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Original Research Article

Thyroid Dysfunction in Patients with Metabolic Syndrome - A Cross Sectional ObservationalStudy from a Single Centre

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Abstract:

Aims and Objectives: The metabolic syndrome consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus. This study was to look for prevalence of thyroid dysfunction, which is known to increase the morbidity when it is associated with metabolic syndrome.

Materials and Methods: An Unaccented cross sectional study was done over 18 months and patients who were over 18 years of age and those who satisfied the criteria for Metabolic Syndrome (as per NTEP ATP III criteria) were included. Patient demographics, blood investigations to include thyroid profile, lipid profile and vital data were included. Data were statistically analysed and presented.

Results: In this study of 84 patients, thyroid dysfunction (Hypothyroidism/ Subclinical hypothyroid state) was prevalent in 17.9% (15/84) of metabolic syndrome patients which was statistically significant (P <0.001).

Conclusion: Sublinical and to a lesser extent overt hypothyroidism is seen in patients with metabolic syndrome and early recognition and appropriate treatment is indicated.

Keywords: Cardiovascular disease, diabetes mellitus, metabolic syndrome, subclinical hypothyroidism, overt hypothyroidism.

Introduction

The metabolic syndrome (syndrome X, insulin resistance syndrome) consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus [1]. Metabolic syndrome constitutes a cluster of risk factors characterized by hypertension, atherogenic dyslipidemia, hyperglycemia, and prothrombotic and proinflammatory conditions. The prevalence of the metabolic syndrome varies around the world and increases with age.

Metabolic syndrome and thyroid dysfunction are associated with higher risk of Atherosclerotic cardiovascular disease (ASCVD). Not much is known about the relationship between metabolic syndrome and thyroid dysfunction. Related studies that were performed were only a few.

Third National health and Nutrition Examination Surveys (NHANES III) revealed the age adjusted prevalence of metabolic syndrome to be 34% in men and 35% in women in the United States. [2] In a multi-ethnic study in Singapore, 28.8% of Indians, 24.2% of Malaysians, and 14.8% of Chinese had metabolic syndrome [3]. There is increasing evidence that thyroid dysfunction affects lipid and glucose metabolism, blood pressure, and body weight, which are associated with various metabolic parameters and may lead to the development or aggravation of components of metabolic syndrome [4]

Aims and Objectives

Primary objective was to study the prevalence of thyroid dysfunction in metabolic syndrome. Secondary objective would be to find the types of thyroid dysfunction in metabolic Syndrome.

Materials and Methods

This was an unicentre cross sectional study (18 months) done in the department of medicine at Dr. BRAMC, Bangalore. An Ethical and Research Committee clearance from Dr. B. R. Ambedkar Medical College, Kadugondanahalli, and Bangalore

before start of the study. All Patients (Both in patients and out patients) above 18years of age who satisfy the criteria of Metabolic Syndrome (as per NTEP ATP III criteria) were included. (NCEP ATP III Criteria. Clinical Identification of the Metabolic Syndrome Risk Factor Defining Level Abdominal obesity, given as waist circumference for Men 102 cm (40 in) Women 88 cm (35 in). Triglycerides 50 mg/dL: HDL cholesterol (Men 40 mg/dL/ Women 50 mg/dL): Blood pressure ->130/85 mm Hg and Fasting glucose >110 mg/dL). Patients with established thyroid disease, pregnant women and less than 18 year old were excluded.

A total of 84 patients with metabolic syndrome, who are admitted or visited OPD, were chosen for the study after satisfying the inclusion and exclusion criteria. Cases selected from the patients admitted or OPD basis satisfying criteria for Metabolic Syndrome, after taking consent, were analyzed clinically and biochemically. The laboratory evaluation in all patients included- Thyroid profile (TSH, freeT3, freeT4), Lipid profile, fasting and post prandial blood glucose and HbA1C. Additional investigations in some patients included Renal Function Test, Electrocardiogram, Ultrasound abdomen & pelvis, TPO antibodies and FNAC of thyroid.

Informed Consent

All the patients fulfilled selection criteria were explained about the details of the disease process, options of treatment, ultimate outcome, possible effects, complications and chances of recurrence in both procedure and a written informed consent was obtained before enrollment. They were informed of their right to withdraw from the study at any stage.

Ethical Clearance. Was obtained from college ethical committee after submitting the proposal before starting the study. (Ref No: EC No: 63. Dated 18/12/2020)

Statistical Analysis

The collected data was entered into Microsoft Excel Worksheet-2010 and data was taken into IBM SPSS Statistic for windows, version 24(IBM Corp., Armonk, N.Y., USA) software for calculation of frequency, percentage, mean, standard deviation and probability value.

Qualitative data was represented in the form of frequency and percentage. Association between qualitative variables was assessed by Chi Square test with continuity correction for 2 x 2 tables and Fisher's exact test for all 2 x 2 tables, where P value of chi square test was not valid due to small counts.

Quantitative data was represented using mean & Standard deviation. Analysis of quantitative data within the groups was done using paired t test if data passes 'Normality test'. One Way Analysis (ANOVA) was used to compare more than two groups. A 'P' value of <0.05 was considered statistically significant.

Results

Eighty-Four patients (Aged 21-85 years) who satisfied the criteria for metabolic syndrome were included and half of patients were in age group 41-60 years (Fig.1) with an equal sex distribution.

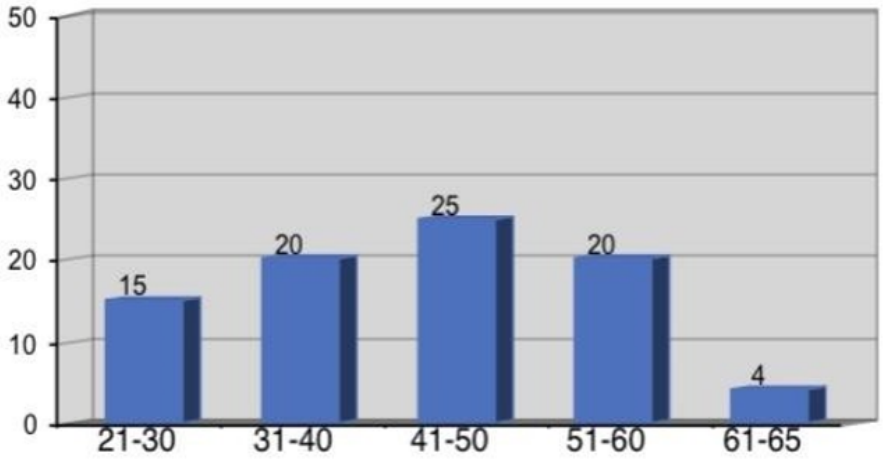


Figure 1: Age distribution of patients with metabolic syndrome in the current study

The prevalence of associated comorbidities in the study population were highest with Diabetes seen in 95% of study population and Low HDL (84.5%), Obesity (77.4%), Hyperlipidaemia (71.4%) and hypertension (70.2%) were also prevalent in decreasing order of frequency (Table-1).

Table 1: Prevalence of associated comorbidities as criteria for metabolic syndrome inpresent study

Criteria	No. of MetS subjects	%
Obese	65	77.4
Hypertension	59	70.2
Diabetes	80	95.2
Low HDL	71	84.5
Hypertriglyceridemia	60	71.4

Thyroid dysfunction (was Hypothyroidism/ Subclinical hypothyroid state) was prevalent in17.9% (15/84) of metabolic syndrome patients in our study. (Fig. 2).

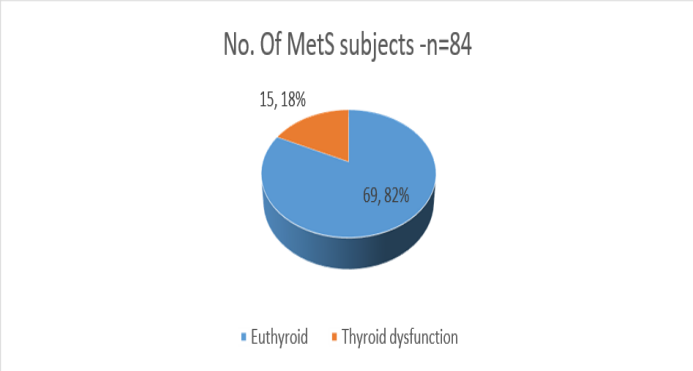


Figure 2: Overall prevalence of Thyroid dysfunction and Euthyroid in study subjects ofMetabolic Syndrome

There was statistically significant (P <0.001) with high TSH values in patients with thyroid dysfunction, with no significant difference in T4 levels (P 0.61) in the same group (Table 2). (Unpaired t- test: P <0.001 Significant**)**

Table 2: Comparison of Thyroid parameters between Euthyroid & Thyroid dysfunction

Parameter	Thyroid status	No. of cases	Mean	SD	t value	P value
S TSH (ulU/ml)	Euthyroid	69	2.49	1.26	12.71	< 0.001, HS
	Thyroid Dysfunction	15	10.53	4.61		
F T4 (pg/ml)	Euthyroid	69	1.98	8.07		NS
	Thyroid Dysfunction	15	0.89	0.42	0.52	0.61.

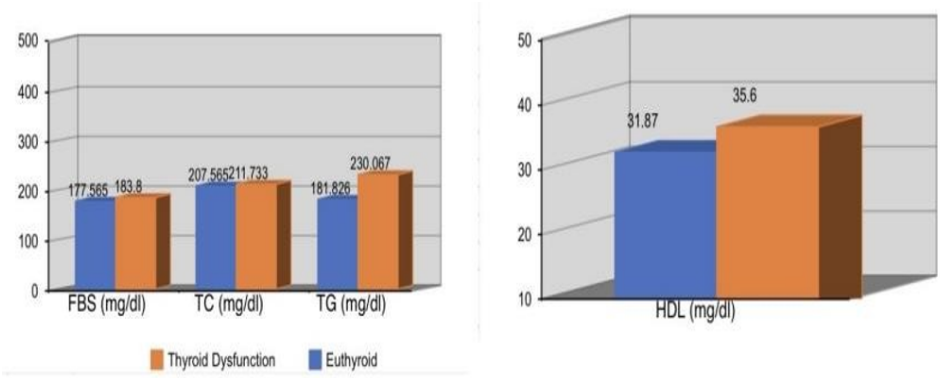
Subclinical hypothyroidism was seen twice as commonly in females (9/84- 20.9%) compared to males (4/84 (9.8%). Subclinical Hypothyroidism was noted in 15.5% of metabolic syndrome patients and commonly occurred in around 40-60 years of age. Overt Hypothyroidism, which was seen in 2.4% of study group were all under 40 years of age.

Table 3: Association of Thyroid dysfunction and metabolic syndrome parameters

MS		Total cases	Euthyroid		Thyroid	Dysfunction		Significance
	parameters		No.	%	No.	%	X2	P value
	Normal	19	18	94.7	1	5.3	2.66	
Obesity	Obese +	65	51	78.5	14	21.5		0.10, ns
Hypertension	Normal	25	19	76.0	6	24.0	0.92	0.34. ns
	HTN +	59	50	84.7	9	15.3		
Diabetes	Normal	4	3	75.0	1	25.0	0.15	0.70, ns
	Diabetes +	80	66	82.5	14	17.5		
	Normal	13	9	69.2	4	30.8		
HDL	Low HDL +	71	60	84.5	11	15.5	1.75	0.19, ns
Trigl.	Normal	24	22	91.7	2	8.3	2.08	0.15, ns
	Hyper Trigl +	60	47	78.3	13	21.7		

The prevalence of subclinical hyperthyroidism is 1.7% with no overt or clinical hyperthyroidism. There was no statistically significant difference in prevalence of associated comorbidities of metabolic syndrome (Diabetes,

hypertension, high triglycerides or obesity) in patients in study group who had overt or subclinical hypothyroidism. (Fig-3a/b)



3a 3b

Figure 3 a& b: Thyroid dysfunction with obesity (3a) and lipid profile (3b) in Euthyroid & Thyroid dysfunction

Discussion

The metabolic syndrome is a cluster of metabolic abnormalities wherein people are obese and have hypertension in addition to high triglyceride level, low high density lipoprotein cholesterol and abnormal fasting glucose levels. [5]

People with metabolic syndrome are at high risk for developing cardiovascular disease and type-2 diabetes. Hypothyroidism is associated with lipid abnormalities like high triglycerides and low high density lipoproteins, weight gain, glucose intolerance and hypertension [6]. Thus, hypothyroidism mimics the parameters of metabolic syndrome. In this study, thyroid dysfunction was prevalent in 17.9% of patients with metabolic syndrome. In various studies [7,8,9], the rate of subclinical hypothyroidism ranged from 14.6- 53% and the rate of overt hypothyroidism was between 3.5 -7.4%. In the current study Subclinical Hypothyroidism was evident in15.5% and Overt Hypothyroidism in 2.4%. In a multicenter cross-sectional study in India (432 patients) by Deshmukh V et al, [10] 28 % of subjects had thyroid dysfunction.

Our study is also consistent with study done by Uzunulu et al, [11] as 16.4% of metabolic syndrome patients had hypothyroidism in Japan and in a study by Khatiwada S et al, [12] (184 patients with metabolic syndrome) a higher rate of subclinical hypothyroidism was noted in 26.6 % of patients with overt hypothyroidism in 3.5 % and subclinical hyperthyroidism in 1.7 % patients.

In the current study the prevalence of subclinical hyperthyroidism is 1.7% and there is no overt or clinical hyperthyroidism. Levothyroxine replacement in all overt or clinical hypothyroid patients, can reduce all the metabolic parameters and cardiovascular risk associated with metabolic syndromes. [13] Managements of patients sub clinical hypothyroidism remain controversial as the scientific evidence available to guide clinical decision is limited. The risk of progression from subclinical hypothyroidism to overt hypothyroid is 2-5% per year. [14] And this progression is faster in Indian population (15). A meta-analysis report shows that levothyroxine therapy in individuals with sub clinical 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. [16]. another double-blind placebo-controlled trial (Basal Thyroid Study) shows that an important risk reduction of cardiovascular mortality of 9 – 31% possible by improvement in low density lipoprotein cholesterol in subclinical hypothyroidism patients treated with levothyroxine therapy.

There are various studies to recommend treating sub clinical hypothyroidism associated with type 2 diabetes and hypertension with improvement in lipid profile and subsequent decrease in atherosclerotic complications and cardiovascular events. [17,18]. As the metabolic syndrome patients have hyperlipidaemia, diabetes, hypertension and increased cardiovascular risk, its look logical to treat metabolic syndrome patients having sub clinical hypothyroidism by levothyroxine replacement therapy. While there appears to be no adverse effects of initiating levothyroxine treatment in this setting, inadvertent over treatment occurs in 14-21% of levothyroxine treated patients,[19,20] carrying potential risks of osteoporosis and atrial fibrillation when serum TSH falls below 0.1 mU/L.[21].

Subclinical hypothyroidism should be confirmed by repeat thyroid function testing after three to six months to exclude transient causes of elevation which include the effects of non-thyroidal illness and medication, and routine prescription of thyrox-

ine is not recommended. The current study shows that the prevalence of thyroid dysfunction in metabolic syndrome patients is higher than in normal subjects. This finding indicates a need for investigating the presence of thyroid dysfunction routinely during managing metabolic syndrome patients. As shown in previous evidences, managing these hypothyroid in metabolic syndrome patients leads to improvement in the metabolic parameters and reducing potential cardiovascular risks prevalent in patients with metabolic syndrome patients.

Conclusion

Thyroid dysfunction occurs at a higher rate in metabolic syndrome patients, with subclinical hypothyroidism being common and occurs twice as commonly in females compared to males. Overt Hypothyrodism also occurs at a higher frequency in these. Thyroid dysfunction adds to morbidity and hence needs to be evaluated and managed accordingly in patients presenting with metabolic syndromes.

References

1. Khatiwada S, Sah SK, Kc R, Baral N, Lamsal M. Thyroid dysfunction in metabolic syndrome patients and its relationship with components of metabolic syndrome. Clin Diabetes Endocrinol. 2016 Feb 1; 2:3
2. Lakka M et al., The metabolic syndrome and cardiovascular disease mortality. JAMA 2002; 228: 2709-16.
3. Chugh K, Goyal S, Shankar V, Chugh SN. Thyroid function tests in metabolic syndrome. Indian J Endocrinol Metab. 2012; 16(6):958–61
4. He J, Lai Y, Yang J, Yao Y, Li Y, Teng W, Shan Z. The Relationship between Thyroid Function and Metabolic Syndrome and Its Components: A Cross-Sectional Study in a Chinese Population. Front Endocrinol (Lausanne). 2021; 12:661160
5. Amihaesei IC, Chelaru L. Metabolic syndrome a widespread threatening condition; risk factors, diagnostic criteria, therapeutic options, prevention and controversies: an overview. Rev Med Chir Soc Med Nat Iasi. 2014; 118(4):896–900.
6. Mavromati M, Jornayvaz FR. Hypothyroidism-Associated Dyslipidemia: Potential Molecular Mechanisms Leading to NAFLD. Int J Mol Sci. 2021 Nov 26; 22(23):12797
7. Agarwal G., Sudhakar M., Singh M., Senthil N., and Rajendran A., The prevalence of thyroid dysfunction among South Indian women with metabolic syndrome, Journal of Clinical and Diagnostic Research. (2011) 5, 213–216,
8. Jayakumar R. V., Hypothyroidism and metabolic syndrome, Thyroid Research and Practice. (2013) 10, no. 4, 1–2.
9. Deshmukh V, Farishta F, Bhole M. Thyroid Dysfunction in Patients with Metabolic Syndrome: A Cross-Sectional, Epidemiological, Pan-India Study. Int J Endocrinol.; 2018:2930251
10. Uzunulu M et al., Prevalence of sub clinical hypothyroidism in patients with metabolic syndrome. Endocr J. 2007; 54: 171 – 76
11. Khatiwada S, Sah SK, Kc R, Baral N, Lamsal M. Thyroid dysfunction in metabolic syndrome patients and its relationship with components of metabolic syndrome. Clin Diabetes Endocrinol. 2016 Feb 1; 2:3.
12. Gluvic Z, Sudar E, Tica J, Jovanovic A, Zafirovic S, Tomasevic R, Isenovic ER. Effects of levothyroxine replacement therapy on parameters of metabolic syndrome and atherosclerosis in hypothyroid patients: a prospective pilot study. Int J Endocrinol. 2015; 2015:147070
13. Surks MI et al., Subclinical Thyroid Disease: Clinical applications. JAMA 2004; 291: 239-243
14. Singh SK, Singh R, Singh SK, Iquebal MA, JaiswalS, Rai PK. Risk of progression to overt hypothyroidism in Indian patients with subclinical hypothyroidism: a prospective observational study. Int J Adv Med 2022; 9:1183-7
15. Michalaki MA, Vagenakis AG, Leonardou AS, Argentou MN, Habeos IG, Makri MG, Psyrogiannis AI, Kalfarentzos FE, Kyriazopoulou VE. Thyroid function in humans with morbid obesity. Thyroid. 2006; 16(1):73-8.
16. Col NF, Surks MI, Daniels GH. Subclinical Thyroid Disease: Clinical Applications. JAMA. 2004; 291(2):239–243.17. Danese MD, Ladenson PW, Meinert CL Powe NR. Effect of Thyroxine Therapy on Serum Lipoproteins in Patients with Mild Thyroid Failure: A Quantitative Review of the Literature, the Journal of Clinical Endocrinology & Metabolism. 2000. 85(9); 2993–3001
17. Caraccio N, Ferrannini E, Monzani F. Lipoprotein profile in subclinical hypothyroidism: response to levothyroxine replacement, a randomized placebo-controlled study. J Clin Endocrinol Metab. 2002; 87(4):1533-8
18. Ross DS et al., The use and limitation of thyrotropin assay as a single thyroid function test. J Clin Endocrinol Metab 1990; 71: 764-769.
19. Parle JV et al., Thyroxine prescription in the community. Br J Gen Pract 1993; 43: 107-109.50
20. Cappola AR, Fried LP, Arnold AM, Danese MD, Kuller LH, Burke GL, Tracy RP, Ladenson PW. Thyroid status, cardiovascular risk, and mortality in older adults. JAMA. 2006 Mar 1; 295(9):1033-41.