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Original Research Article

Study of thyroid dysfunction in metabolic syndrome in patients of Amalapuram, Andhra Pradesh, India

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ABSTRACT

Background: Both metabolic syndrome and thyroid dysfunction are associated with increased risk of atherosclerotic heart disease. The present study was conducted to study the Association of thyroid dysfunction and Metabolic syndrome and to find out the type of thyroid dysfunction in metabolic syndrome patients.
Methods: Sixty cases were defined according to the IDF Criteria. Detailed history and necessary investigations like fasting blood sample was analyzed for total triiodothyronine (T3), total thyroxine (T4), thyroid-stimulating hormone (TSH), lipid profile, and blood glucose were undertaken.
Results: In this study population of metabolic syndrome cases, the thyroid dysfunction is present in 16.7% patients. Among the thyroid dysfunction, sub clinical hypothyroidism is highly prevalent - 11.7%, The hypothyroidism is 3.3% prevalent in metabolic syndrome patients (one patient had TSH levels of more than 150 mU/L) and sub clinical hyperthyroidism is 1.7% prevalent. There were no overt hyperthyroidism patients in the study.
Conclusions: This study clearly shows that, 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

Keywords: Correlation, Hyperlipidemia, Metabolic syndrome, Subclinical hypothyroidism, Thyroid dysfunction

INTRODUCTION

The "deadly quartet" -- also known as "metabolic syndrome" and "syndrome X" -- is the cluster of metabolic abnormalities where in people are obese, and have hypertension, high triglyceride levels, low high density lipoproteins and abnormal fasting glucose levels.[1,2]

People with metabolic syndrome are at high risk for developing cardiovascular disease and are twice likely to die from and three times as likely to have myocardial infarction, stroke compared with people without this syndrome.[3]Insulin resistance is supposed to be the central pathophysiological phenomenon underlying the clustering.[4] Thyroid disease is associated with atherosclerotic cardiovascular disease.[5,6] This association may be in part be explained by thyroid hormones regulation of lipid metabolism and its effects 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 metabolic process and may be associated with metabolic syndrome.

Both metabolic syndrome and thyroid dysfunction are associated with increased risk of atherosclerotic heart

disease. Little is known about the relationship between metabolic syndrome and thyroid dysfunction. Only a few small studies have been performed.[7,8]

In a cross sectional study in 220 metabolic syndrome patients, it was found that subclinical hypothyroidism was prevalent in 16.4 % of metabolic syndrome patients.[7] In a study from Nepal, Chandra L et al, found that metabolic syndrome was prevalent in 21.1% of thyroid dysfunction patients.[8] The study done by Lin St et al, found that lower free thyroxin level are associated with metabolic syndrome in Chinese population.[9] There is no information available in literature regarding this association in this part of country. Therefore, the association of thyroid dysfunction with metabolic syndrome was evaluated in this study.

METHODS

Source of data were gained from the patients who were diagnosed as metabolic syndrome and fulfill inclusion and exclusion criteria, getting admitted to Department of General medicine KIMS and RF hospital who fulfil the inclusion and exclusion criteria during the period of August 2017 to August 2019.

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 - defined as waist circumference with ethnicity specific values (for south Asians: ≥90 cm for Men and ≥80cm for women were used), and any two of the following:

- Raised triglycerides: >150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality.
- Reduced HDL cholesterol: <40 mg/dL in males, <50 mg/dl in females, or specific treatment for this lipid abnormality.
- Raised blood pressure: systolic BP >130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension.
- Raised fasting plasma glucose: (FPG)>100 mg/dl, or previously diagnosed type 2 diabetes mellitus.

Inclusion criteria

- Patients of Age more than 18 years, who fulfilled the criteria for metabolic syndrome by International diabetic foundation (IDF) were taken into study.
- Patients with metabolic syndrome not on any medications - newly detected metabolic syndrome patients.

Exclusion criteria

- Known hypothyroid or sub-clinical hypothyroid or hyperthyroidism patients.
- Patients taking medications for diabetes mellitus, hypertension, thyroid disorders, dyslipidemia.
- Taking steroids.
- Individual less than 18 years age

Detailed history of medication, and anthropometric measurements like height, weight, waist circumference were noted in a semi-structured proforma. Blood pressure was recorded in right upper limb in sitting posture. After eight hours of fasting, blood drawn for fasting blood sugar, lipid profile and thyroid assay in a single sitting.

The fasting blood sugar was done by enzymatic calorimetric method using semi auto analyzer. The high density lipoprotein cholesterol and triglycerides were done enzymatically on XL-300 ERBA fully automated clinical chemistry analyzer. The thyroid hormone assay (TSH, T3 and T4) were done by Chemiluminescence Immuno Assay (CLIA) using ADVIA Centaur equipment.

RESULTS

Thyroid function test results

The TSH in this study was ranging from 0.17 mU/L to 150 mU/L and T4 levels ranging from 6.2 microg/dl to 7.3 microg/dl. Patients were grouped into four groups according to the definitions based on TSH and T4 levels and further statistical analysis was done based on these groups. According to definitions, 50 patients found to be euthyroid and two patients were hypothyroid. Seven patients had sub clinical hypothyroidism and one patient had sub clinical hyperthyroidism. There were no overt hyperthyroid patients in this study (Table 1).

Table 1: Thyroid dysfunction.

Group	No.	%	Male	Female
Euthyroid	50	83.33%	26	24
Hypothyroid	2	3.33%	1	1
Subclinical hypothyroidism	7	11.67%	0	7
Subclinical hyperthyroidism	1	1.67%	0	1
Hyperthyroidism	0	0	0	0

The thyroid dysfunction is 16.7% prevalent in metabolic syndrome patients. Among the thyroid dysfunction, sub clinical hypothyroidism is highly prevalent - 11.7%. The hypothyroidism is 3.3% prevalent in metabolic syndrome patients (one patient had TSH levels of more than 150mU/L) and sub clinical hyperthyroidism is 1.7% prevalent. There were no overt hyperthyroidism patients in this study (Table 1).

As there were a considerable number of patients only in euthyroid group (50) and sub-clinical hypothyroid group both groups were analyzed statistically using student t-test. But these analyses were not statistically significant, as they were very small no of individuals in both

subgroups and variants are very high in both subgroups. Correlation between the T4, TSH and metabolic parameters were also analyzed.

Table 2: Metabolic syndrome parameters wise thyroid dysfunction.

MS criteria fulfilled	Total no	Euthyroid	Hypothyroid	Subclinical hypothyroid	Subclinical hyperthyroid
3	19	16	1	2	0
4	19	17	0	1	1
5	22	17	1	4	0

(p value = 0.36 not significant).

Table 3: Distribution of thyroid dysfunction.

MS parameters	Euthyroid		Sub clinical hypothyroidism		p value
	Mean	SD	Mean	SD	
WC	97.16	6.98	98.57	8.32	0.626
SBP	139.88	14.14	140.29	14.40	0.944
DBP	89.52	7.28	88.29	9.20	0.689
FBS	158.28	51.04	141.43	37.82	0.405
HDL	43.46	6.25	43.43	4.58	0.990
TGL	234.20	170.18	185.57	93.75	0.434

(p value >0.05 not significant at 5% level).

As per Table 3 mean SBP was 139.99±14.14 mm of hg in euthyroid group and 140.29±14.40 mm of hg in subclinical hypothyroidism group. The mean DBP was 89.52±7.28mm of hg in euthyroid group and 88.29±9.20 mm of hg in subclinical hypothyroidism group. The mean FBS was 158.28 mg/dl in euthyroid group and 141.43 mg/dl in subclinical hypothyroidism group. The mean HDL was 43.46mg/dl in euthyroid group and 43.43 mg/dl in subclinical hypothyroidism group.

Table 4: Correlation between T4, TSH and metabolic syndrome parameters in euthyroid patients.

MS parameter	T4	p value	TSH	p value
WC	0.243	0.08	-0.029	0.839
SBP	0.078	0.59	0.076	0.60
DBP	0.125	0.38	-0.416	0.77
FBS	0.175	0.22	-0.095	0.59
HDL	0.067	0.64	-0.108	0.45
TGL	0.056	0.69	-0.066	0.30

(p value >0.05 not significant at 5% level).

As per Table 4 the correlation value of T4 and SBP was 0.078 and p value was 0.59.The correlation value between DBP and T4 was 0.125 with p value 0.38 and with TSH it was -0.416 the p value was 0.77.The correlation value between FBS and T4 was 0.175 and with TSH it was -0.095. The correlation value between HDL and T4 was 0.067and with TSH it was -0.108. The correlation value between TGL and T4 was 0.056 and with TSH it was -0.066.

Correlation coefficient values between T4, TSH and metabolic parameters are not significant in this study, because of limited number of study subjects and variants are high.

Table 5: Correlation between T4, TSH and metabolic syndrome parameters in subclinical hypothyroid patients.

MS parameter	T4	p value	TSH	p value
WC	6.5	0.11	-0.577	0.17
SBP	5.14	0.23	-0.511	0.24
DBP	-4.9	0.91	0.060	0.89
FBS	7.41	0.05	-0.576	0.17
HDL	4.6	0.29	-0.249	0.58
TGL	-4.04	0.82	-0.134	0.77

(p value >0.05 not significant at 5% level)

As per Table 5 the correlation value of T 4 and SBP was 5.14 and p value was 0.23. The correlation value between DBP and T4 was -4.9 with p value 0.91and with TSH it was 0.060 the p value was 0.89. The correlation value between FBS and T4 was 7.41 and with TSH it was-0.576. The correlation value between HDL and T4 was 4.6 and with TSH it was -0.249. The correlation value between TGL and T4 was -4.04 and with TSH it was -0.134.

DISCUSSION

The metabolic syndrome is a cluster of metabolic abnormalities wherein people are obese and have hypertension, high triglyceride level, low high density lipoprotein cholesterol and abnormal fasting glucose levels.4 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. Thus, hypothyroidism mimics the parameters of metabolic syndrome. This study was conducted in 60 cases of metabolic syndrome, who had been admitted to Department of General medicine KIMS and RF hospital who fulfil the inclusion and exclusion criteria during the period of August 2017 to August 2019.

Table 6: Comparison of association of thyroid dysfunction in metabolic syndrome with other studies.

Studies	Percentage of thyroid dysfunction
Uzunula et al[7]	16.4 %
Chandra L et al[8]	21.1 %
P Gyawali[10]	31.25 %
Present study	16.7 %

Table 7: Comparison of type of thyroid dysfunction with other studies.

Studies	Euthyroid	Subclinical hypothyroid	Hypothyroid	Subclinical hyperthyroid
Ghanshyam PS Shantha et al[11]	70 %	21.9 %	7.4 %	0 %
P Gyawali[10]	68.75 %	28. 9 %	1.55 %	0.8 %
Present study	83.33 %	11.67 %	3.33 %	1.7 %

In this study, thyroid dysfunction is 16.7% among metabolic syndrome patients. Hypothyroidism is 15% prevalent in metabolic syndrome patients (Overt Hypothyroidism 3.3% and sub clinical hypothyroidism 11.7%). The Association of thyroid dysfunction and hypothyroidism in metabolic syndrome patients are higher than in the normal population, which is 5.9% for thyroid dysfunction and 4.6% for hypothyroidism (0.3% overt and 4.3% sub clinical hypothyroidism).This study is consistent with study done by Uzunulu et al, as 16.4% of metabolic syndrome patients had hypothyroidism in Japan (Table 6).[10]

In this study, sub clinical hypothyroidism is highly prevalent - 11.7%. The reason may be we are getting TFT done in all metabolic syndrome patients now. The hypothyroidism is 3.3% prevalent in metabolic syndrome patients (one patient had TSH levels of more than 150 mU/L) and sub clinical hyperthyroidism is 1.7% prevalent. There were no overt hyperthyroidism patients in our study.

In this study one sixth of metabolic syndrome patients or every sixth patient with metabolic syndrome has hypothyroidism. 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. There is some controversy in treating sub clinical hypothyroidism patients.

Managements of patients sub clinical hypothyroidism remain controversial because the body of scientific evidence available to guide clinical decision is limited. The risk of progression from subclinical hypothyroidism to overt hypothyroid is 2-5% per year. 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 pretreatment cholesterol levels.[12]

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 sub clinical hypothyroidism patients treated with levothyroxine therapy Surks et al, recommends treating sub clinical hypothyroidism associated with type 2 diabetes and hypertension in his scientific review.[13] As the metabolic syndrome patients have hyperlipidemia, 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 overtreatment occurs in 14-21% of levothyroxine treated patient carrying potential risks of osteoporosis and atrial fibrillation when serum TSH falls below 0.1 mU/L. These patients need frequent thyroid function tests to avoid this complication. 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 evidences, managing these hypothyroid in

metabolic syndrome patients are rewarding by improvement in the metabolic parameters and reducing cardiovascular risk.[14]

CONCLUSION

Thyroid dysfunction is common in metabolic syndrome patients and it occurred in 16.7% of metabolic syndrome patients in our study. Sub clinical hypothyroidism is present in 11.7% and over hypothyroidism is 3.3% in metabolic syndrome patients in our study. One sixth of metabolic syndrome patients or every sixth metabolic syndrome had hypothyroidism either overt or subclinical. It is better to exclude the presence of Thyroid dysfunction while managing metabolic syndrome patients, for better outcome.

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