International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Study of Thyroid Dysfunction in Patient with Metabolic Syndrome in a Tertiary Care Centre of Kumaon Region

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Abstract: ***Background: Metabolic syndrome (MetS) is a clustering of multiple risk factors for atherosclerotic cardiovascular disease such as central obesity, impaired fasting glucose or type 2 diabetes mellitus, elevated triglyceride, reduced high - density lipoprotein cholesterol and hypertension. MetS is closely associated with thyroid dysfunction (TD) due to the impact of thyroid hormones on lipid metabolism, glucose, blood pressure, and cardiovascular dysfunction. This study was done to assess the underlying thyroid dysfunction among MetS patients and also to assess the clinical profile and demography of these patients. Methods: This was an observational study of 100 metabolic syndrome patients with thyroid dysfunction. Anthropometric measurements and vital signs were noted. Blood samples were tested for hemogram, correlogram, lipid profile, and thyroid function, and fasting plasma glucose. we aim to assess the underlying thyroid dysfunction among these patients. Results were analyzed by using percentages and proportions whenever possible. Results: A total of 100 patients with metabolic syndrome were taken among which 25 were males and 75 were females, most common age group affected was 40 - 49 years and 60 - 69years. Thyroid dysfunction was present in 27.0% of patients. Hypothyroidism was present in 23% of patients (Overt Hypothyroidism was 7% and sub - clinical hypothyroidism was 16.0%). In patients with metabolic syndrome diabetes was present in 78% of patients, systemic hypertension in 75%, and hypertriglyceridemia in 60% of patients. Conclusion: Hypothyroidism was the most common thyroid dysfunction in patients with metabolic syndrome. A large proportion of thyroid dysfunction cases diagnosed during the study highlight the need for vigilant thyroid screening in patients with metabolic syndrome.***

Keywords: Atherosclerotic cardiovascular disease, Metabolic syndrome, Subclinical hypothyroidism, Thyroid dysfunction

1. Introduction

Metabolic syndrome is a clustering of multiple risk factors for atherosclerotic cardiovascular disease (ASCVD) such as central obesity, impaired fasting glucose (IFG) or type 2 diabetes mellitus (T2DM), elevated triglyceride (TG), reduced high - density lipoprotein cholesterol (HDL - C) and hypertension (HTN). [1, 2] It is estimated that one out of four people around the world suffer from Metabolic syndrome. [2]

Metabolic syndrome is characterized by inflammation [3] and it increases the risk of cardiovascular morbidity and mortality. The cluster includes various combinations of elevated blood pressure (BP), atherogenic dyslipidemia, obesity, abnormal glucose tolerance, and insulin resistance (IR) as well as such other abnormalities as pro - inflammatory and prothrombotic states. [3]The presence of Metabolic syndrome is associated with an approximate doubling of the risk of cardiovascular disease (CVD) and mortality. Similarly, in those without diabetes, the risk of developing type 2 diabetes mellitus (T2DM) is increased 5 to 20 - fold in the presence of Metabolic syndrome. [4]

According to the new IDF definition, [4] for a person to be defined as having the metabolic syndrome they must have: Central obesity (defined as waist circumference ≥ 94cm for Europid men and ≥ 80cm for Europid women, with ethnicity - specific values for other groups i. e ≥90cm for South Asian men and ≥80cm for South Asian women.) plus any two of the following four factors: • Raised TG level: > 150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality • Reduced HDL cholesterol: < 40 mg/dL (1.0 mmol/L) in males and < 50 mg/dL (1.3 mmol/L) 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 (5.6 mmol/L), or previously diagnosed type 2 diabetes If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define the presence of the syndrome. Thyroid diseases are among the most prevalent endocrine disorders worldwide. Based on the estimation from various studies, it has been projected that about 42 million people in India suffer from thyroid diseases. [5] MetS is closely associated with thyroid dysfunction (TD) due to the impact of thyroid hormones on lipid metabolism, glucose, blood pressure, and cardiovascular dysfunction. [6] Functional changes in the thyroid gland might have an association with MetS and its related components including obesity, insulin resistance (IR), lipid and glucose metabolism abnormalities, raised blood pressure, and cardiovascular dysfunction. MetS and TD are both characterized by a cluster of common abnormalities such as abdominal obesity, hyperglycemia, hypertension, reduced high - density lipoprotein cholesterol (HDL - C), and elevated triglycerides (TG). Moreover, IR, identified as a basic mechanism for MetS, also plays a role in hypothyroidism. [7]

Aim

To study thyroid dysfunction in patients with metabolic syndrome in a tertiary care center of Kumaun region of Uttarakhand.

Objectives

1) To study the pattern of thyroid dysfunction in patients presenting with metabolic syndrome and vice - versa.
2) To analyze the association of thyroid dysfunction with components of metabolic syndrome.

2. Materials and Method

It was a cross - sectional observational hospital - based study inpatients presenting to the OPD/IPD of the General medicine department, Haldwani from 2020 to 2022. All the patients enrolled in the study were evaluated for thyroid dysfunction including overt hypothyroidism, subclinical hypothyroidism, and hyperthyroidism. Patients were also evaluated for hypertriglyceridemia.

Inclusion criteria

1) Patients with CENTRAL OBESITY, waist circumference ≥90cm for Men and ≥80cm for women.
2) Plus any two of the following:
   - Raised triglycerides ≥150mg/dl, or specific treatment for this lipid abnormality.
   - Reduced HDL cholesterol<40 mg/dl in males, <50mg/dl in females, or specific treatment for this lipid abnormality.
   - Raised blood pressure: Systolic BP ≥130 mm Hg or Diastolic BP ≥85 mm Hg or treatment of previously diagnosed hypertension.
   - Raised fasting plasma glucose (FPG) ≥100mg/dl, or previously diagnosed type 2 diabetes

Exclusion criteria

1) Known Hypothyroid patients or Sub - clinical hypothyroid patients or Hyperthyroid patients or On treatment for hypo/hyperthyroidism.
2) Individuals less than 16 years of age.
3) Patients with Liver disorders, Renal disorders, Congestive cardiac failure, Pregnant women.

3. Results

A total of 100 patients with metabolic syndrome satisfying the inclusion criteria were enrolled in the study. The prevalence of Euthyroid was 73%, Hypothyroidism was 7%, subclinical hypothyroidism was 16% and subclinical hyperthyroidism was 16%.

Table 1: Prevalence of Thyroid Dysfunction

Thyroid Function	Number	Percentage
Euthyroid	73	73.0%
Hypothyroidism	7	7.0%
Sub - clinical hypothyroidism	16	16.0%
Sub - clinical hyperthyroidism	4	4.0%

Table 2: Relation of Thyroid Dysfunction with Metabolic abnormalities

Metabolic abnormalities	Euthyroid	Sub - clinical hypothyroidism	Sub - clinical hyperthyroidism	Hypothyroidism	p - value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Waist circumference	96.63±6.98	110.44±6.74	120.00±9.52	82.75±6.60	< 0.05*
Systolic blood pressure	118.88±4.85	111.56±5.11	110.57±10.91	143.00±5.94	< 0.05*
Diastolic blood pressure	80.68±3.04	71.75±3.44	70.86±7.01	104.25±2.50	< 0.05*
Fasting blood sugar	107.42±21.63	84.06±17.64	75.71±7.83	171.75±52.32	< 0.05*

(p - valve < 0.05 significant at 5% level)

Among Euthyroid patients mean waist circumference was 96.63±6.98, the mean systolic blood pressure was 118.88±4.85, the mean diastolic blood pressure was 80.68±3.04 and the mean fasting blood sugar was 107.42±21.63 respectively. Among sub - clinical hypothyroidism patients mean waist circumference was 110.44±6.74, mean systolic blood pressure was 111.56±5.11, mean diastolic blood pressure was 71.75±3.44 and mean fasting blood sugar was 84.06±17.64. Among hypothyroidism patients, the mean waist circumference was 82.75±6.60, the mean systolic blood pressure was 143.00±5.94, the mean diastolic blood pressure was 104.25±2.50 and the mean fasting blood sugar was 171.75±52.32 respectively. Waist circumference, SBP, DBP, and fasting blood sugar were significantly higher among subjects with Sub - clinical hypothyroidism and Hypothyroidism.

Table 3: Relation of Thyroid status with the number of patients meeting Metabolic syndrome criteria

Thyroid status	No of patients meet Metabolic syndrome criteria			Total
	3	4	5	
Euthyroid	49	24	0	73
	67.1%	32.9%	.0%	100.0%
Sub - clinical hypothyroidism	6	2	8	16
	37.5%	12.5%	50.0%	100.0%
Hypothyroidism	1	1	5	7
	14.3%	14.3%	71.4%	100.0%
Sub - clinical hyperthyroidism	0	1	2	4

	.0%	25.0%	75.0%	100.0%
Total	56	28	16	100
	56.0%	28.0%	16.0%	100.0%
Chi - square value = 52.160, p - value < 0.001*				

The number of patients meeting metabolic syndrome criteria was compared among subjects with different thyroid status using the chi - square test. Subjects with Hypothyroidism and Sub - clinical hyperthyroidism had more number of patients meeting metabolic syndrome criteria (71.4% and 75.0% respectively).

4. Discussion

In this study, thyroid dysfunction was 27.0% among metabolic syndrome patients. Among thyroid dysfunction, sub - clinical hypothyroidism was highly prevalent (16%). Hypothyroidismwas 7.0% prevalentand sub - clinical hyperthyroidism was 4.0% prevalent. There were no overt hyperthyroidism patients in our study. The Association of thyroid dysfunction and hypothyroidism in metabolic syndrome patients is higher than in the normal population, which is 5.9% for thyroid dysfunction and 4.6% for hypothyroidism (0.3% for overt and 4.3% for sub - clinical hypothyroidism). [8] This study is consistent with a study done by *Uzunulu et al*, as 16.4% of metabolic syndrome patients had hypothyroidism in Japan. [9]

Age - wise distribution
In the present study, the age incidence was more between the age group 40 - 49 years which was comparable to the *Shantha et al*. [10] In a cross - sectional study, which was a population - based Nord Trøndelag Health Study, the risk of mortality due to coronary heart disease was significantly higher in people with an average age of about 60.1 years. [11]

In the current study, hypothyroidism was more among the 40 - 49 and 60 - 69 years age groups, Sub - clinical hyperthyroidism was more among the 40 - 49 years group and Sub - clinical hypothyroidism was more among 40 - 49 years, 50 - 59 years, and 60 - 69 years.

A considerable number of persons with subclinical hypothyroidism eventually develop overt hypothyroidism at a yearly rate of 4.3 - 8%, with a larger predisposition in the aged population. [12] On a similar note, the Wickham survey revealed 10% of women aged 55-64 years had higher TSH levels. [13] This proposes that our study population might reasonably represent the general population. However, increasing the sample size might show any potential relationship between other factors under study with subclinical hypothyroidism.

Gender - wise
In the present study, females (75.0%) predominated males (25.0%) which was comparable to the Shantha et al. [10] In our study, out of 25 males 21 (84%) patients were euthyroid, 2 (8%) patients were hypothyroid and 2 (8%) patients were subclinical hypothyroid. Out of 75 females, 52 (69.3%) were euthyroid, 5 (6.7%) were hypothyroid, 4 (5.3%) were sub clinical hyperthyroid and 14 (18.7%) were having subclinical hypothyroid. Sub - clinical hypothyroidism and hypothyroidism was significantly more among women.

Women in all age groups had higher occurrence of the thyroid disorder. Our study was in similarity to the findings by *Deshmukh et al*, [14] both men and women in the higher age group (>45 years of age) had a higher incidence of TD (men: 63% vs.37%; women: 59% vs.41%).

Prevalence of diabetes and hypertension
In our study Diabetes was present in 78 (78%) patients of metabolic syndrome and 12 (12%) patients were not satisfying the criteria for diabetes. The prevalence of thyroid disease in patients with diabetes is significantly higher than that in the general population. [15]

One double - blind placebo - controlled trial (Basal Thyroid Study) showed 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. [16, 17] Col et al. recommended treating sub - clinical hypothyroidism associated with type 2 diabetes and hypertension. [18] As metabolic syndrome patients have hyperlipidemia, diabetes, hypertension, and increased cardiovascular risk, it looks logical to treat metabolic syndrome patients having subclinical hypothyroidism with levothyroxine replacement therapy.

Patients with subclinical hypothyroidism are at an enhanced risk for atherosclerosis and myocardial manifestations and thus, the thyroxine replacement in these patients has a beneficial effect on the low - density lipoprotein cholesterol levels and the clinical symptoms of hypothyroidism. An improvement in low - density lipoprotein cholesterol levels in turn reduces cardiovascular mortality by 9 - 31%. [19, 20]

Correlation of metabolic syndrome parameters with thyroid dysfunction
Among euthyroid patients, the mean value of total cholesterol was 174.45±30.36, the mean value of HDL was 42.79±5.75, and the mean triglycerides value was 129.68±142.41 respectively. Among subclinical hypothyroid patients, the mean value of total cholesterol was 235.38±25.18, the mean value of HDL was 34.25±6.51, and the mean triglycerides value was 224.25±25.95 respectively.

Among Hypothyroid patients, the mean value of total cholesterol was 277.29±26.42, the mean value of HDL was 31.29±7.36, and mean triglycerides value was 271.57±63.76 respectively. In the current study, the total cholesterol and Triglycerides were significantly higher among subjects with Sub - clinical hypothyroidism and Hypothyroidism compared to Euthyroid. Whereas, the mean HDL was significantly lower among Sub - clinical hypothyroidism and Hypothyroidism. The correlation of Correlation coefficient values of T4 with HDL was statistically significantly negative and triglycerides and fasting blood sugar were positively significant among subjects with Sub - clinical hypothyroidism and Hypothyroidism.

In line with our study, *Kota et al*. found a significant association between subclinical hypothyroidism and MetS with the relationship between TSH levels and TC, TG, LDL, and HDL - C levels among Indian patients. [21] and *Deshmukh et al*, [14] MetS components observed in patients diagnosed with TD were high waist circumference, reduced HDL - C, raised HOMA - IR, systolic blood pressure, diastolic blood pressure, fasting glucose, and TG.

Thyroid hormones affect lipid metabolism and thus the components of metabolic syndrome, and there is positive relation between TSH and LDL cholesterol, whereas negative relation between TSH and HDL cholesterol. [22] Similar to our study, one of the studies showed that subclinical hypothyroidism was significantly associated with metabolic syndrome, and a linear association was observed between TSH levels and total cholesterol, triglycerides, LDL, and HDL cholesterol levels across the metabolic syndrome group. [23] However, in a study in Turkey, TSH was not related to any metabolic syndrome parameters. [24]

Relation of Thyroid Dysfunction with Metabolic abnormalities

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Relation of Thyroid status with the number of patients meeting Metabolic syndrome criteria

The number of patients meeting metabolic syndrome criteriawas compared among subjects with different thyroid statuses using the chi - square test. Subjects with Hypothyroidism and Sub - clinical hyperthyroidism had more number of patients meeting metabolic syndrome criteria (71.4% and 75.0% respectively).

5. Conclusion

Hypothyroidism was the most common thyroid dysfunction in patients with metabolic syndrome. A large proportion of thyroid dysfunction cases diagnosed during the study highlight the need for vigilant thyroid screening in patients with metabolic syndrome

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