Study of Thyroid Volume in Patients with Metabolic Syndrome

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Abstract:

Background: Insulin resistance (IR) is a primary component of metabolic syndrome (MetS), a collection of disorders related to metabolism. Recently, there has been discussion on the potential link between MetS and its constituent parts and changes in the morphology and function of the thyroid gland. Owing to the elevated morbidity rate associated with TNs and enlarged thyroid, research on the disease's risk factors is necessary.

Aim: To determine the effect of components of the metabolic syndrome as causes of increased thyroid volume.

Methods: This study was conducted at Internal Medicine Department, Faculty of Medicine, Zagazig University on 32 patients with metabolic syndrome who were divided into 20 patients with enlarged throid volume and 12 patients without enlarged thyroid volume. Thyroid profile and ultrasound were measured.

Results: The prevalence of enlarged thyroid volume among patients diagnosed with MetS was (62.5%). There was significant increase in TSH, anti TPO and anti-thyroglobulin in enlarged thyroid group than normal volume thyroid group

Conclusion: Our findings revealed a high prevalence of enlarged thyroid volume (62.5%) among patients diagnosed with MetS. Our findings suggest a potential link between MetS and enlarged thyroid with possible underlying mechanisms such as metabolic dysregulation.

Keywords: Thyroid Volume, Metabolic Syndrome, Thyroid Nodule.

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Introduction

Any kind of swelling of the thyroid gland is referred to as a "goitre." There may be a diffuse, nodular, or multinodular enlargement in people with normal thyroid function, hyperthyroidism, or hypothyroidism. A nodular goitre (NG) is a thyroid enlargement that can be diagnosed clinically. It is defined by the overabundance of development and structural or functional changes to one or more regions of normal thyroid tissue **[1, 2].**

One of the most prevalent clinical thyroid problems are thyroid nodules (TNs). According to a recent cross-sectional nationwide survey, up to 20.43% of people worldwide are estimated to have TNs **[3].**

The significant prevalence of occult nodules is demonstrated by the fact that only about 5% of even if nodules are palpable, up to 70% of patients have nodules that ultrasonography unintentionally finds. Furthermore, compared to their counterparts, Women are more likely to have TNs than men the elderly, those with iodine deficiency, and people who have been exposed to radiation **[4].**

Many cardiovascular risk factors are linked to the metabolic syndrome (MetS). IR is thought to be the primary pathogenic connection between these risk variables. Metabolic syndrome (MetS) is associated with a number of cardiovascular risk factors. IR is thought to be the primary pathogenic connection between these risk variables. The metabolic syndrome is associated with numerous cardiovascular risk factors (MetS). IR is thought to be the primary pathogenic connection between these risk variables **[5, 6].**

Although previously published studies reported variable alterations in thyroid function, elevated TSH levels in the subjects seems to be a constant observation. These studies' contradictory results could be attributed to their design, which included people with varying degrees of obesity and iodine intake **[7].** Additionally, a recent study discovered that individuals with IR were living for the first time in an iodine-sufficient environment also had higher thyroid volume and nodule prevalence **[8].**

Patients and Methods

This study was conducted at Internal Medicine Department, Faculty of Medicine, Zagazig University during the period from April 2023 to October 2023 on 32 patients with metabolic syndrome who were divided into 20 patients with enlarged thyroid volume and 12 patients without enlarged thyroid volume. All study participants provided informed written agreement, and the local ethical committee authorised the research.

Exclusions from the study included people with a history of thyroid disorders, people who had ever had thyroid therapy, including L-thyroxine or antithyroid gland medication, people who had had surgery or radiation therapy for the head and neck, people with certain chronic illnesses (hepatic or renal dysfunction, heart failure), pregnant or nursing women, people with significant mental or neurological disorders (schizophrenia, depression, or epilepsy), people who had ever had cancer, people who had ever been exposed to iodinated contrast material within the previous six months, and people who had ever taken amiodarone were not allowed to participate in the study.

A complete medical history, anthropometric measurements, a general clinical examination, laboratory investigations (CBC, liver and kidney function tests, FBS and PPBS, HbA1C, fasting insulin level), and an estimation of insulin resistance (IR) based on the homeostasis model assessment (HOMA) index for each patient were performed on all patients. Utilizing the formula (fasting plasma glucose (mmol/l) X fasting plasma insulin (IU/ml)) ÷ O22.5, this was computed. **[9].** Also, FT4, FT3, TSH, anti-thyroid peroxidase and antithyroglobulin were measured.

Thyroid Ultrasound Scan.

The ultrasound was done by utilizing a 10-MHz linear probe (Logiq 5 Pro, GE Medical Systems, WI, USA) by the same radiologist to perform thyroid ultrasonography on each patient. Every subject underwent examination while lying down with their heads cocked back. Both longitudinal and transverse planes yielded images. To determine the volume, measurements of the bilateral thyroid gland's length, width, and thickness were taken. The ellipsoid formula was utilised to quantify the volumes of thyroid glands and nodules. Zdepth (cm), X Width (cm), X Length (cm), Volume (ml) X π /6 **[10].** The location, dimensions, quantity, borders, and computation of TNs were recorded concurrently. A fine needle aspiration biopsy (FNAB) was administered to all individuals whose thyroid nodules measured more than one centimeter. A TNs was described as a radiologically identifiable, isolated lesion within the thyroid gland that was not part of the surrounding thyroid parenchyma **[4].**

Statistical Analysis:

IBM©, Armonk, NY, USA provided SPSS v28 for the statistical study. The mean and standard deviation (SD) of the quantitative parametric data were analyzed using the unpaired student t-test. Frequency and percentage (%) were used to describe the qualitative factors. The Fisher's exact test or the Chi-square test were used for analysis when suitable. The two-tailed P value of a result was deemed statistically significant if it was less than 0.05.

Results:

Table 11: Comparison of demographic and Clinical Characteristics of the Metabolic Variables and thyroid volume in patient group.

		Patient group (MetS (+)) (n=32)		P value
		Enlarged thyroid (n=20)	**Normal thyroid volume (n=12)**	
Age (years)	**Mean ± SD**	48.8 ± 11.11	47.5 ± 12.66	0.84
	Range	30 - 65	32 - 65	
Sex	**Male**	16 (55%)	6 (91.7%)	0.7
	Female	4 (45%)	6 (8.3%)	
Weight (Kg)	**Mean ± SD**	107.1 ± 2.8	100.83 ± 3.92	**0.001***
	Range	90 - 113	89 - 117	
Height (cm)	**Mean ± SD**	159.35 ± 6.6	159.42 ± 3.4	0.97
	Range	151 - 171	154 - 165	
BMI (Kg/m^2)	**Mean ± SD**	44.3 ± 3.5	40.9 ± 3.7	**0.014***
	Range	35.3 - 48.5	34.3 - 46.3	
Waist circumference (cm)	**Mean ± SD**	110.4 ± 7.04	103.1 ± 5.4	**0.004***
	Range	91 - 116	98 - 117	
HTN		9 (45%)	4 (33.3%)	0.51
DM		8 (40%)	4 (33.3%)	0.7
Dyslipidemia		20 (100%)	12 (100%)	-

BMI: body mass index, WC: waist circumference, DM: diabetes mellitus, HTN: hypertension, IR: insulin resistance, chi square test, Student t-test, *: statistically significant as P value <0.05

The anthropometric measurements, weight, BMI, and waist circumference were all noticeably greater. with enlarged thyroid volume than patient with normal thyroid volume while age, sex and height was insignificantly different among the patient group. While the associated comorbidities, there was no significant difference between patient group with enlarged thyroid volume than with normal thyroid volume Patient group**(Table 1).**

Table 2: Clinical Biochemistry Baseline Value Among patient group with enlarged thyroid volume and Normal thyroid volume.

		Patient group (MetS (+)) (n=32)		P value
		Enlarged thyroid (n=20)	**Normal thyroid volume (n=12)**	
FBG (mg/dL)	**Mean ± SD**	119.3 ± 19.7	116 ± 16.7	0.63
	Range	102 - 160	101 - 142	
PPBS (mg/dL)	**Mean ± SD**	204.3 ± 52.6	209.9 ± 46.6	0.76
	Range	147 - 310	150 - 310	
HbA1C (%)	**Mean ± SD**	6.8 ± 0.9	6.8 ± 1	1.0
	Range	5.9 - 8.5	6 - 8.9	
HOMA- IR	**Mean ± SD**	3.7 ± 0.8	2.8 ± 0.9	**0.006***
	Range	2.2 - 4.1	1.1 - 3.9	
Fasting insulin (mIU/L)	**Mean ± SD**	12.8 ± 3.1	10 ± 3.3	**0.02***
	Range	4.5 - 14.9	4.2 - 14.7	

HDL: high density lipoprotein, LDL: low density lipoprotein, FBG: fasting blood glucose, PPBS: post prandial blood sugar, Student t-test, *: statistically significant as P value <0.05

HOMA- IR and fasting insulin were significantly increased in patient with enlarged thyroid volume than with normal thyroid volume among the patient group while other tests were insignificant (Table 2).

Table 32: show thyroid function and thyroid antibodies Biochemistry baseline value among patient group with enlarged thyroid volume and with normal thyroid volume Patient group.

		Patient group (MetS (+)) (n=32)		P value
		Enlarged thyroid (n=20)	Normal thyroid volume (n=12)	
TSH (mIU/L)	**Mean ± SD**	2.9 ± 0.2	2.4 ± 0.6	**0.001***
	Range	1.7 - 5.3	1.9 - 4.2	
FT3 (pg/ml)	**Mean ± SD**	3.7 ± 0.8	4 ± 0.7	0.29
	Range	1.8 - 4.6	1.9 - 4.7	
FT4 (ng/dL)	**Mean ± SD**	1.4 ± 0.2	1.3 ± 0.2	0.18
	Range	1 - 1.6	1 - 1.6	
Anti TPO (IU/mL)	**Mean ± SD**	28.4 ± 2.5	25.3 ± 2.6	**0.002**
	Range	22.1 - 33.1	24.8 - 33.2	
Anti-thyroglobulin (IU/mL)	**Mean ± SD**	18.6 ± 6.3	14.2 ± 4.7	**0.04**
	Range	10.7 - 35.8	6.9 - 29.3	

TSH: thyroid stimulating hormone, FT3: free triiodothyronine, FT4:free thyroxine, Anti TPO: Anti-thyroid peroxidase, Student t-test

There was significant increase in TSH, anti TPO and anti-thyroglobulin in patient with enlarged thyroid volume than with normal thyroid volume Patient grwhile there was no significant difference according to FT3 and FT4 among the patient group (Error! Reference source not found.**3).**

Table 4: Comparison of presence thyroid nodule among patient group with enlarged thyroid volume and with normal thyroid volume group.

		Patient group (MetS (+)) (n=32)		P value
		Enlarged Thyroid (n=20)	Normal thyroid volume (n=12)	
Thyroid nodule	**Yes**	15 (75%)	7 (58.3%)	0.32
	No	5 (25%)	5 (41.7%)	

Student t-test, chi square, *: statistically significant as P value <0.05

There was no significant difference according to presence thyroid nodule between both group with enlarged thyroid volume than with normal thyroid volume Patient group **(Table 32 4).**

Discussion

Numerous elements are known to be involved in the production of TNs and thyroid volume (TV). Furthermore, iodine not only makes up a significant portion of thyroid hormones but also creates an environment that is conducive to the growth of thyroid cells. Numerous studies have shown that an increased prevalence of thyroid problems might be caused by iodine excess or shortage **[11].**

Obesity and poor glucose metabolism have been identified as risk factors for thyroid disorders in earlier research. Furthermore, recent research has shown that enhanced thyroid proliferation and nodule formation may result from insulin resistance (IR), one of the primary characteristics of metabolic syndrome (MetS) **[12].**

MetS is known to be associated with central obesity, dyslipidemia, hypertension, and hyperglycemia. Worldwide, the prevalence of MetS has been rapidly increasing due to changes in hazardous lifestyle choices. Consequently, the increased incidence of TNs and increased thyroid volume are caused by the high prevalence of MetS. **[13].**

In our study, regarding the anthropometric measurements, weight, BMI and waist circumference were significantly higher in enlarged thyroid group than normal thyroid volume while height was insignificantly different among the enlarged thyroid groups.

This came in agreement with **Xiao et al. [14]** who reported that, Waist circumference was risk factor for thyroid enlargement. The thyroid volumes of the overweight and obese groups were substantially higher than those of the normal thyroid volume group.

Research has demonstrated that when body mass index (BMI) or body surface area increases, TV increases as well **[15].** Hyperinsulinemia and IR brought on by a high BMI cause thyroid cell proliferation to rise and goitre development to occur **[16].**

Additionally, a number of studies have shown a correlation between thyroid volume and a number of risk variables, including BMI **[17, 18].**

In our study, HOMA- IR and fasting insulin were significantly increased in enlarged thyroid than normal thyroid volume group. While, FBG, PPBS and HbA1C were insignificantly different.

This agrees with **Xiao et al. [14]** who reported that, HOMA-IR and insulin level were positively correlated with increasing thyroid volume.

Insulin resistance could be a primary contributor of MetS. Thyroid cells express insulin receptors. Overindulgence in insulin can bind to thyroid cell receptors, and AMP can activate pathways including protein kinase (AMPK) to cause mitosis **[19].** Conversely, insulin also causes the insulin growth factor (IGF)-1 receptors to become active. Goitre results from prolonged insulin stimulation of thyroid follicular cells, which promotes cell proliferation. In addition, IGF-1 can boost TSH sensitivity, encourage thyroid cell proliferation, and raise colloidal volume, all of which help to partially explain the pathophysiology of thyroid enlargement **[20].** Adult goitre and thyroid tumour incidence have been demonstrated to be positively correlated with insulin resistance **[21].**

Contrary to the findings of previous studies, a different study finds that the thyroid volume significantly correlates with the components of the metabolic syndrome, such as serum lipid profiles, fasting plasma glucose, and blood pressure, and waist circumference. In the group of people with non-nodular thyroid, the thyroid volume was also positively correlated with serum insulin and HOMA-IR levels **[16].**

Additionally, a number of studies have shown a connection between thyroid volume and a number of risk factors, including diabetes mellitus and impaired fasting glucose **[17, 18].**

Also**, Zhu et al. [22]** discovered that patients with insulin resistance (IR) had a considerably higher frequency of TNs than patients without IR.

In a case-control research involving 146 patients, the group of patients with thyroid nodules (15.87%) had a considerably higher HOMA index—a marker of insulin resistance—than the control group (10.8%) **[23].**

There has been evidence linking increased thyroid volume and nodule prevalence to insulin resistance, although the precise molecular processes and pathogenesis remain unclear **[24].** The implication was that IR may stimulate the growth of thyroid cells and nodule development **[25].**

In agreement with our study, **Blanc et al. [26]** has insisted that no connection has been discovered between thyroid nodule and insulin sensitivity measures.

In disagreement with our study, **Su et al. [12]** furthermore unable to identify any other associated insulin sensitivity measures with TNs. Also, **Aydogan et al. [27]** found that there was no correlation found between thyroid nodules and HOMA-IR.

In our study, there was significant increase in TSH in enlarged thyroid group than normal thyroid volume group while there was no significant difference regarding FT3 and FT4 among the patient group.

In accordance, **Ayturk et al. [28]** reported that it was discovered that TSH independently predicted an increase in thyroid volume.

In our study, there was no significant difference regarding thyroid nodule among the enlarged thyroid groups.

Between the groups with and without insulin resistance, a prospective study did not find any differences in thyroid volume or the presence of nodular thyroid disorders. Thyroid volume, however, was substantially correlated with the Metabolic Syndrome. These findings imply that, while each of the syndrome's constituent parts can affect thyroid nodularity to some degree, the thyroid gland is ultimately affected cumulatively by them all **[29].**

In our study, anti TPO and anti-thyroglobulin were significantly higher in enlarged thyroid group than normal thyroid volume group (P<0.001).

Greater levels of TSH and IL-6 have been seen in both MetS and AITD, indicating a potential relationship between the two conditions **[30].**

Chen et al. [31] found a positive correlation between AITD and HOMA-IR, central obesity, hyperlipidemia, obesity, and MetS.

We showed that a strong positive association existed between thyroid volume and each of weight, BMI, waist circumference, TSH, anti TPO and anti-thyroglobulin.

In agreement with our study, **Anil et al. [32]** demonstrated that the waist circumference and thyroid volume continued to have an independent correlation. Also, **Duran et al. [18]** shown that there was a positive correlation between thyroid volume and TSH (r = 0.435, p < 0.001).

In addition, **Su et al. [12]** discovered that, after adjusting for age and sex, only WC was associated with thyroid volume (P = 0.02 < 0.05). Consequently, they postulated that WC constituted a separate risk factor for increased thyroid volume.

Conclusion:

Our findings revealed a high prevalence of enlarged thyroid volume (62.5%) among patients diagnosed with MetS. Our findings suggest a potential link between MetS and enlarged thyroid with possible underlying mechanisms such as metabolic dysregulation.

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