

**Association of Thyroid Dysfunction with Metabolic Syndrome: A Real-world Study**

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**Objective:** Objective of this study was to determine the prevalence of thyroid dysfunction in metabolic syndrome and to find out the association of thyroid dysfunction and metabolic syndrome. **Material and methods:** In this retrospective observational real world study 110 consecutive patients with metabolic syndrome criteria were included. Detailed history including medications, and anthropometric measurements were collected in a semi-structured proforma. **Result:** In this study, prevalence of thyroid dysfunction in metabolic syndrome patients is 20%. Thyroid dysfunction is more common in female (58.18%) than male (41.82%) with metabolic syndrome. Among the thyroid dysfunction patients 3.6% and 16.4% had overt hypothyroidism and subclinical hypothyroidism respectively. No patients had either subclinical hyperthyroidism or overt hyperthyroidism. A significant negative correlation between T4 and waist circumference ( $r=-0.169$ ;  $p=0.05$ ) and a positive correlation between TSH and waist circumference ( $r=0.189$ ;  $p=0.042$ ) was found. **Conclusion:** Thyroid dysfunction is prevalent in metabolic syndrome and more common in female. Subclinical hypothyroidism is the most common thyroid dysfunction in metabolic syndrome patients. There is a significant negative correlation between T4 and waist circumference and a significant positive correlation between TSH and waist circumference.

**Keywords:** Hypothyroidism, Metabolic syndrome, Obesity, Cardiovascular disease.

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**Introduction**

The impact of metabolic syndrome on morbidity and quality of life has been emphasized by the findings of the national commission (USA) on diabetes and DCCT trial [1], which clearly mentioned its role in developing neuropathy, nephropathy, retinopathy, IHD, and large vessel obstruction through the complications that affect the small and large vessels [2]. Metabolic syndrome affected 25 - 35% of the adult population in India according to available studies [3].

When any patient has at least 3 of the five conditions is diagnosed as metabolic syndrome according to the National Cholesterol Education Programme Adult Treatment Panel-III guidelines [4]. The above stated five conditions are (1) Fasting glucose  $\geq 110$  mg/dL (or receiving drug therapy for hyperglycaemia) (2) Blood pressure  $\geq 130/85$  mm Hg (or receiving drug therapy for hypertension) (3) Triglycerides  $\geq 150$  mg/dL (or receiving drug therapy for hypertriglyceridemia) (4) HDL-Cholesterol  $< 40$  mg/dL in men or  $< 50$  mg/dL in women (or receiving drug therapy for reduced HDL-C) (5) Waist circumference  $\geq 90$  cm in men or  $\geq 80$  cm in women. Abnormal fasting blood glucose levels, high triglyceride levels, high blood pressure along with the presence of central obesity and insulin resistance is the characteristic of patients having metabolic syndrome [5]. In people who have metabolic syndrome, there is a high risk of developing cardiovascular and cerebrovascular disease [6]. Incidence of obesity and metabolic syndrome are in rise with the changing lifestyle and food habits [7].

Atherosclerotic cardiovascular disease was directly associated with thyroid disorders, because of its effect on blood pressure and its role in regulation of lipid metabolism. Metabolic process is generally

accelerated by thyroid hormone and thus, may be both are associated with each other along with increased risk of atherosclerotic heart disease [8]. Thyroid dysfunction, prominently subclinical hypothyroidism and metabolic syndrome both are independent risk factors for cardiovascular diseases (CVD) [9]. Patients who are at high risk of developing CVD need to be assessed the thyroid function as their association were demonstrated in many recent studies [10].

Slow metabolism as a result hypothyroidism leads to obesity and on the other hand obesity causes alterations in thyroid hormones [11]. Thus, it is still under investigation that whether the change in thyroid hormone level a cause or an effect of metabolic syndrome or obesity [12]. The objective of this study was to evaluate the association of thyroid dysfunction in the patients with metabolic syndrome.

**Material and Methods**

**Study design:** This is was a retrospective observational real world study conducted among 110 patients. Patients who were maintaining their medical history or whose clinical data were recorded at the treating center were analyzed in this study. A proforma which include past medical history, demographic details (weight, height, BMI, and waist circumference), biochemical test results (blood glucose, lipid profile, thyroid hormone i.e. TSH, T4 and T3 along with clinical data, were used for the data collection and further analysis.

**Inclusion and exclusion criteria**

Patients whose all clinical data were present and also fulfils criteria of metabolic syndrome as defined by NCEP, ATP-III was included. Any patient whose clinical data was not maintained properly or has not given his or her consent to participate in the study were excluded from the analysis. Any patient who had chronic illness or severe micro or macro vascular complication and pregnant and lactating women were also excluded from this study. Patients who are taking any medication that could alter the thyroid functions or the lipid levels also excluded from the study.

**Parameters**

When the FT4 levels were low ( $FT4 < 0.93$  ng/dl) and when the TSH levels were high ( $TSH > 10$   $\mu$ U/ml) patients were classified as overt

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hypothyroid. Patients were considered to be euthyroid with normal TSH (0.27-4.2 µIU/ml) and FT4 (0.93-1.7 ng/dl).

**Statistical Analysis**

SAS® version 9.2 (SAS Institute Inc., USA), a statistical software, were used to perform all statistical analysis. Categorical variables were presented as numbers and percentages. mean ± standard deviation were used to express the mean data value of continuous variables. P < 0.05 was considered as statistical significant.

**Result**

Based on the inclusion and exclusion criteria of metabolic syndrome a total of 110 patients were selected for this retrospective study. Of these 110 patients 46 were male and 64 were female. As demonstrated in table 1, 11.8% were <36 years of age group, whereas, 40% and 31.8% belongs to 36 to <46 years and 46 to <55 years age group respectively and 16.4% were above 55 years age group (Table 1).

**Table 1: Age distribution of study population**

Age Group	Total No (%)	Male/Female
<36 yrs.	13 (11.8%)	5/7
36 to <46 yrs.	44 (40%)	14/29
46 to <55 yrs.	35 (31.8%)	15/21
>55 yrs.	18 (16.4%)	12/7
Total	110 (100%)	46/64

It was observed that 80% patients were euthyroid, whereas, 3.6% and 16.4% had overt hypothyroid and subclinical hypothyroidism respectively (Table 2).

No patients had either subclinical hyperthyroidism or overt hyperthyroidism.

**Table 2: Thyroid status of the study population**

Group	No (%)	Male/ Female
Euthyroid	88 (80%)	41/47
Overt Hypothyroid	4 (3.6%)	1/3
Sub clinical hypothyroidism	18 (16.4%)	2/16

Of 88 euthyroid patients 41 were male and 47 were female, whereas in the hypothyroid group, only 1 was male and 3 were female and in subclinical hypothyroidism group, 2 were male and 16 were female. Table 3 demonstrated the association between thyroid status and metabolic syndrome criteria. Twenty two subjects had all the five criteria of metabolic syndrome among which 20 were euthyroid, one

had overt hypothyroidism and one had subclinical hypothyroidism. Fifty one subjects had fulfilled four criteria of metabolic syndrome among which 39 were euthyroid, 2 had overt hypothyroidism and 10 had subclinical hypothyroidism.

**Table 3: Distribution of subjects with thyroid dysfunction in relation to the fulfilment of criteria for metabolic syndrome**

Metabolic Syndrome Criteria Fulfilled	Number of Subjects	Euthyroid	Overt Hypothyroid	Subclinical hypothyroid
3	37	29	1	7
4	51	39	2	10
5	22	20	1	1

37 subjects had fulfilled three criteria of metabolic syndrome among which 29 were euthyroid, one had overt hypothyroidism and 7 had sub clinical hypothyroidism. Among all individual components of the metabolic syndrome waist circumference and fasting blood sugar are found to be significantly associated with T4 and/or TSH. There was a

significant negative correlation between T4 and waist circumference (r= -0.169; p=0.05) and a positive correlation between TSH and waist circumference (r= 0.189; p=0.042) and a significant positive correlation between fasting blood sugar and T4 (r= 0.163; p=0.05) (Table 4)

**Table 4: Correlation of components of metabolic syndrome with T4 and TSH**

Metabolic Syndrome Parameters	TSH		T4	
	r	p	r	p
Waist circumference	0.189	0.042	-0.169	0.05
Systolic blood pressure	-0.105	0.311	0.81	0.416
Diastolic blood pressure	0.081	0.426	-0.71	0.52
Fasting blood glucose	-0.78	0.379	0.163	0.05
Triglyceride	0.14	0.91	0.3	0.89
HDL Cholesterol	-0.04	0.895	0.136	0.144

**Discussion**

Metabolic syndrome is characterized by inflammation and also is a cluster of cardiometabolic risk factors [13]. Among the females with metabolic syndrome the prevalence of thyroid dysfunction was more in this study and also supported by many previous study [14-16]. As compared to general population, the prevalence of the thyroid disease in patients with diabetes is significantly higher [17]. This indicate there is a possible interplay between the insulin sensitivity and thyroid status [18]. In concordance with that in this study, among all individual components of the metabolic syndrome waist circumference and fasting blood sugar are found to be significantly associated with T4 and/or TSH. Bakker et al suggested that the

deleterious effect of hypothyroidism on the lipid profile is mainly because of its effect on insulin resistance [19]. Hyperlipidaemia, hypercoagulability, insulin resistance and low grade inflammation are established risk factors for sub-clinical hypothyroidism and overt hypothyroidism [20,21]. Association between subclinical hypothyroidism and insulin resistance remains unclear, despite several studies have proved the association between hypothyroidism and insulin resistance for overt hypothyroidism. Thyroid dysfunction occurs in 20% of metabolic syndrome patients and this finding was in agreement with previous studies showing an association between thyroid dysfunction and metabolic syndrome [22-25]. The prevalence of overt hypothyroidism (3.6%) and

subclinical hypothyroidism (16.4%) in metabolic syndrome patients is higher than that of the general population which also in line with the findings of Meher LK et al [22] and Shantha GP et al [23]. Raising obesity in the middle age group and consistent with the changing lifestyle patterns were probably the principle reason for maximum number of patients were from 36 to 55 years group.

There are few limitations of the study. Firstly, a cause and effect of relationship could not be determined as because this was a retrospective observational cross-sectional study. Secondly, this was studied with a small number of populations. Larger prospective cohort study is needed to determine the deleterious effect on cardiovascular disease and metabolic functions by thyroid dysfunction.

#### Conclusion

Thyroid dysfunction is common in metabolic syndrome and more common in female. Subclinical hypothyroidism is the most common thyroid dysfunction in metabolic syndrome patients. Among all individual components of the metabolic syndrome waist circumference and fasting blood sugar are found to be significantly associated with T4 and/or TSH.

#### References

- Nathan DM. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview. *Diabetes Care*. 2014;37(1):9-16
- Nathan DM, Bayless M, Cleary P, et al. Diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: advances and contributions. *Diabetes*. 2013;62(12):3976-3986
- Thiruvagounder M, Khan S, Sheriff DS. The prevalence of metabolic syndrome in the local population in India. *Biochemia Medica* 2010;20(2):249-52.
- Parikh RM, Mohan V. Changing definitions of metabolic syndrome. *India J Endocrinol Metab*. 2012;16(1):7-12.
- Alberti KG et al. Diagnosis, and definition - provisional report of WHO consultation. *Diabet Med*. 1998; 15:539-553.
- Alshehri AM. Metabolic syndrome and cardiovascular risk. *J Family Community Med*. 2010;17(2):73-78.
- Jeffrey J, VanWormer, Jackie L, Boucher, Abbey C, Sidebottom, Arthur Sillah, Thomas Knickelbine, Lifestyle changes and prevention of metabolic syndrome in the Heart of New Ulm Project, *Preventive Medicine Reports*, 2017;6: 242-245
- Balkau B et al. European Group for Study of Insulin Resistance (EGIR). *Diabet Med* 1999; 16:442-443.
- Boden G et al. Free fatty acids in obesity and type 2 diabetes – Insulin resistance. *Eur J Clin Invest* 2002; 32:14-23.
- Cappola AR et al., Hypothyroidism and atherosclerosis *J Clin Endocrinol Metab* 2003; 88:2438-2444.
- Kara O. Influence of subclinical hypothyroidism on metabolic parameters in obese children and adolescents. *Clin Exp Pediatr*. 2020;63(3):110-114
- Pacifico L, Anania C, Ferraro F, Andreoli GM, Chiesa C. Thyroid function in childhood obesity and metabolic comorbidity. *Clin Chim Acta*. 2012;413:396–405.
- Leclere J, Cousty C, Schlienger JL, Wemeau JL. Subclinical hypothyroidism and quality of life of women aged 50 or more with hypercholesterolemia: results of the HYOGA study. *Presse Med*. 2008; 37(11):1538-46.
- Singh BM, Goswami B and Mallika V. Association between insulin resistance and hypothyroidism in females attending a tertiary care hospital. *Indian Journal of Clinical Biochemistry*. 2010; 25(2):141-145.
- Bauer DC, Ettinger B, Browner WS. Thyroid functions and serum lipids in older women: a population-based study. *Am J Med*. 1998;104(6):546-51.
- Chubb SA, Davis WA, Inman Z, Davis TM. Prevalence and progression of subclinical hypothyroidism in women with type 2 diabetes: the Fremantle. *Diabetes Study. Clin Endocrinol*. 2005;62:480-486.
- Elisabeth HA, Huibert APP, Visser JT, Drexhage HA, Hofman A, Jacqueline CVW. Subclinical Hypothyroidism Is an Independent Risk Factor for Atherosclerosis and Myocardial Infarction in Elderly Women: The Rotterdam Study. *Annals of Internal Medicine*. 2000;132(4):270-278.
- Reaven GM. Role of insulin resistance in human disease. *Diabetes*. 1988; 37:1595-607.
- Bakker SJL, Maaten JCT, Popp-Snijders C, Slaets JPJ, Heine RJ, Gans ROB. The relationship between thyrotropin and low density lipoprotein cholesterol is modified by insulin sensitivity in healthy euthyroid subjects. *J Clin Endocrinol Metab*. 2001; 86:1206-11.
- Serter R, Demirbas B, Culha C, Cakal E. The effect of L-thyroxine replacement therapy on lipid based cardiovascular risk in sub clinical hypothyroidism. *Invest J Endocrinol*, 2004; 27:897-903.
- American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. *Endocr Pract*. 2002; 8:457-69.
- Meher LK, Raveendranathan SK, Kota SK, Sarangi J, Jali SN. Prevalence of hypothyroidism in patients of metabolic syndrome. *Thyroid Res Pract*. 2013;10:60-4.
- Shantha GP, Kumar AA, Jeyachandran V, Rajamanickam D, Rajkumar K, Salim S, et al. Association between primary hypothyroidism and metabolic syndrome and the role of C reactive protein: a cross-sectional study from South India. *Thyroid Res*. 2009;2:2.
- Wang JY, Wang CY, Pei D, Lai CC, Chen YL, Wu CZ, et al. Association between thyroid function and metabolic syndrome in elderly subjects. *J Am Geriatr Soc*. 2010;58:1613-4.
- Gyawali P, Takanche JS, Shrestha RK, Bhattarai P, Khanal K, Risal P, et al. Pattern of Thyroid Dysfunction in Patients with Metabolic Syndrome and Its Relationship with Components of Metabolic Syndrome, *Diabetes Metabolism J*. 2015;39:66-73.

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