http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v9i2.06

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Article

A Study of Thyroid Dysfunction in Patients with Metabolic Syndrome

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Abstract
Introduction: *Metabolic syndrome (MetS) is a combination of risk factors such as hypertension, atherogenic dyslipidemia, hyperglycemia, truncal (central) obesity, and prothrombotic and proinflammatory conditions, which could increase the risk of cardiovascular illness, diabetes, and death. Metsare closely associated with thyroid dysfunction (TD) due to the impact of thyroid hormones on lipid metabolism, glucose, blood pressure, and cardiovascular dysfunction.*
Aim of the Study: *To study the prevalence and to find the types of thyroid dysfunction in Metabolic Syndrome and to find the association of Thyroid Dysfunction and Metabolic Syndrome.*
Materials and Methods: *A total of 60 Patients with metabolic syndrome fulfilling IDF criteria have selected the study. A detailed history of medication and anthropometric measurements were noted in a semi-structured proforma. Blood pressure was recorded in the right upper limb in a sitting posture. After eight hours of fasting, blood was drawn for fasting blood sugar, lipid profile, and thyroid assay in a single sitting.*
Results: *In this study, thyroid dysfunction prevalence is 18.33% among metabolic syndrome patients. Subclinical Hypothyroidism is 15% prevalent in metabolic syndrome patients and Overt Hypothyroidism is 3.3% prevalent. There is no incidence of either overt or subclinical Hyperthyroidism in our study population. The prevalence of thyroid dysfunction and hypothyroidism in metabolic syndrome patients is higher than the prevalence in the normal population, which is 5.9% for thyroid dysfunction and 4.6% for hypothyroidism (0.3% overt and 4.3% subclinical hypothyroidism). The incidence of metabolic syndrome is significantly higher in women (25.8) than in men (8%) with metabolic syndrome.*
Conclusion: *Thyroid dysfunction occurs in 18.33% of metabolic syndrome patients. The prevalence of Subclinical hypothyroidism (15.0%) and Overt Hypothyroidism (3.33%) in metabolic syndrome patients is higher than that of the general population. One-sixth of metabolic syndrome patients or every sixth metabolic syndrome had Subclinical Hypothyroidism. Prevalence of thyroid dysfunction is much more common in Females with thyroid dysfunction than males. Exclude the presence of Thyroid dysfunction while managing metabolic syndrome patients.*
Keywords: *Metabolic Syndrome, Body Mass Index, Free Thyroxine, Thyroid Stimulating Hormone.*

Introduction

Each year mortality due to coronary artery disease and cerebrovascular disease are on the rise. Though multiple risk factors are leading to these terminal illnesses, few of these risk factors appear in groups. The characteristic of this group is the presence of central obesity and insulin resistance; they also have high blood pressure, high triglyceride levels, and abnormal fasting blood sugar levels. These groups of risk factors are known as Metabolic Syndrome.[1] M There is a high risk of developing cerebrovascular disease and cardiovascular events in people who have metabolic syndrome. With the changing lifestyle and food habits, there is a rise in the incidence of obesity and Metabolic Syndrome. Thyroid disease is associated with atherosclerotic cardiovascular disease. This association may be in part be explained by the thyroid hormones regulation of lipid metabolism and its effect on blood pressure. Thyroid hormones have ubiquitous effects and influence the function of most organs. This hormone appears to serve as a general pacemaker accelerating the metabolic process and may be associated with metabolic syndrome.[2] Both Metabolic syndrome and thyroid dysfunction are associated with an increased risk of atherosclerotic heart disease. Thyroid dysfunction, prominently subclinical hypothyroidism has been observed more frequently in metabolic syndrome patients than in the general population Both metabolic syndrome and hypothyroidism are independent risk factors for cardiovascular diseases (CVD).[3] The presence of both conditions may be compounded to increase the risk for CVD and considerable overlap occurs in the pathogenic mechanisms of atherosclerotic cardiovascular disease by metabolic syndrome and hypothyroidism There are reports about higher thyroid-stimulating hormone (TSH) level in metabolic syndrome patients than in healthy ones, and high prevalence of metabolic syndrome in subjects with TSH level higher than normal as compared to those with normal TSH level However the association between thyroid dysfunction and components of metabolic syndrome is still debatable. There is evidence that thyroid function may need to be assessed in patients with metabolic syndrome who are also at higher risk for CVD.[4] Metabolic syndrome and thyroid dysfunction association were demonstrated in many recent studies. Thyroid dysfunction is altered states of thyroid-stimulating hormone level with or without alteration in Triiodothyronine (T3), Tetra iodothyronine (T4). People with high Thyroid-stimulating hormone (TSH) levels were found to have a twofold rise in the prevalence of metabolic syndrome.[5] Subclinical hypothyroidism with increased TSH level was also seen to be associated with an increased risk of coronary heart disease. Both atherosclerosis and dyslipidemia are common in hypothyroidism. As both metabolic syndrome and thyroid dysfunction are individual and independent risk factors for the development of atherosclerotic Cardiovascular Disease (CVD), the concurrent existence of both in the same individual will further increase cardiovascular risk in the individual.[6]

Materials and Methods

This study Tamil Nadu Government Multi Super Speciality Hospital, Omandurar Government Estate, Chennai. from January 2018 to December 2019 (24 months)A total of 60 Patients with metabolic syndrome fulfilling IDF criteria have selected the study. The detailed history of medication and anthropometric measurements were noted in a semi-structured proforma. Blood pressure was recorded in the right upper limb in a sitting posture. After eight hours of fasting, blood was drawn for fasting blood sugar, lipid profile, and thyroid assay in a single sitting. A detailed history of medication and anthropometric measurements like height, weight, waist circumference were noted in a semi-structured proforma. Blood pressure was recorded in the right upper limb in a sitting posture. After eight hours of fasting, blood was drawn for fasting blood sugar, lipid profile, and thyroid assay in a

single sitting. The patients who fulfilled the criteria for metabolic syndrome by IDF were taken into the study. –For a person to be defined as having the metabolic syndrome they must have: Central obesity – waist circumference ≥ 90 cm for men and ≥ 80 cm for women. Plus any two of the following four factors: Raised TG level ≥ 150 mg/dl or any specific treatment. Reduced HDL cholesterol < 40 mg/dl in males and < 50 mg/dl in females. Raised blood pressure ≥ 130/85 mm Hg or medication. Raised fasting glucose ≥ 100 mg/dl or previously diagnosed type 2 diabetes.

Inclusion Criteria: The patients who fulfilled the criteria of metabolic syndrome as defined by IDF 2005 were taken up for this study.

Exclusion Criteria: Known Hypothyroid / Subclinical Hypothyroid. Patients with chronic illness.

Statistical Analysis: The data of each patient will be collected on a proforma specially designed for this study and which includes demographic details, past medical history, clinical data, and biochemical results will be analyzed for statistical significance and correlation. All statistical analyses were performed using SAS® version 9.2 (SAS Institute Inc., USA). The prevalence of TD in MetS patients was calculated as a number and percentage with 95% CI.

Results

Table: 1 Age Distribution & Population Characteristic Features of Cases

AGE GROUP	TOTAL NO	PERCENTAGE	CUMULATIVE PERCENTAGE	Male	Female
Up to 35 yrs.	7	11.7%	11.7%	3	**4**
36 - 45 yrs.	24	40.0%	51.7%	8	**16**
46 - 55 yrs.	19	31.7%	83.3%	8	**11**
Above 55 yrs.	10	16.7%	100.0%	6	**4**
Total	**60**	**100.0%**	**100.0%**	**25**	**35**

Table: 1 Total of 60 patients included in the study based on the inclusion and exclusion criteria of metabolic syndrome. Among them 33 were women and 27 were men. Women constitute around 55% of total cases and the rest 45% by men. The age of the women ranges from 33 to 62 years with a mean age of 45.1 and a Standard Deviation of 7.6. The age of the men ranges from a minimum of 30 to a maximum of 67 with a mean of 46.5 and a Standard deviation of 9.7. According to age, 7 patients were less than 35 years old. 24 patients were in the age 35-45 age group, 19 were in the 45-55 age group and 10 patients were above 55 years. As we can see most patients fall in the middle age group from 36 to 55 years, consistent with the changing lifestyle patterns and raising obesity in the middle age group. Among the sixty study subjects, twenty-eight members (47%) fulfilled three parameters for metabolic syndrome, twenty members (33%) fulfilled four parameters and twelve members (20%) fulfilled all criteria for metabolic syndrome.

Table: 2 Thyroid Function Test Results

	N	Minimum	Maximum	Mean	Standard Deviation
FT4	60	0.17	2.27	1.07	**0.265**
TSH	60	0.56	154	5.4	**19.809**
Valid N (listwise)	**60**				

Table: 2 The TSH in this study was ranging from 0.56mU/L to 154 mU/L and free T4 levels ranging from 0.17ng/dl to 2.21ng/dl. Patients were grouped into four groups according to the definitions based on TSH and FT4 levels and further statistical analysis was done based on these groups. According to our definitions, 49 patients were found to be euthyroid and two patients were hypothyroid. Nine patients had subclinical hypothyroidism. There were no overt hyperthyroid or sub-clinical hyperthyroidism patients in our study.

Table 3: Thyroid Status of the study Population

GROUP	NO	%	MALE	FEMALE
EUTHYROID	49	83.33%	23	**26**
HYPOTHYROID	2	3.33%	1	**1**
SUB CLINICAL HYPOTHYRODISIUM	9	15.00%	1	**8**
SUBCLINICAL HYPERTHYRODISIUM	0	0%	0	**0**
HYPERTHYRODISM	**0**	**0%**	**0**	**0**

Table: 3 According to our definitions, 49 patients were found to be euthyroid and two patients were hypothyroid. Nine patients had subclinical hypothyroidism. There were no overt hyperthyroid or sub-clinical hyperthyroidism patients in our study. According to age, among patients age less than 35, there were seven subjects. Six were Euthyroid and one is Overt hypothyroid. No subclinical hypo or hyperthyroid in this group. In the age group 36-45, there were 24 subjects, among them, eighteen were Euthyroid, and the remaining six were Subclinical hypothyroid. There were no overt hypo or hyperthyroid in this group.

Table 4: Metabolic Syndrome Parameters Wise Thyroid Dysfunction

MS CRITERIA FULFILLED	TOTAL NO	EUTHYROID	HYPOTHYROID	SUBCLINICAL HYPOTHYROID	SUBCLINICAL HYPERTHYROID
3	28	25	1	2	0
4	20	17	0	3	0
5	12	7	1	4	0
TOTAL	60	49	2	9	0

Table: 4 Presence of thyroid dysfunction based on several criteria present is statistically significant in our study possibly due to the limited number of study subjects. Women havea higher incidence of thyroid dysfunction when compared to men with metabolic syndrome. Chi-square tests did not any signs of thyroid status distribution with respect to sex in study subjects possibly due to a limited number of study subjects. Analysis of study subjects concerning the number of criteria fulfilled for Metabolic syndrome

Table 5: Distribution- Thyroid Status Concerning No. of MS Parameter

Thyroid status		MS parameter			Total
		3	4	5	
Euthyroid	Count	25	17	7	49
	% within MS parameter	89.3%	85.0%	58.3%	81.7%
Subclinical Hypothyroid	Count	2	3	4	9
	% within MS parameter	7.1%	15.0%	33.3%	15.0%
Hypothyroid	Count	1	0	1	2
	% within MS parameter	3.6%	0.0%	8.3%	3.3%
Total	Count	28	20	12	60
	% within MS parameter	100.0%	100.0%	100.0%	100.0%

Table: 5 Association between thyroid status and several criteria positive for metabolic syndrome is not significant in our study. Now finally correlation of the individual parameters of metabolic syndrome in thyroid dysfunction and euthyroid in metabolic syndrome is studied.

Table 6: Distribution of MS Parameters in Euthyroid and Thyroid Dysfunction

Thyroid status		N	Mean	Std. Deviation	Std. Error Mean
WBC	Euthyroid	49	98.2	6.7	0.961
	Thyroid Dysfunction	11	97.6	8.7	2.609
SBP	Euthyroid	49	140.7	15.7	2.246
	Thyroid Dysfunction	11	137.6	16	4.83
DBP	Euthyroid	49	87.2	10.5	1.5
	Thyroid Dysfunction	11	87.5	9.1	2.751
FBS	Euthyroid	49	138	25.4	3.622
	Thyroid Dysfunction	11	126.1	10.3	3.111
TC	Euthyroid	49	193.3	34.5	4.934
	Thyroid Dysfunction	11	197.4	26.8	8.086
HDL	Euthyroid	49	43.9	6.3	0.902
	Thyroid Dysfunction	11	47.3	6	1.799
TGL	Euthyroid	49	171.8	54.7	7.808
	Thyroid Dysfunction	11	161.5	42.8	12.893

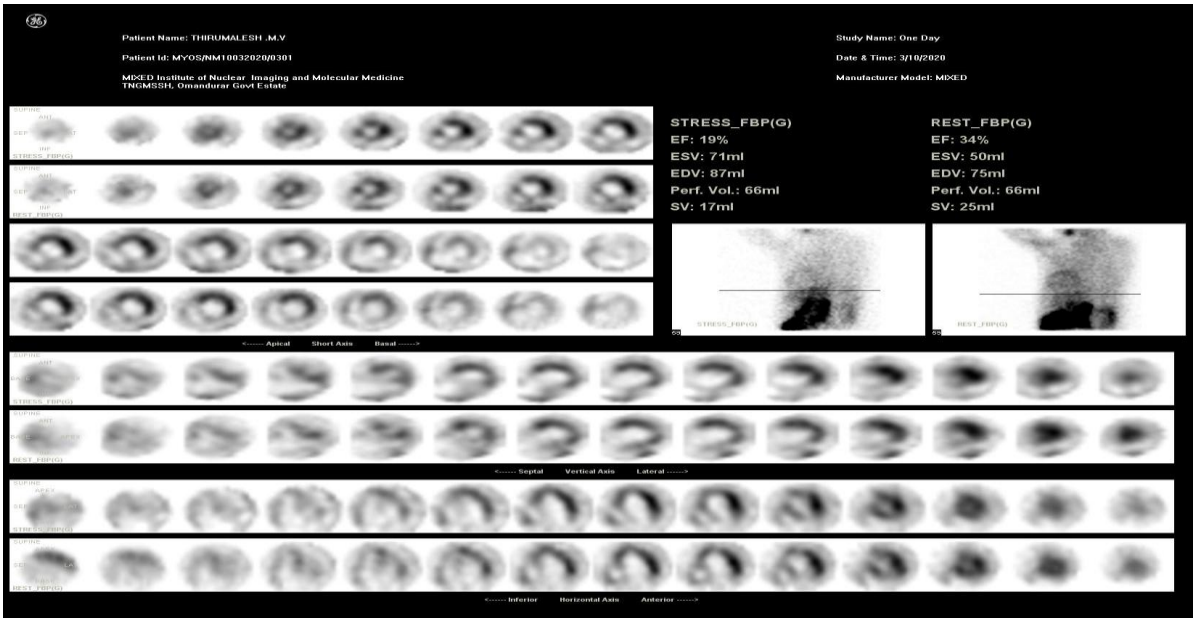
Table: 6 Due to a small number of study subjects correlation of metabolic syndrome parameters between euthyroid and thyroid dysfunction is not significant. Lastly, the correlation between TSH and FT4 is analyzed against metabolic syndrome parameters in euthyroid and thyroid dysfunction is analyzed. Correlation is not significant in our study.

Table 7: Distribution of Indices

	EUTHYROID		THYROID DYSFUNCTION	
	MEAN	SD	MEAN	SD
AGE	46.35	8.82	43.45	7.49
HEIGHT	158.49	9.02	154.18	8.05
WEIGHT	85.67	7.78	83.09	9.62
BMI	27.01	1.59	26.94	2.68
WC	98.18	6.73	97.64	8.65
SBP	140.65	15.72	137.64	16.02
DBP	87.18	10.5	87.45	9.13
FBS	138.04	25.36	126.09	10.32
TC	193.27	34.54	197.36	26.82
HDL	43.55	6.24	47.27	5.97
TGL	171.76	54.65	161.55	42.76
FT4	1.13	0.24	0.82	0.24
TSH	1.75	0.79	21.6	44.25

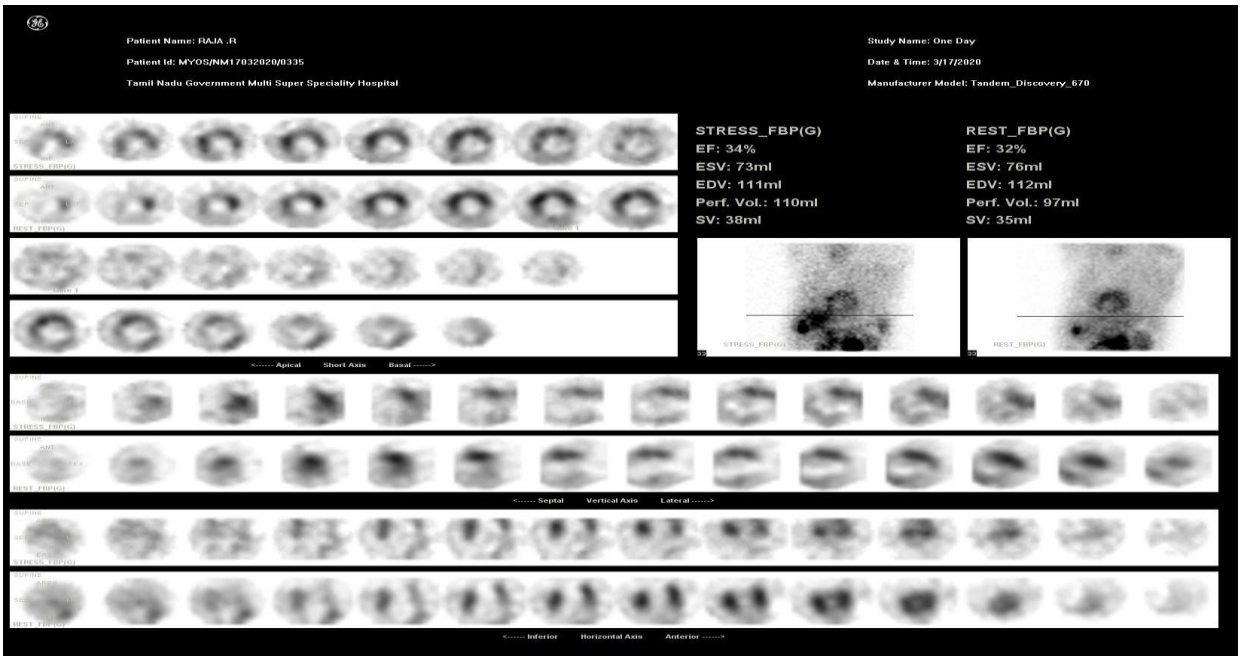
Table: 7 as there was a small no of patients with very high variants, statistically Significant results were not found in our study. (P valve > 0.05 not significant at 5% level)

Picture 1: Region Corresponding and Wall Invoveled in Metabolic Syndrome



Picture :1 Study demonstrates relatively decreased tracer concentration in the region corresponding to the anterior wall, septum, and the inferior wall indicating the involvement of LAD and RCA territories. The entire Left ventricle is grossly enlarged with reduced tracer concentration.

Picture 2: Systolic and Diastolic Dysfunction



Picture 2: Depicts significantly decreased tracer concentration in the Inferior and Lateral wall regions corresponding to the RCA and LCX territories. The entire ventricle is enlarged with evidence of systolic and diastolic dysfunction

Discussion

Metabolic syndrome is a cluster of metabolic abnormalities where in people are obese and have hypertension, high triglyceride levels, low high-density lipoprotein cholesterol, and abnormal fasting glucose levels. People with metabolic syndrome are at high risk of developing cardiovascular disease and type-2 diabetes.[7] Hypothyroidism is associated with lipid abnormalities like high triglycerides and low high-

density lipoproteins, weight gain, glucose intolerance, and hypertension. Thus hypothyroidism mimics the parameters of metabolic syndrome.[8] In this study, thyroid dysfunction prevalence is 18.33% among metabolic syndrome patients. Subclinical Hypothyroidism is 15% prevalent in metabolic syndrome patients and Overt Hypothyroidism is 3.3% prevalent. There is no incidence of either overt or subclinical Hyperthyroidism in our study population.[9] The prevalence of thyroid dysfunction and hypothyroidism in metabolic syndrome patients is higher than the prevalence in the normal population, which is 5.9% for thyroid dysfunction and 4.6% for hypothyroidism (0.3% overt and 4.3% subclinical hypothyroidism.[10] This study is consistent with the study done by Hak AE et al, as 16.4% of metabolic syndrome patients had hypothyroidism. In this study prevalence of subclinical hyperthyroidism is 1.7% and there is no overt or clinical hyperthyroidism. In this study, one- sixth of metabolic syndrome patients or every sixth patient with metabolic syndrome has Subclinical hypothyroidism. And one in every 30 patients has overt hypothyroidism. In these hypothyroidism patients, treatment with levothyroxine replacement reverses the symptoms and signs of hypothyroidism, thereby those factors which mimic metabolic syndrome. It is well known and proven that, by treating with levothyroxine replacement in all overt or clinical hypothyroid patients, we can reduce all the metabolic parameters and cardiovascular risk.[11] Controversy in treating sub-clinical hypothyroidism patients. Managements of patients subclinical hypothyroidism remain controversial because the body of scientific evidence available to guide clinical decisions is limited. The risk of progression from subclinical hypothyroidism to overt hypothyroid is 2-5% per year.[12] A meta-analysis report shows that levothyroxine therapy in individuals with subclinical hypothyroidism lowers mean serum total and low-density cholesterol concentration significantly and the reduction in serum cholesterol may be larger in individuals with higher pre-treatment cholesterol levels. Another double-blind placebo-controlled trial (Basal Thyroid Study) shows that an important risk reduction of cardiovascular mortality of 9 – 31% possible by the improvement in low-density lipoprotein cholesterol in subclinical hypothyroidism patients treated with levothyroxine therapy.[13] Lakka HM et al., et al., recommends treating subclinical hypothyroidism associated with type 2 diabetes and hypertension in his scientific review. As metabolic syndrome patients have hyperlipidemia, diabetes, hypertension,and increased cardiovascular risk, it looks logical to treat metabolic syndrome patients having subclinical hypothyroidism by levothyroxine replacement therapy. While there appear to be no adverse effects of initiating levothyroxine treatment in this setting, inadvertent overtreatment occurs in 14-21% of levothyroxine treated patients, carrying potential risks of osteoporosis and atrial fibrillation when serum TSH falls below 0.1 mU/L.(52) These patients need frequent thyroid function tests to avoid this complication.[14] This study shows that the prevalence of thyroid dysfunction in metabolic syndrome patients is higher than in normal subjects. One-sixth of metabolic syndrome patients or every sixth metabolic syndrome had hypothyroidism either overt or subclinical. This finding indicates a need for investigating the presence of Thyroid dysfunction during managing metabolic syndrome patients. As shown in previous evidence, managing these hypothyroid in metabolic syndrome patients is rewarding by improvement in the metabolic parameters and reducing cardiovascular risk.[15]

Conclusions

Thyroid dysfunction occurs in metabolic syndrome patients. Thyroid dysfunction occurs in 18.33% of metabolic syndrome patients. Prevalence of Subclinical hypothyroidism is15.0%in metabolic syndrome patients is higher than that of the general population. The prevalence of Overt Hypothyroidism is 3.33% in

metabolic syndrome patients which is higher than that of the general population. One-sixth of metabolic syndrome patients or every sixth metabolic syndrome had Subclinical Hypothyroidism. One in every thirty metabolic syndrome patients had Subclinical Hypothyroidism. Prevalence of thyroid dysfunction is much more common in Females with thyroid dysfunction than males. Exclude the presence of Thyroid dysfunction while managing metabolic syndrome patients. This study clearly shows that the prevalence of thyroid dysfunction in metabolic syndrome patients is higher than in normal subjects. One-sixth of metabolic syndrome patients or every sixth metabolic syndrome had Subclinical Hypothyroidism. One in every thirty metabolic syndrome patients had Subclinical Hypothyroidism This finding indicates a need for investigating the presence of Thyroid dysfunction during managing metabolic syndrome patients.

Source of Support- Nil
Conflict of Interest- None
Ethical Committee Clearance Was Approved By Institutional Ethical Committee

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