ORIGINAL ARTICLE

Prevalence of thyroid dysfunction in metabolic syndrome

Saajid Anwar[1], Yoganathan Chidambaram[2], Clement Jenil Dhas C P[2], Sujith Kumar[2]*

[1]Sri Ramachandra Institute of Higher Education and Research, Porur Chennai-600116 (Tamil Nadu) India, [2]Department of General Medicine, PSG Institute of Medical Sciences & Research, Peelamedu, Coimbatore-641004 (Tamil Nadu) India

Abstract

Background: Metabolic syndrome is a pathologic state characterized by abdominal obesity, hypertension, insulin resistance, and hyperlipidemia. Thyroid hormones significantly affect lipid metabolism and dysfunction of the same can potentially increase the risk of coronary heart disease. *Aim and Objectives:* To assess the changes in thyroid parameters in patients suffering from metabolic syndrome. *Material and Methods:* The present study was a cross-sectional study conducted at a tertiary healthcare centre and included subjects aged more than 18 years with a waist circumference > 90 cm for men and > 80 cm for women along with any two of the criteria: Triglycerides > 150 mg/dL, HDL< 40 mg/dL (men), < 50 mg/dL (women), Systolic Blood Pressure (SBP) > 130 mmHg, Diastolic Blood Pressure (DBP) > 85 mm Hg, Fasting Blood Glucose (FBS) > 100 mg/dL. Blood samples were taken from patients for glucose, lipid profile, and thyroid function tests and correlation was obtained. *Results:* Among the 141 patients enrolled in the study, 59.6% individuals had TSH in the euthyroid range, 39.7% in hypothyroid range, and 0.7% in the hyperthyroid range. Additionally, 75% individuals had free T4 in the euthyroid range, 6% in the hyperthyroid range and 19% in the hypothyroid range. Of the participants in the hypothyroid range, 45.7% were overweight, 33.3% were obese, and 25% were severely obese. There was only one hyperthyroid participant who was overweight. However, none of the assessed parameters showed a statistically significant association with TSH levels among the participants. *Conclusion:* The results show that there is no direct association between thyroid dysfunction and individual parameters of metabolic syndrome, However, subclinical hypothyroidism is prevalent among metabolic syndrome patients hence making evaluation for thyroid disease in these patients a priority.

Keywords: Metabolic syndrome, Thyroid disease, Triglyceride, Hyperthyroid

Introduction

Metabolic Syndrome (MetS) can be defined as a cluster of various interrelated metabolic disorders of metabolic, environmental and/or genetic origin. This is also known as Insulin Resistance Syndrome (IRS), or syndrome X[1]. World Health Organization has defined MetS as a pathologic state which is characterized by abdominal obesity, hypertension, insulin resistance, and hyperlipidemia [2, 3].

Studies have reported an overall 25% (approximately 18.5% in men and 31% in women) age-adjusted prevalence of MetS in urban Indian populations [4]. According to the National Cholesterol Education Program (NCEP) Adult Treatment Panel III criteria, MetS is diagnosed if three or more of the following five criteria are met: waist circumference > 40 inches (men) or > 35 inches (women), hypertension (> 130/85 mmHg), fasting Triglyceride (TG) level > 150 mg/dL, fasting high-density lipoprotein (HDL) cholesterol level < 40 mg/dL (men) or < 50 mg/dL (women) and fasting

blood glucose > 100 mg/dL [5].

The risk factors for MetS are of metabolic origin and comprises elevated Blood Pressure (BP), atherogenic dyslipidemia, increased plasma glucose, as well as a prothrombotic and proinflammatory state. Atherogenic dyslipidemia consists of elevated apolipoprotein B, triglycerides, small particles of Low-Density Lipoprotein (LDL), and low levels of HDL. Elevated plasma glucose refers to the state of pre-diabetes or diabetes. A prothrombotic state is one where we can observe anomalies in procoagulant factors such as elevated factor VII and fibrinogen, anti-fibrinolytic factors (such as elevated plasminogen activator inhibitor- 1), platelet abnormalities, and endothelial dysfunction. We can define proinflammatory state as high levels of circulating cytokines and acute phase reactants like C-reactive protein [6]. The pathophysiology of MetS is complex and is not completely elucidated. An ongoing debate exists regarding whether the individual components of MetS are responsible for distinct pathologies or are they the manifestations of a common pathogenic mechanism. Amongst the proposed mechanisms, factors that play major roles in the inception, development, and transformation of MetS to Cardiovascular Disease (CVD) include insulin resistance, chronic inflammation, and neurohormonal activation [7].

Thyroid Dysfunction (TD) refers to an altered serum Thyroid Stimulating Hormone (TSH) level with normal or altered Free Triiodothyronine (FT3) and Free Thyroxine (FT4) [8]. MetS and TD share a cluster of common clinical features like abdominal obesity, hypertension, hyperglycemia, reduced HDL levels, and elevated triglycerides [9-10]. Thyroid hormones significantly affect the synthesis, mobilization, and metabolism of lipids and has adverse effects on lipid profile; thus, it might have the potential to increase the risk of Coronary Heart Disease (CHD) [11]. The deviation of TSH levels from normal values has also been proven to be partially associated with lipid components and can increase the total cholesterol level in CHD patients independent of thyroid hormone status[12, 13]. If a correlation is found between thyroid dysfunction and MetS, it will eventually help in decreasing morbidity and mortality risk as thyroid dysfunction is closely associated with CVD. Thus, the primary objective of the present study was to assess the association between thyroid parameters and MetS with the secondary objective being to assess the correlations between various elements of thyroid indices and MetS.

Material and Methods

This was a cross-sectional study conducted at PSG Institute of Medical Science and Research from April 2021 to October 2022. The study was initiated after obtaining approval from the Institutional Human Ethics Committee (IHEC; Registration No. PSG/IHEC/2021/Appr/Exp/062) dated April 02, 2021.

The study population included adult subjects of more than 18 years of age with waist circumference more than 90 cm for men and more than 80 cm for women. The waist circumference measured was by the International Diabetes Federation and was ethnicity-specific (South Asian). It was measured halfway between the lowermost border of the costal edge and the topmost border of the iliac crest. Apart from this, any two of the below-mentioned criteria were necessary to be included in the study- Triglycerides - more than 150 mg/dL, HDL - less than 40 mg/dL in men, 50 mg/dL in women, Systolic blood pressure (SBP) more than 130 mm

of Hg, Diastolic Blood Pressure (DBP) more than 85 mm of Hg, FBS >100 mg/dL, age- more than 18 years. Patients not willing to participate in the study, or who were on oral contraceptive pills, or patients with history of pancreatitis were excluded from the study.

The following formula was used to calculate the sample size based on the results of a previously conducted study [14]:

$N = 4 \times p \times q/d^2$

With 20 percent non respondents, sample size required was found to be 141.

Detailed history of the study participants was taken and examination carried out as per proforma. Blood samples were then collected from the patients and tested for plasma glucose using hexokinase enzymatic method, TSH and ft4 using electrochemiluminescence immunoassay (ECLIA) method, HDL by using direct method and TG using enzymatic end point method. These tests provided data related to glucose and lipid profile as well as thyroid function. The collected data was then analysed and necessary statistical methods were used to check for association.

Statistical analysis

Descriptive statistics was used to determine percentage data. Chi-square test was utilized to determine association between variables. Statistical Package for the Social Sciences version 22 software was used to perform statistical analysis and p-value < 0.05 was considered statistically significant.

Results

Based on the eligibility criteria, a total of 141 patients (males n = 92, 65.2%, females n = 49, 34.8%) were enrolled in the study, with a mean (SD) age of 56.73 ± 13.03 years.

Baseline characteristics

Among the total study population, 74% of individuals were suffering from type 2 diabetes mellitus. Most of the patients (n=93, 66%) had an SBP > 130 mmHg, and the rest (n=48, 34%) had an SBP < 130mm Hg; 65 (46.1%) individuals had a DBP > 85 mmHg and 76 (53.9%) individuals had DBP < 85 mm Hg. Based on the BMI among the selected individuals, 92 (65.2%) individuals were overweight, 36 (25.5%) were obese, 8 (5.7%) belonged to the severely obese category and 5 (3.5%) belonged to the morbidly obese category. Lipid profile was also assessed in the patients; 39% of individuals had a normal triglyceride (TG) level, 61% had a high TG level; 63% of individuals had low HDL levels and 37% had normal HDL levels.

Thyroid parameters

Eighty four (59.6%) individuals had TSH in the euthyroid range, 56 (39.7%) in the hypothyroid range, and 1 (0.7%) in the hyperthyroid range (Figure 1). When FT4 was measured, 106 (75%) individuals had free T4 in the euthyroid range, 9 (6%) in the hyperthyroid range, and 26 (19%) in the hypothyroid range (Figure 2).

Various components of thyroid indices and metabolic syndrome

Triglyceride was elevated in 33 individuals (38.4%) while 23 (41.8%) had normal triglyceride levels among subjects belonging to the hypothyroid range. TG level was elevated in 1 (1.2%) participant belonging to the hyperthyroid range; It was elevated in 52 (60.5%) participants and was within normal levels in 32 (58.2%) participants belonging to the euthyroid range. On analysis, 38 (42.7%) participants who were in the hypothyroid range had low HDL levels and 18 (34.6%) had

normal HDL and 1 (1.9%) participant in the hyperthyroid range had normal HDL levels. Further analysis showed that 33 (35.5%) hypothyroid participants had an SBP > 130 mmHg and 23 (47.9%) had SBP < 130 mmHg; 1 (1.1%) individual belonging to the hyperthyroid range had an SBP >130 mm of Hg. On analysis of hypothyroid individuals, 23 (41.1%) had a DBP > 85 mmHg and 33 (58.9%) had DBP < 85 mmHg; 1 (1.5%) hyperthyroid individual had DBP > 85 mm Hg. Among the subjects, 24 (49%) participants in the hypothyroid group were females and 32 (34.8%) were male; 1 (2%) hyperthyroid participant was female (Table 1).

Of the participants who were in the hypothyroid range, 42 (45.7%) were overweight, 12 (33.3%) were obese, and 2 (25%) were severely obese. There was only one hyperthyroid individual who was overweight (Figure 3). On analysis of hypothyroid participants, 36 (64.3%) had subclinical hypothyroidism and 20 (35.7%) had primary/ overt hypothyroidism (Figure 4).

Association between different parameters and TSH of participants

The different parameters were checked for association with differing levels of TSH and the results show that parameters such as TGL, HDL, BMI, SBP, DBP, age and gender were not associated with TSH levels of the participants. (Tables 2 and 3).

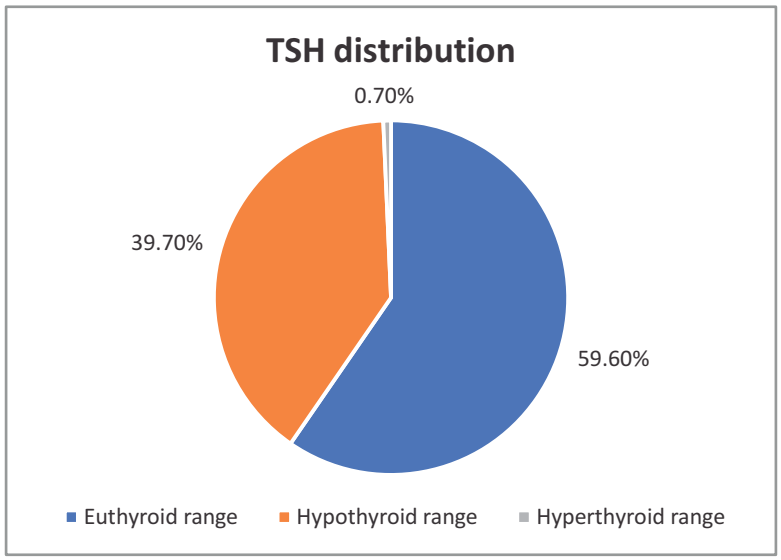

Figure 1: Thyroid Stimulating Hormone (TSH) distribution

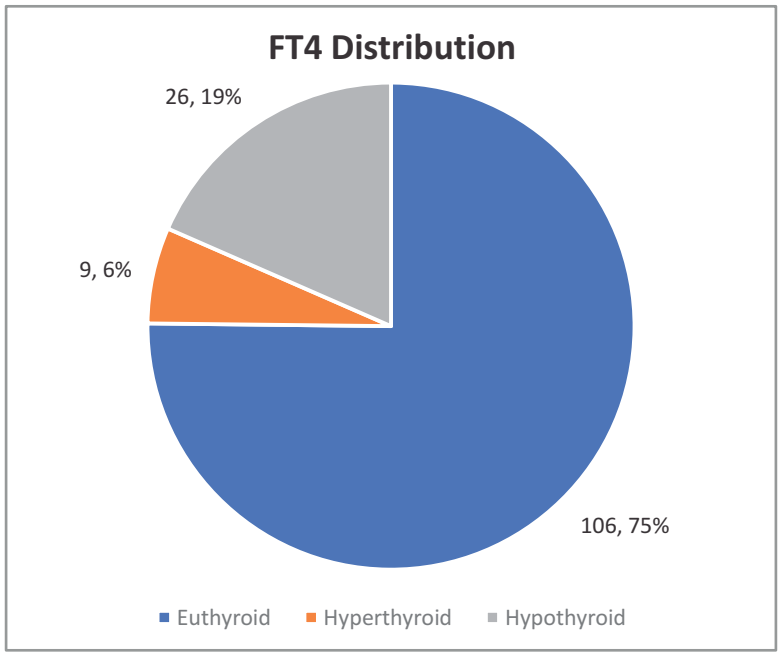

Figure 2: Free T4 (FT4) distribution

Table 1: Changes in TSH based on variation in TGL, HDL, SBP, DBP and gender

		Euthyroidism	Hyperthyroidism	Hypothyroidism
TGL	**Normal**	32	0	23
	High	52	1	33
HDL	**Low**	51	0	38
	Normal	33	1	18
SBP	**>130 mm Hg**	59	1	33
	<130 mm Hg	25	0	23
DBP	**>85 mm Hg**	41	1	23
	<85 mm Hg	43	0	33
Gender	**Male**	60	0	32
	Female	24	1	24

TSH - Thyroid Stimulating Hormone; TGL - Triglycerides; HDL - High Density Lipoprotein; SBP - Systolic Blood Pressure; DBP - Diastolic Blood Pressure

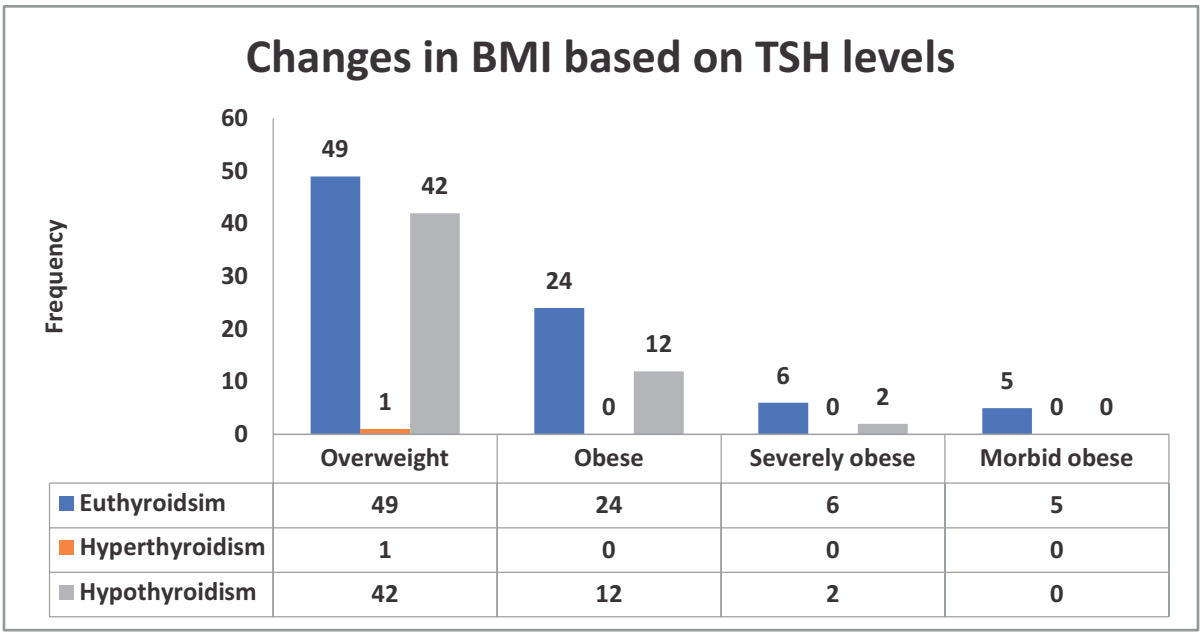

Figure 3: Changes in BMI based on TSH levels

BMI -Body Mass Index, TSH -Thyroid Stimulating Hormone

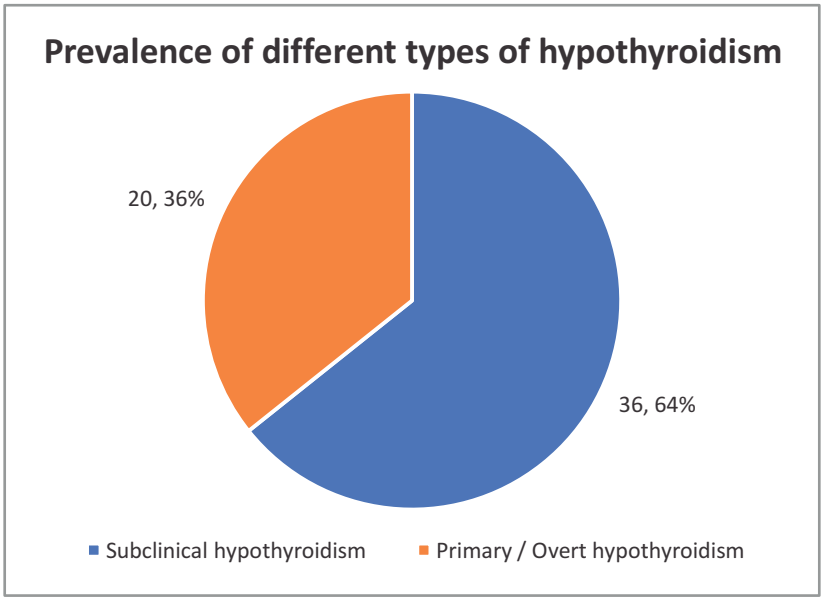

Figure 4: Prevalence of different types of hypothyroidism

Table 2: Association of different parameters with TSH of the study participants

Variables		TSH			*p*
		Normal	Hyperthyroidism	Hypothyroidism	
TGL	**Normal**	32(58.2%)	0(0.0%)	23(41.8%)	0.682
	High	52(60.5%)	1(1.2%)	33(38.4%)	
HDL	**High**	51(57.3%)	0(0.0%)	38(42.7%)	0.292
	Normal	33(63.5%)	1(1.9%)	18(34.6%)	
BMI	**Overweight**	49(53.3%)	1(1.1%)	42(45.7%)	0.345
	Obese	24(66.7%)	0(0.0%)	12(33.3%)	
	Severely obese	6(75.0%)	0(0.0%)	2(25.0%)	
	Morbidly obese	5(100.0%)	0(0.0%)	0(0.0%)	
SBP	**>130 mm hg**	59(63.4%)	1(1.1%)	33(58.9%)	0.296
	<130 mm hg	25(52.1%)	0(0.0%)	23(41.1%)	
DBP	**>85 mm hg**	41(63.1%)	1(1.5%)	23(35.4%)	0.370
	<85 mm hg	43(56.6%)	0(0.0%)	33(43.4%)	
Gender	**Male**	60(65.2%)	0(0.0%)	32(34.8%)	0.086
	Female	24(49.0%)	1(2.0%)	24(49.0%)	

TSH - Thyroid Stimulating Hormone; TGL - Triglycerides; HDL - High Density Lipoprotein; BMI – Body Mass Index; SBP - Systolic Blood Pressure; DBP - Diastolic Blood Pressure

Table 3: Association of age with TSH of the study participants

	N	Minimum	Maximum	Mean	SD	*p*
Normal	84	29	81	55.57	12.005	0.356
Hyperthyroidism	1	67	67	67.00	0	
Hypothyroidism	56	29	85	58.29	14.439	

TSH - Thyroid Stimulating Hormone

Discussion

Metabolic syndrome might be associated with non-endocrine and endocrine disorders as well as have numerous consequences [15]. Metabolic syndrome is a risk factor for cardiometabolic disorders and specific cancer types, and it has progressively garnered attention in numerous research investigating the impact of hypothyroidism on metabolic syndrome [16]. Thyroid dysfunction, although well known, is not clinically manifested and evidence reporting has shown inconsistency in terms of thyroid function about metabolic syndrome [17].

In this present study, a considerable number of patients (39.7%) had TSH levels in the higher range suggesting a degree of hypothyroidism in such patients. Moreover, in 26 (18.4%) patients, the FT4 level was above normal suggesting hyperthyroidism. In a similar study, Hamlaoui ML *et al.*, found that the most observed endocrine thyroid disease was found to be hypothyroidism (45.3%) which was followed by hyperthyroidism (14.0%) [18]. On analysis of hypothyroid participants in our study, 64.3% had subclinical hypothyroidism and 35.7% had primary/overt hypothyroidism. Another study also identified that the most common endocrine disorder in metabolic syndrome patients was thyroid dysfunction; within which subclinical hypothyroidism (26.6%) was mostly observed along with overt hypothyroidism among 3.5% of patients and subclinical hyperthyroidism in 1.7% of patients [16]. Gyawali *et al.* in their study concluded that thyroid dysfunction was reported in 31.84% of included metabolic syndrome patients and that the most common types of dysfunctions seen were subclinical hypothyroidism (29.32%), overt hypothyroidism (1.67%) which was then followed by subclinical hyperthyroidism (0.83%) and these results contrasted with the results of the present study [19]. A study conducted by Meher *et al.* reported a high prevalence rate of subclinical hypothyroidism (22%) as well as overt hypothyroidism (4%) in patients suffering from metabolic syndrome [20]. Oh JY *et al.* in their study, found that the prevalence of metabolic syndrome was significantly more observed in the high-TSH group (7.5%) than in the low-TSH group (4.8%), using a TSH level of 2.5 mU/L as an upper reference limit in euthyroid subjects [21]. Other studies have also shown that in euthyroidism, subjects with a TSH in the upper normal range were more likely to have metabolic syndrome [22], and a slight increase in serum TSH could be considered a risk factor for the same [23]. In the present study, 106 (75%) individuals had free T4 in the euthyroid range. Similarly, the prevalence of MetS in the euthyroid population was estimated at 34.2% in a study by Khatiwada S *et al.* [15].

The present study reported that 42.7% of patients who were in the hypothyroid range had low HDL levels and 34.6% had normal HDL levels. Triglyceride was elevated in 38.4% of patients while 41.8% had normal triglyceride levels among subjects belonging to the hypothyroid range. In a similar study, the hyperthyroid group was found to have significantly lower levels of total cholesterol, LDL, and HDL [18]. Another study found a significant positive correlation between circulating TSH and total cholesterol, or LDL concentrations and this is consistent with the well-established association between hypothyroidism and elevated levels of total cholesterol and LDL [24]. Khatiwada S *et al.* observed that patients with subclinical hypothyroidism presented with high triglyceride and low HDL levels [15]. Triglyceride was found to be

elevated in 60.5% of participants of the euthyroid range and 38.4% of participants of the hypothyroid range in our study. However, Garduño-Garcia Jde J *et al.* reported that subclinical hypothyroid patients presented with higher triglyceride levels when compared to euthyroid patients [25].

Of the hypothyroid participants included in the present study, 45.7% were overweight, 33.3% were obese, and 25% were severely obese. Khatiwada S *et al.* observed a negative association between BMI about free T3 and free T4 levels as well as a weak positive correlation with relation to TSH [15]. A study conducted in Germany found that euthyroid subjects whose TSH levels were in the upper normal range (2.5–4.5 mU/L) were found to be more obese (BMI > 30 Kg/m^2), showed higher triglyceride levels as well as an increased susceptibility to metabolic syndrome [22]. Similarly, other studies have also reported high BMI and higher prevalence of abdominal obesity in hypothyroid subjects [18].

The results of the present study showed that among the hypothyroid participants, 58.9% had a SBP > 130 mm Hg and 41.1% had SBP < 130 mm Hg; However, Bojin Xu *et al.* found that there was no linear association between TSH levels and DBP or SBP [24].

Among the subjects in the present study, 49% of participants in the hypothyroid group were females and 34.8% were male; 2% of the hyperthyroid participant was female. The results are similar to those of a study where thyroid dysfunction was more commonly seen in females (39.7%) when compared to males (26%) [15]. Contrary to this, thyroid dysfunction was reported to be more prevalent in men (68.7%) than in women (57.1%) in a study by Hamlaoui ML *et al.* [18].

The results of the present study also showed that demographic details such as age and gender as well as parameters such as age, BMI, TGL, HDL, SBP and DBP were not associated with changes in TSH levels in the selected participants. This result was in complete contrast with the results of studies with regard to TGL, BMI and HDL [15, 18, 22, 24, 25]. However, it was similar to the results of a previously conducted study wherein no association was found between SBP and DBP with regard to TSH [24]. Gender has provided mixed results with the present study showing a female predominance which was supported by another study, but a different study has shown male predominance [15, 18]. However, analysis has shown that it bears no association with TSH levels.

The study has certain limitations. It has not statistically correlated the association between various thyroid dysfunction indices with components of metabolic syndrome. Further studies with larger populations are needed to emphasize the correlation between the incidence and level of thyroid dysfunction among individuals suffering from metabolic syndrome

Conclusion

It can be concluded from the study that the incidence of thyroid dysfunction and metabolic syndrome are interlinked, largely being subclinical hypothyroidism. However, individual parameters do not show any association with the condition. Nevertheless, it is of utmost importance to also evaluate for thyroid disease in individuals with metabolic syndrome keeping in view its associated cardiovascular risk and morbidity.

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Author for Correspondence:
Dr. Yoganathan Chidambaram, Department of General Medicine, PSG IMS & R, Peelamedu, Coimbatore 641004, Tamil Nadu, India
Email: yoganathancc@gmail.com Cell: 9942460735

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