (ECLIA method). Normal range for TSH was 0.27–4.2 μIU/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 μIU/ml) and normal FT3 and FT4 levels were required for the diagnosis of subclinical hypothyroidism. 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.

The data was arranged in suitable tables for analysis under the relevant headings. The results were averaged as (mean ± standard deviation) for each parameter subgroups separately. Each variable, including BMI, Blood Pressure, Waist Circumference (WC), Serum levels of Glucose, Total Cholesterol, LDL-C, HDL-C, Triglyceride, TSH, FT3 and FT4 were analysed by *Paired Sample t-test*. Statistical analysis was done using IBM SPSS Statistics 20 package. *p-value* <0.05 was considered as statistically significant and *p-value* of <0.005 was considered as statistically highly significant.

RESULTS

Among 100 subjects of Metabolic Syndrome and 100 subjects of control group, in our present study, significant differences were found between the two groups. Mean BMI, SBP, DBP of Metabolic Syndrome group was found to be 25.09, 153.76, 86.32 while for control group it was 20.01, 137.27, 79.18.

The mean values of Serum Glucose level, Waist Circumference, Total Cholesterol, HDL-Cholesterol, LDL-Cholesterol, and Total Glycerides for Metabolic Syndrome Group were 132.31, 89.92, 212.60, 52.58, 111.51, 161.87 while for Control Group were found to be 75.63, 86.92, 183.65, 54.60, 94.56,

134.56. Similarly, the mean values of TSH, FT4 & FT3 for Metabolic syndrome group and control group were found to be 5.48, 1.89, 2.44 and 3.43, 2.78, 3.34 respectively.

Table-1: Paired Samples Statistics of Metabolic Syndrome Group and Control Group

		Mean	N	Std. Deviation	Std. Error Mean
BMI	MetSynGr	25.09	100	4.744	.474
	ControlGr	20.01	100	4.480	.448
SBP	MetSynGr	153.76	100	13.849	1.385
	ControlGr	137.27	100	15.837	1.584
DBP	MetSynGr	86.32	100	8.512	.851
	ControlGr	79.18	100	7.699	.770
Glucose (mg/dl)	MetSynGr	132.31	100	20.456	2.046
	ControlGr	75.63	100	13.757	1.376
WC (cms)	MetSynGr	89.92	100	2.415	.241
	ControlGr	86.92	100	2.541	.254
Total Chol	MetSynGr	212.60	100	19.366	1.937
	ControlGr	183.65	100	14.586	1.459
HDL-C	MetSynGr	52.58	100	15.331	1.533
	ControlGr	54.60	100	13.234	1.323
LDL-C	MetSynGr	111.51	100	16.299	1.630
	ControlGr	94.56	100	13.255	1.325
Tg	MetSynGr	161.87	100	16.324	1.632
	ControlGr	134.56	100	13.255	1.325
TSH	MetSynGr	5.48	100	1.856	.186
	ControlGr	3.43	100	1.343	.134
FT4	MetSynGr	1.89	100	.680	.068
	ControlGr	2.78	100	.719	.072
FT3	MetSynGr	2.44	100	.592	.059
	ControlGr	3.34	100	1.139	.114

Table-2: Paired Samples Correlations of Metabolic Syndrome Group and Control Group

		N	Correlation	Sig.
BMI	MetSynGr & ControlGr	100	.957	.000
SBP	MetSynGr & ControlGr	100	-.037	.712
DBP	MetSynGr & ControlGr	100	-.101	.316
Glucose(mg/dl)	MetSynGr & ControlGr	100	-.080	.429
WC(cms)	MetSynGr & ControlGr	100	.985	.000
Total Chol	MetSynGr & ControlGr	100	.002	.985
HDL-C	MetSynGr & ControlGr	100	.058	.567
LDL-C	MetSynGr & ControlGr	100	.023	.822
Tg	MetSynGr & ControlGr	100	.066	.511
TSH	MetSynGr & ControlGr	100	.131	.193
FT4	MetSynGr & ControlGr	100	.012	.906
FT3	MetSynGr & ControlGr	100	.016	.878

On analysis, there was a significant change in the levels of BMI, SBP, DBP, WC, Serum Glucose, Total Cholesterol, LDL-Cholesterol, Triglycerides, TSH, FT4 & FT3 among the Metabolic Syndrome Group when compared to Control Group. But, the levels of HDL-Cholesterol among Metabolic Syndrome and Control Group were found to be non-significant.

DISCUSSION

Thyroid hormones increase the Basal Metabolic Rate (BMR), there by metabolic pathways are up-regulated resulting in resting energy expenditure. In our present study as observed significant increase in TSH and decrease in FT3, FT$ levels was noted. It can be hypothesized that, in metabolic syndrome there can be insulin resistance and similarly thyroid receptor resistance operating in these Metabolic Syndrome subjects.

Table-3: Paired Samples Test of Metabolic Syndrome Group and Control Group

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
BMI	MetSynGr & ControlGr	5.080	1.383	.138	4.806	5.354	36.731	99	.000
SBP	MetSynGr & ControlGr	16.490	21.424	2.142	12.239	20.741	7.697	99	.000
DBP	MetSynGr & ControlGr	7.140	12.042	1.204	4.751	9.529	5.929	99	.000
Glucose(mg/dl)	MetSynGr & ControlGr	56.680	25.548	2.555	51.611	61.749	22.186	99	.000
WC(cms)	MetSynGr & ControlGr	3.000	.449	.045	2.911	3.089	66.746	99	.000
Total Chol	MetSynGr & ControlGr	28.950	24.223	2.422	24.144	33.756	11.952	99	.000
HDL-C	MetSynGr & ControlGr	-2.020	19.664	1.966	-5.922	1.882	-1.027	99	.307
LDL-C	MetSynGr & ControlGr	16.950	20.772	2.077	12.828	21.072	8.160	99	.000
Tg	MetSynGr & ControlGr	27.310	20.332	2.033	23.276	31.344	13.432	99	.000
TSH	MetSynGr & ControlGr	2.050	2.143	.214	1.625	2.475	9.565	99	.000
FT4	MetSynGr & ControlGr	-.890	.984	.098	-1.085	-.695	-9.048	99	.000
FT3	MetSynGr & ControlGr	-.900	1.275	.128	-1.153	-.647	-7.057	99	.000

In a study done by Chugh *et al*. evaluating the thyroid function tests in individuals with metabolic syndrome to explore the possibility of thyroid receptor resistance, a significant increase was found in TSH levels in patients as compared to controls, while T3 and T4 levels were comparable in patients and controls concluding that raised TSH in patients with metabolic syndrome independent of lowered T3 and T4 suggest it to be a part and parcel of this syndrome [18]. Another similar studies done by Meher *et al*. & Jayakumar RV *et al*. found that body mass index, waist circumference, mean systolic pressure, diastolic pressure, fasting blood sugar, total cholesterol, LDL-C, triglycerides, and TSH were significantly higher, and FT3, free thyroxine (FT4), and HDL-C were significantly lower in the metabolic syndrome patients compared to the control group concluding that there is a significant association between subclinical hypothyroidism and metabolic syndrome, and it highlights the importance of thyroid function tests in patients with metabolic syndrome.[19,20] It is still not clear whether alterations in thyroid hormones are a cause or an effect of obesity (metabolic syndrome) suggesting need for further evaluation on a large scale with inclusion of various hormones elaborated by adipose tissue (like leptin, resistin, adiponectin, etc.).

CONCLUSION

Metabolic Syndrome is related to increased BMI, SBP, DBP, WC, Serum Glucose, Total Cholesterol, LDL-C, Tg and TSH. This confirms that the persons with Metabolic syndrome are more prone to diseases related to Cardio-vascular System. Hence, an early detection of altered Cardio-vascular functioning followed by early intervention may either decrease or may even postpone the severity of the Cardio-vascular complications. Decreased levels of FT3 and FT4, suggesting hypothyroidism in the persons with Metabolic syndrome suggest an early detection in the complications.

Thus, altered thyroid functioning is found to be prevalent among patients with metabolic syndrome specially the subclinical hypothyroidism contributing to thyroid dysfunction with or with-out altered cardio-vascular complications. From the present findings, it can be concluded that thyroid function status should always be done as a routine investigation in patients with metabolic syndrome. Further, the persons with increased waist circumference should be screened at the earliest as there is increased prevalence of thyroid

dysfunction in metabolic syndrome. It is also well known that both thyroid dysfunction and metabolic syndrome are independent risk factors for cardiovascular disease. The study concludes that thyroid dysfunction is one of the most common endocrine disorders in metabolic syndrome patients. Subclinical hypothyroidism was more common pattern among thyroid dysfunction. Hence we recommend study of thyroid function status in all patients with metabolic syndrome or it should be included as a diagnostic criterion for diagnosing metabolic syndrome.

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