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PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN PATIENTS WITH METABOLIC SYNDROME IN SOUTH INDIA

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INTRODUCTION

Metabolic syndrome is a cluster of risk factors and is characterized by hypertension, atherogenic dyslipidemia, hyperglycemia, prothrombotic, and pro-inflammatory conditions.[1] The metabolic syndrome is also known as syndrome X, insulin resistance syndrome, and the deadly quartet. The metabolic syndrome is more common in genetically susceptible populations. Being overweight or obese, physical inactivity and an atherogenic diet commonly elicit clinical manifestations.[2] The risks of metabolic syndrome include cardiovascular disease and diabetes mellitus. In addition, Metabolic Syndrome (MetsS) is associated with several other comorbidities such as Non-Alcoholic Fatty Liver disease, sleep disorders, reproductive tract disorders, and microvascular disease.[3]

Subclinical hypothyroidism (SCH) is defined as an elevated serum concentration of thyroid-stimulating hormone (TSH) while the levels of circulating thyroid hormone are within the normal range. Thyroid dysfunction is associated with dyslipidemia, a well-known cardiovascular risk factor.[4] Cross-sectional studies have demonstrated that serum levels of total cholesterol and LDL cholesterol are higher in patients with subclinical hypothyroidism than in euthyroid control.[5] It acts through altered insulin sensitivity in healthy subjects and patients with type 2 diabetes mellitus.[6]

A study on thyroid dysfunction in the MetS population may help us to know the magnitude of overlap of these two groups and may highlight the importance of thyroid function tests in identifying the hypothyroid population from MetS as the relation between the two is not yet identified. This study intended to assess the prevalence of hypothyroidism in patients with MetS and to investigate the association between hypothyroidism and MetS.

MATERIAL AND METHOD

This cross-sectional study was conducted in Vijaya health care. One hundred patients with MetS who met the criteria for the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP) III [three out of five criteria positive, that includes blood pressure greater than or equal to 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 protein cholesterol (HDL-C) 102 cm in men and 88 cm in women] were included in the study group.[7] Fifty patients with no clinical manifestations of MetS (0 out of 5 criteria for MetS) are included in the control group.

Patients with disorders of the liver, renal, congestive cardiac failure, pregnant females, patients taking oral contraceptive pills, statins, and other medications that alters lipid levels and thyroid function, and those under treatment for any thyroid-related disorder were excluded from the study. Blood pressure is measured over the right arm with the patient lying supine. A mean value of three blood pressure readings was taken as the final recording. Waist circumference is measured at the plane between the anterior superior iliac spine and lower costal margin, narrow part at the waistline while the patient was standing and in full expiration.

Fasting blood samples (venous blood samples taken after a minimum of 8 hours of overnight fast) of glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), High-density lipoprotein cholesterol (HDL-C), and triglyceride levels were obtained. Serum thyroid stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) measurements were made using electrochemiluminescence immunoassay (ECLIA method). A high serum TSH level (4.2–10 µIU/ml) and normal FT3 and FT4 levels were required to make a diagnosis of subclinical hypothyroidism.

RESULTS

Table 1: Patient characteristics.

S.no	Variables		MetS group(n=100)	Control group(n=100)	p-value
1	Age(years)		46.6±12.4	47±11.2	0.081
2	Gender(n%)	Female	61(61.00)	66(66.00)	0.822
		Male	39(39.00)	34(34.00)	
3	Smoking(n%)		17(17.00)	13(13.00)	0.324
4	Alcohol(n%)		9(9.00)	6(6.00)	0.629
5	Body mass index(kg/m^2)		30.62±5.9	27±2.1	**0.0001**
6	Systolic blood pressure(mmHg)		148±26.92	123.21±15.8	**0.0001**
7	Diastolic blood pressure(mmHg)		95.32±8.90	78±9.32	**0.001**
8	Waist circumference(cm)		95.9±6.9	89±9.34	**0.001**
9	Total cholesterol(mg/dl)		218.53±43.8	172.5±39.12	**0.0001**
10	LDL cholesterol(mg/dl)		124.43±41.76	113±32.90	**0.003**
11	HDL cholesterol(mg/dl)		39.6±9.52	51.42±13.98	**0.0021**
12	Triglycerides(mg/dl)		195.42±94.73	118.6±68.42	**0.001**
13	Fasting blood glucose(mg/dl)		105.52±13.95	96.42±12.98	**0.001**
14	Mean number of MetS criteria		3.8±0.6	1.6±0.6	**0.001**
15	FT_4 (ng/dl)		1.4±0.5	1.5±0.4	0.162
16	TSH(µIU/ml)		2.5±1.7	1.6±1.4	0.023

A total of 200 patients were included in the study in which both groups contain 100 patients each

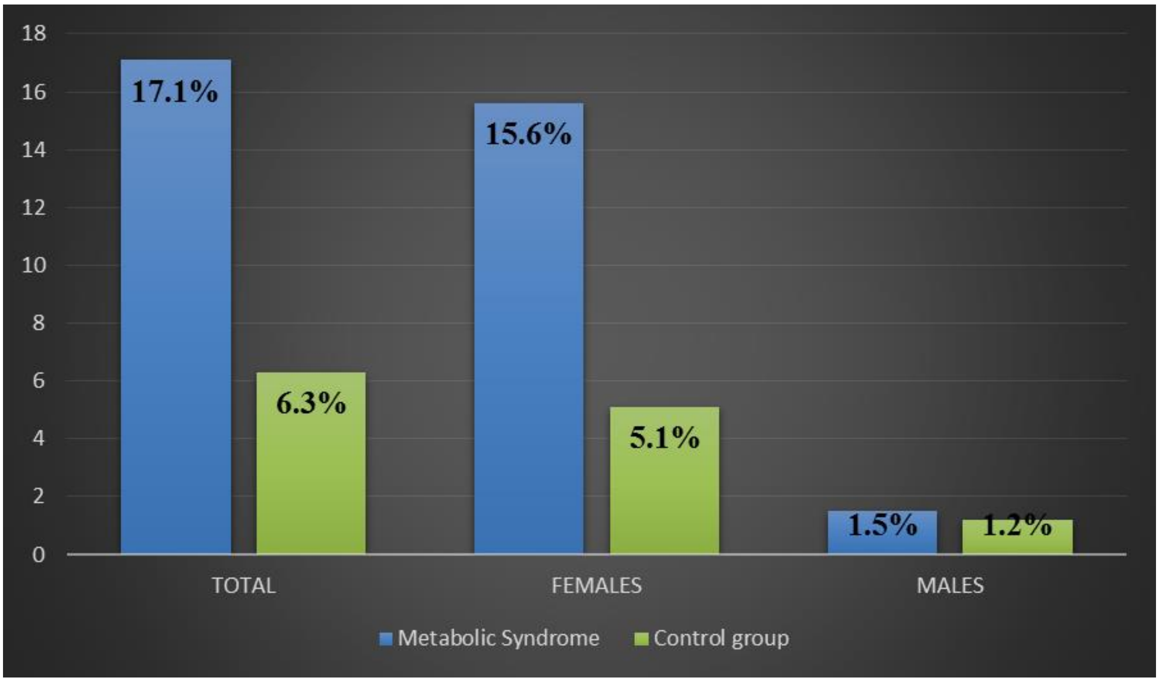
Table 2: Bivariate analysis for subclinical hypothyroidism in patients with metabolic syndrome

S.no	Variables	Categories	SCH(+) n,%	SCH(-) n, %	p Value
1	Gender	Female	11(18.03)	50(81.96)	**0.001**
		Male	5(12.82)	34(87.17)	
2	Age(Year)	< 50	5(9.43)	48(90.56)	0.523
		≥ 50	7(14.89)	40(85.10)	
3	Body mass index(kg/m^2)	≥ 30	7(10.14)	62(89.85)	0.173
		< 30	3(9.67)	28(90.32)	
4	Waist circumference(cm)	Female > 88	12(24.48)	37(75.51)	0.952
		Female≤ 88	2(1.66)	10(83.33)	
		Male> 102	7(30.43)	16(69.56)	0.518
		Male≤ 102	5(31.25)	11(68.75)	
5	Blood pressure(mmHg) (Systolic, diastolic)	≥ 130, ≥85	19(21.83)	68(78.16)	0.257
		<130, <85	2(15.38)	11(84.61)	
6	Triglycerides(mg/dl)	≥ 150	12(17.39)	57(82.60)	0.639
		< 150	10(32.25)	21(67.74)	
7	HDL cholesterol(mg/dl)	Female ≥50, male≥40	7(9.45)	67(90.54)	0.638
		Female<50, male<40	4(15.38)	22(84.61)	
8	Fasting blood glucose(mg/dl)	≥ 110	16(23.88)	51(76.11)	0.258
		<110	7(21.21)	26(78.78)	
9	FT_4 (ng/dl, mean ±SD)		1.42±0.53	1.94±0.42	**0.001**
	TSH(µIU/ml, mean ±SD)		8.42±2.1	2.84±0.73	**0.021**

Table 3: Multivariate analysis for subclinical hypothyroidism in patients with metabolic syndrome.

S.no	Variables	Categories	Clinical Model OR (95% CI)
1	Gender	Female	5.123(1.342- 12.853)
		Male	
2	Age(Year)	< 50	0.941(0.312- 1.632)
		≥ 50	
3	Body mass index(kg/m^2)	≥ 30	2.951(0.358- 4.961)
		< 30	
4	Waist circumference(cm)	Female > 88	0.642(0.127- 2.963)
		Female≤ 88	
		Male> 102	0.537(0.037- 3.961)

		Male≤ 102	
5	**Blood pressure(mmHg) (Systolic, diastolic)**	**≥ 130, ≥85**	2.963(0.627-9.635)
		<130, <85	
6	**Triglycerides(mg/dl)**	**≥ 150**	0.753(0.167- 1.974)
		< 150	
7	**HDL cholesterol(mg/dl)**	**Female ≥50, male≥40**	1.846(0.496-4.163)
		Female<50, male<40	
8	**Fasting blood glucose(mg/dl)**	**≥ 110**	0.942(0.275-1.852)
		<110	



DISCUSSION

Hypothyroidism is often accompanied by serum lipid concentrations that are associated with an enhanced risk of cardiovascular or heart disease. Subclinical hypothyroidism, characterized by thyroid hormones within the reference range combined with elevated thyroid-stimulating hormone (TSH), may also be associated with unfavorable serum lipids.[8,9] MetS is a state of chronic low-grade inflammation because of the complex interplay between genetic and environmental factors. Several factors are associated with MetS including Insulin resistance, atherogenic dyslipidemia, hypercoagulable state, visceral adiposity, endothelial dysfunction, genetic susceptibility, elevated blood pressure, and chronic.[10]

Hypothyroidism and metabolic syndrome are the most important risk factors for atherogenic cardiovascular disease. The common pathogenicity in both the disorders is Insulin resistance, which can cause a considerable overlap between the hypothyroid and metabolic syndrome populations. The role of insulin resistance in the development of dyslipidemia in hypothyroidism has been suggested in recent studies.[11]

In the present study, the mean systolic pressure, diastolic pressure, fasting blood sugar, 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 findings were similar to those obtained in Chennai urban population by Shantha et al.[12] On the other hand, Fernandes et al suggest the absence of a significant relationship between thyroid function with total or LDL cholesterol.[6] There was a strong association observed between SCH and several indices of metabolic syndrome in women in a one-year follow-up study done by Nakajima et al.[13]

In this study, SCH was found in 17.1% of cases in the Mets group and 6.3% in the control group. Similarly, the high prevalence was observed by Ruhla et al and Chang et al in their studies respectively.[14,15] Prevalence of SCH was higher in females in the Mets group as compared to the control group, while it was almost similar in males in both the groups in this study. In both groups, all the cases with SCH had TSH levels above the upper limit and FT_4 within the normal limit. According to our present study, MetS patients with higher BMI are more prone to having associated subclinical hypothyroidism. However, Kota et al, have recently demonstrated the absence of any significant relationship between the severity of obesity and serum TSH levels.[16] A cross-sectional study was conducted by Knudsen et al which concluded that even slightly elevated serum TSH levels are associated with an increase in the occurrence of obesity.[17]

Various reviews stated that there is convincing evidence for a major impact of thyroid function on all components of the metabolic syndrome, reflecting profound alterations of energy homeostasis at many levels and a slight increase in serum TSH might be a risk factor for metabolic syndrome.[18,19] The prevalence of obesity and the MetS is rapidly increasing in South Asians residing in the Indian subcontinent (e.g., India, Pakistan, Bangladesh, and Nepal), leading to increased morbidity and mortality due to T2DM.[20]

The prevalence of Thyroid disorders (TD) is high in patients with MetS, particularly in SCH and females can be at an increased risk. Although thyroid hormone substantially can affect every element of MetS, it showed that there exists no relationship between TD and any element of MetS. It showed an increased incidence of TD, with elevated TSH and normal levels of T3 and T4 in MetS. The findings in our study indicate more impact in placing investigations in the presence of Thyroid disorder while evaluating and treating patients with MetS.

CONCLUSION

The prevalence of subclinical hypothyroidism in patients with MetS has been observed to be higher. Thyroid disorders should be considered when evaluating and treating patients with MetS to reduce the impending risk.

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