Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2025.383049.3943 Volume 31, Issue 7 July. 2025
Manuscript ID:ZUMJ-2505-3943
DOI:10.21608/zumj.2025.383049.3943

ORIGINAL ARTICLE

Study of Thyroid Nodules and Volume in Patients with Metabolic Syndrome

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Submit Date:08-05-2025
Accept Date:29-05-2025

ABSTRACT

Background: Metabolic syndrome (MetS) is well distinguished by insulin resistance, obesity, dyslipidemia, as well as hypertension, it has been increasingly associated with thyroid dysfunction. Thyroid nodules in addition to enlarged thyroid volume are commonly seen in MetS patients, though the link remains unclear, especially in iodine-deficient areas like Egypt. The purpose of this work was evaluation of the possible relationship between components of MetS and changes in thyroid morphology, particularly thyroid volume and nodularity, and to explore possible metabolic contributors to these changes.

Methods: We carried out this case–control study on 64 individuals at Zagazig University Hospital, comprising 32 MetS patients and 32 individuals who were age- and sex-matched as healthy controls. All individuals underwent comprehensive assessments including anthropometric measurements, thyroid function tests, metabolic profiling, and thyroid ultrasonography. Anti-thyroid antibodies were also measured.

Results: Compared to controls, MetS patients had significantly higher BMI, waist circumference, TSH (mean 2.7 vs. 1.9 mIU/L, $p = 0.0004$), and thyroid volume (mean 17.8 vs. 12.9 mL, $p < 0.001$). Thyroid nodules were found in 68.75% of MetS patients versus none among the controls ($p < 0.001$). Among MetS cases, those with enlarged thyroids had significantly higher insulin resistance (HOMA-IR: 3.7 vs. 2.8, $p = 0.006$) and fasting insulin levels ($p = 0.02$). Anti-TPO as well as anti-thyroglobulin antibodies were also significantly elevated in those with both enlarged thyroids and nodules. Thyroid volume exhibited positive correlations with BMI, waist circumference, TSH, and thyroid antibodies.

Conclusions: Metabolic syndrome is closely correlated with higher thyroid volume and higher incidence of thyroid nodules, potentially driven by insulin resistance and autoimmune activity. These findings highlight the importance of thyroid evaluation in MetS patients for early detection and management of thyroid abnormalities.

Keywords: Thyroid Nodules; Volume; Metabolic Syndrome

INTRODUCTION

A goitre stands for any enlargement of the thyroid gland, that could appear as diffuse, single, or multiple nodules. This enlargement could occur among individuals with normal thyroid function, or those with hypothyroidism or hyperthyroidism [1]. When the gland shows discrete overgrowth in one or more regions, it is termed a nodular goitre (NG), and it typically results from structural and/or functional alterations within otherwise normal thyroid tissue [1,2].

Thyroid nodules are a common finding in clinical practice, representing one of the most prevalent abnormalities affecting the thyroid gland. Their detection has become increasingly frequent with the widespread use of sensitive imaging techniques, and they may be encountered in a significant proportion of patients, particularly as incidental findings during routine investigations. Data from recent global surveys estimate the prevalence of TNs to be approximately 20% [3]. While only about 5% of individuals have nodules that can be felt during a physical exam, incidental nodules are detected in up to 70% of patients undergoing neck ultrasonography, reflecting a high rate of subclinical or "silent" nodules. These nodules are more common in women, older adults, individuals with iodine deficiency, and those exposed to radiation [4].

Metabolic syndrome is marked by the co-occurrence of several cardiovascular risk factors. Of these, insulin resistance is considered a fundamental mechanism that not only contributes to the initial development of the syndrome but also drives its progression over time. Thyroid hormones are crucial regulators of metabolic processes, influencing glucose and lipid metabolism, energy balance, and blood pressure. Given these functions, thyroid dysfunction is hypothesized to be linked to the development of MetS and its associated features like obesity, dyslipidemia, as well as hypertension [5,6].

Growing attention has been directed at the relationship between MetS and TNs. Evidence from case-control research involving cases in a mildly iodine-deficient region showed a significantly higher incidence of TNs and larger thyroid volumes in those with MetS compared to healthy controls. Each component of MetS was found to independently lead to higher thyroid volume. Notably, individuals with insulin resistance face a threefold increased risk of developing thyroid nodules [7,8].

While earlier studies have reported variable thyroid function results in patients with MetS, elevated serum TSH levels have emerged as a recurring observation. These discrepancies could arise from variations in the design of the study, especially those involving populations with differing degrees of obesity and iodine status [9]. More recently, a positive correlation between insulin resistance and increased thyroid volume and nodule frequency has been confirmed even in iodine-sufficient populations [10].

Historically, Egypt experienced iodine deficiency, prompting implementation of regional iodine supplementation programs [11]. Even after the implementation of iodine supplementation programs, previous studies have demonstrated that both metabolic syndrome as a whole and its individual components continue to be correlated with an increased occurrence of thyroid nodules in regions that are iodine-deficient or have only borderline iodine sufficiency [4].

Despite increasing recognition of the relation between metabolic syndrome and thyroid dysfunction, particularly in the context of thyroid nodule prevalence and increased thyroid volume, significant gaps remain in understanding the specific mechanisms and clinical implications, especially among elderly cases with chronic kidney disease (CKD). Recent studies have largely focused on general adult populations or those with isolated metabolic or endocrine disorders, often overlooking the compounded effects of aging, renal insufficiency, and metabolic derangements on thyroid morphology and function. In regions with a history of iodine deficiency, such as Egypt, where both CKD and MetS are prevalent, the interplay of these factors may further modulate the risk and

presentation of thyroid abnormalities. However, comprehensive data evaluating thyroid function and morphology in elderly CKD patients with MetS-considering both metabolic and autoimmune contributors-are lacking. This underscores the need for targeted research to clarify the correlation between components of MetS, renal dysfunction, and thyroid changes in this vulnerable population [11].

So, the purpose of this work was evaluation of the possible relationship between components of MetS and changes in thyroid morphology, particularly thyroid volume and nodularity, and to explore possible metabolic contributors to these changes.

METHODS

This case–control study was conducted at the Internal Medicine Department, Faculty of Medicine, Zagazig University, over a six-month period from April 2023 to October 2023. A total of 64 participants were enrolled and divided equally into two groups: 32 patients diagnosed with metabolic syndrome (MetS group) and 32 age- and sex-matched healthy individuals serving as controls (non-MetS group). Ethical approval was obtained from the Zagazig University IRB (ZU-IRB#10660/2/4-2023), and written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki.

A total of 64 participants were enrolled, including 32 patients diagnosed with metabolic syndrome (MetS group) and 32 age- and sex-matched healthy individuals as the control group. Controls were selected to match the MetS group in terms of age (±2 years) and sex distribution to minimize confounding. The case group comprised 32 individuals diagnosed with MetS with reference to the International Diabetes Federation (IDF) criteria. This group included 22 men and 10 women. For the diagnosis of metabolic syndrome, we used a modified definition appropriate for populations at increased risk of insulin resistance: central obesity was defined by a waist circumference of at least 90 cm in men and 80 cm in women, which is lower than the thresholds typically used in Western populations. In addition, participants had to meet at least two additional criteria from the following: elevated triglycerides (≥ 150 mg/dL or on treatment), low HDL cholesterol (< 40 mg/dL in men or < 50 mg/dL in women, or on treatment), high blood pressure (≥ 130/85 mmHg or on antihypertensive medication), or elevated fasting glucose (≥ 100 mg/dL or a known diagnosis of type 2 diabetes). These cutoffs are consistent with recommendations for Asian and other populations at higher risk of metabolic complications [12].

We excluded patients if they had a history of thyroid disease or any form of thyroid therapy, including medications, surgery, or radiotherapy. Additionally, those with chronic conditions such as hepatic, renal, or cardiac dysfunction were excluded. Psychiatric or neurological disorders—including depression, epilepsy, or schizophrenia—also served as exclusion criteria. Pregnant or lactating individuals were not eligible for participation. Furthermore, subjects with exposure to iodinated contrast within the previous six months, or those using medications known to affect thyroid function, such as amiodarone, were excluded. Lastly, participants with a history of cancer, autoimmune diseases, or other endocrine disorders were also excluded from the study.

All participants underwent detailed clinical history taking, which included demographics such as age, gender, and smoking status, as well as past medical history of diabetes, hypertension, and lipid abnormalities. A thorough medication history was recorded, noting the use of antidiabetic, antihypertensive, lipid-lowering

drugs, or any previous thyroid treatments. Additionally, a comprehensive physical examination was conducted to evaluate general health and detect clinical signs suggestive of thyroid dysfunction.

Anthropometric and blood pressure assessments were performed using standardized methods. Participants were weighed and measured for height while wearing light clothing and without footwear. Body mass index (BMI) was calculated for each participant by dividing their weight in kilograms by the square of their height in meters. Waist circumference was measured directly on bare skin at the midpoint between the lower edge of the ribcage and the top of the iliac crest, following standard protocols. Blood pressure was assessed twice on the right arm using a manual sphygmomanometer after participants had rested for at least five minutes; the lower of the two readings was used in the analysis.

Laboratory investigations included venous blood samples collected between 8–9 a.m. after a 12-hour overnight fast. Tests comprised a complete blood count (CBC) measured using the Sysmex XN330 analyzer, as well as liver and kidney function tests conducted via the Olympus AU2700 analyzer. Fasting and postprandial blood glucose levels were measured using the glucose oxidase method (Roche Diagnostics), which employs enzymatic oxidation of glucose to yield a quantifiable colorimetric signal proportional to glucose concentration. Hemoglobin A1c (HbA1c) was quantified by high-performance liquid chromatography (HPLC), a method recognized for its precision and specificity in assessing long-term glycemic control. Fasting insulin concentrations were determined via chemiluminescent enzyme immunoassay. Insulin resistance was assessed using the HOMA-IR index, calculated as (fasting insulin [µU/mL] × fasting glucose [mmol/L]) / 22.5 [13]. This index provides a convenient estimate of peripheral insulin sensitivity and is widely used in clinical practice and research

Additionally, lipid profile measurements—including total cholesterol, HDL, as well as triglycerides were performed using enzymatic methods, with LDL cholesterol assessed via Friedewald's equation. Thyroid function was assessed through measurements of TSH, free T3, and free T4 using immunochemoluminescence assays (Immulite 2000). Thyroid autoantibodies, specifically anti-thyroid peroxidase (>50 U/mL) and anti-thyroglobulin (>40 U/mL), were also assessed using commercial immunoassay kits.

All participants underwent thyroid ultrasonography utilizing a 10-MHz linear transducer (Logiq 5 Pro, GE Medical Systems). All thyroid ultrasonographic assessments were conducted by a board-certified consultant radiologist (MD in Diagnostic Radiology) with over 10 years of experience in thyroid and neck ultrasonography. To minimize variability, a standardized scanning protocol was used for all participants. A trained assistant was present for patient positioning but did not participate in image interpretation.

The thyroid lobe volume was determined using the ellipsoid formula: volume = depth × width × length × π/6 [14]. The ultrasound examination evaluated total thyroid volume, individual nodule volume, and detailed characteristics including nodule location, number, margins, size, and presence of calcifications. Nodules larger than 1 cm were assessed for suitability for fine-needle aspiration biopsy (FNAB). A thyroid nodule was defined as a distinct lesion clearly distinguishable from the surrounding thyroid tissue on imaging studies, such as ultrasound. This definition aligns with standard radiological criteria, where a nodule is identified as any discrete area that

can be delineated from the adjacent thyroid parenchyma during imaging [15].

Specific definitions were applied throughout the study. Euthyroidism was defined by TSH levels between 0.35 and 4.60 mIU/L, FT3 levels of 3.50–6.50 pM, and FT4 levels of 8.90–20.60 pM [16]. Goiter was diagnosed when thyroid volume exceeded 18 cm^3 in women or 25 cm^3 in men [17]. Hypothyroidism was identified by TSH levels above 4.60 mIU/L [17], and any deviation in TSH, FT3, or FT4 from their reference ranges indicated thyroid dysfunction. Diabetes was identified according to the diagnostic standards set by the American Diabetes Association (ADA), which rely on specific blood glucose and A1C thresholds or the presence of classic symptoms with elevated random glucose [18]. Hypertension was defined as either a measured blood pressure of 140/90 mmHg or greater, or the current use of antihypertensive drugs. Participants were considered smokers if they reported smoking at least one cigarette per day for a minimum of six months.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 28. Data normality was assessed with the Shapiro–Wilk test and histograms. Normally distributed continuous variables were analyzed with the unpaired t-test and reported as mean ± SD. Categorical variables were described as frequencies and percentages, with comparisons made using Chi-square or Fisher's exact test. A two-sided P-value < 0.05 was considered significant.

RESULTS

Baseline characteristics revealed no significant differences in age or sex between the MetS(+) and MetS(−) groups. However, the MetS(+) group exhibited significantly higher values for weight, BMI, and WC than the MetS(−) group ($p < 0.05$) (Table 1).

Patients with MetS+ showed significantly higher TSH levels (2.7 ± 0.7 mIU/L) than controls (1.9 ± 0.98 mIU/L), ($p = 0.0004$). Additionally, significant differences were observed in thyroid volume (17.8 ± 3.54 vs. 12.9 ± 1.43 mL, $p < 0.001$), percentage with enlarged thyroid volume (62.5% vs. 0%, $p < 0.001$), prevalence of thyroid nodules (68.75% vs. 0%, $p < 0.001$), Anti-TPO levels (28.1 ± 2.49 vs. 25.1 ± 2.4 IU/mL, $p < 0.001$), and Anti-thyroglobulin levels (26.4 ± 4.4 vs. 16.8 ± 5.34 IU/mL, $p < 0.001$) (Table 2).

Patients with an enlarged thyroid had significantly higher weight (107.1 ± 2.8 kg vs. 100.83 ± 3.92 kg, $p = 0.001$), higher BMI (44.3 ± 3.5 kg/m^2 vs. 40.9 ± 3.7 kg/m^2, $p = 0.014$), and larger waist circumference (110.4 ± 7.04 cm vs. 103.1 ± 5.4 cm, $p = 0.004$) compared to those with normal thyroid volume (Table 3).

Patients with enlarged thyroid volume had significantly higher prevalence of insulin resistance (IR: 95% vs. 58.3%, $p = 0.01$), elevated HOMA-IR values (3.7 ± 0.8 vs. 2.8 ± 0.9, $p = 0.006$), and higher fasting insulin levels (12.8 ± 3.1 mIU/L vs. 10 ± 3.3 mIU/L, $p = 0.02$) compared to patients with normal thyroid volume (Table 4).

Patients found to have thyroid nodules demonstrated significantly higher average TSH levels-approximately 3.1 mIU/L-compared to individuals without nodules, with average TSH was around 2.18 mIU/L. This difference was statistically significant ($p < 0.001$). Anti-TPO antibody levels (27.95 ± 2.32 vs. 25.1 ± 2.5 IU/mL, $p = 0.003$), and Anti-thyroglobulin antibody levels (22.39 ± 4.75 vs. 16.86 ± 6.34 IU/mL, $p = 0.01$) than patients without nodules (Table 5).

Patients with enlarged thyroid showed significantly higher Anti-TPO levels (28.4 ± 2.5 vs. 25.3 ± 2.6 IU/mL, $p = 0.002$) and Anti-thyroglobulin levels (18.6 ± 6.3 vs. 14.2 ±

4.7 IU/mL, *p = 0.04*) compared to those with normal thyroid size (Table 6).

Thyroid volume showed significant positive correlations with weight (r = 0.244, p < 0.001), BMI (r = 0.421, p < 0.001), waist circumference (r = 0.493, p < 0.001), TSH levels (r = 0.246, p < 0.001), Anti-TPO antibodies (r = 0.176, p < 0.001), and Anti-thyroglobulin antibodies (r = 0.304, p < 0.001) (Table 7).

Table 1: Demographics and Anthropometric Profile of Study Groups

Parameter	Patient group (MetS+) (n=32)	Control group (MetS-) (n=32)	P value
Age (years) - Mean ± SD	48.3 ± 11.53	43.1 ± 11.54	0.074
Age Range	30 - 65	25 - 62	
Sex - Male	22 (68.8%)	14 (43.8%)	0.079
Sex - Female	10 (31.3%)	18 (56.3%)	
Weight (Kg) - Mean ± SD (P = <0.001*)	102.7 ± 7.58	64.5 ± 5.9	<0.001*
Weight Range	89 - 117	55 - 76	
Height (cm) - Mean ± SD	159.4 ± 5.55	160.5 ± 6.16	0.446
Height Range	151 - 171	150 - 172	
BMI (Kg/m2) - Mean ± SD (P = <0.001*)	40.5 ± 3.5	25.1 ± 2.91	<0.001*
BMI Range	34.29 - 48.48	18.59 - 32.02	
Waist circumference (cm) - Mean ± SD (P = <0.001*)	105.4 ± 6.51	76.7 ± 3.74	<0.001*
Waist Range	91 - 117	71 - 83	

BMI: body mass index, WC: waist circumference. * indicates statistically significant (P < 0.05).

Table 2: Thyroid Function, Volume, and Autoantibodies in Study Groups

Parameter	Patient group (MetS+) (n=32)	Control group (MetS-) (n=32)	P value
TSH (mIU/L) (P = 0.0004*)	2.7 ± 0.7	1.9 ± 0.98	0.0004*
TSH Range	1.7 – 5.3	1.2 - 4.6	
FT3 (pg/ml)	3.8 ± 0.76	3.7 ± 0.79	0.585
FT3 Range	1.8 - 4.7	1.9 - 4.7	
FT4 (ng/dL)	1.4 ± 0.19	1.4 ± 0.2	0.950
FT4 Range	1 – 1.6	1 - 1.7	
Thyroid Volume (mL) (P = <0.001*)	17.8 ± 3.54	12.9 ± 1.43	<0.001*
Volume Range	11.3 - 23.2	10.1 - 16.1	
%Enlarged Thyroid Volume (P = <0.001*)	62.5%	0%	<0.001*
% with Thyroid Nodules (P = <0.001*)	68.75%	0%	<0.001*
Anti-TPO (IU/mL) (P = <0.001*)	28.1 ± 2.49	25.1 ± 2.4	<0.001*
Anti-TPO Range	22.1 - 33.2	20.8 - 29.3	
Anti-thyroglobulin (IU/mL) (P = <0.001*)	26.4 ± 4.4	16.8 ± 5.34	<0.001*
Anti-thyroglobulin Range	6.9 - 35.8	5.8 - 28.5	

* indicates statistically significant (P < 0.05).TSH = thyroid stimulating hormone, FT3 = free triiodothyronine, FT4 = free thyroxine, Anti-TPO = anti-thyroid peroxidase. Statistical Test: Student t-test used for all continuous variables; Chi-square for categorical comparisons.

Table 3: Demographics and Anthropometrics by Thyroid Size in MetS (+)

Parameter	Enlarged Thyroid (n=20)	Normal Thyroid (n=12)	P value
Age (years) - Mean ± SD	48.8 ± 11.11	47.5 ± 12.66	0.84
Age Range	30 - 65	32 - 65	
Sex - Male	16 (55%)	6 (91.7%)	0.7
Sex - Female	4 (45%)	6 (8.3%)	
Weight (Kg) (P = 0.001*)	107.1 ± 2.8	100.83 ± 3.92	0.001*
Weight Range	90 - 113	89 - 117	
Height (cm)	159.35 ± 6.6	159.42 ± 3.4	0.97
Height Range	151 - 171	154 - 165	
BMI (Kg/m2) (P = 0.014*)	44.3 ± 3.5	40.9 ± 3.7	0.014*
BMI Range	35.3 - 48.5	34.3 - 46.3	
Waist circumference (cm) (P = 0.004*)	110.4 ± 7.04	103.1 ± 5.4	0.004*
Waist Range	91 - 116	98 - 117	

* indicates statistically significant (P < 0.05). BMI = body mass index.
Student t-test for continuous variables; Chi-square test for categorical variables.

Table 4: Comorbidities, Lipids, and Laboratory Investigations by Thyroid Size in MetS (+)

Parameter	Enlarged Thyroid (n=20)	Normal Thyroid (n=12)	P value
HTN	9 (45%)	4 (33.3%)	0.51
DM	8 (40%)	4 (33.3%)	0.7
Dyslipidemia	20 (100%)	12 (100%)	-
IR (P = 0.01*)	19 (95%)	7 (58.3%)	0.01*
Total Cholesterol (mg/dL)	237.5 ± 16.6	234.7 ± 15	0.63
Triglycerides (mg/dL)	259.1 ± 15.7	257.7 ± 18.2	0.81
HDL (mg/dL)	34.5 ± 2.9	35.9 ± 3.1	0.2
LDL (mg/dL)	151.2 ± 18	147.2 ± 15.2	0.52
FBG (mg/dL)	119.3 ± 19.7	116 ± 16.7	0.63
PPBS (mg/dL)	204.3 ± 52.6	209.9 ± 46.6	0.76
HbA1C (%)	6.8 ± 0.9	6.8 ± 1	1.0
HOMA-IR (P = 0.006*)	3.7 ± 0.8	2.8 ± 0.9	0.006*
Fasting insulin (mIU/L) (P = 0.02*)	12.8 ± 3.1	10 ± 3.3	0.02*

* indicates statistically significant (P < 0.05). HTN = hypertension, DM = diabetes mellitus, IR = insulin resistance, HDL = high-density lipoprotein, LDL = low-density lipoprotein, FBG = fasting blood glucose, PPBS = postprandial blood sugar, HOMA-IR = homeostatic model assessment for insulin resistance. Student t-test for continuous variables; Chi-square test for categorical variables.

Table 5: Thyroid Profile and Autoantibodies by Thyroid Nodules in MetS (+)

Parameter	Nodule Positive (n=22)	Nodule Negative (n=10)	P value
HTN	9 (40.9%)	4 (40%)	0.47
DM	7 (31.8%)	5 (50%)	0.08
Dyslipidemia	22 (100%)	10 (100%)	-
IR	18 (81.8%)	8 (80%)	0.17

Parameter	Nodule Positive (n=22)	Nodule Negative (n=10)	P value
Total Cholesterol (mg/dL)	238.5 ± 15.89	231.9 ± 15.56	0.28
Triglycerides (mg/dL)	256.41 ± 15.1	263.3 ± 19.03	0.27
HDL (mg/dL)	34.41 ± 3.17	36.4 ± 2.17	0.08
LDL (mg/dL)	152.81 ± 16.45	142.84 ± 16.49	0.12
FBG (mg/dL)	115.55 ± 16.99	123.5 ± 21.18	0.26
PPBS (mg/dL)	201.73 ± 41.57	216.7 ± 65.71	0.43
HbA1C (%)	6.9 ± 0.91	6.47 ± 0.62	0.18
HOMA-IR	3.01 ± 0.77	2.7 ± 1.03	0.35
Fasting insulin (mIU/L)	10 ± 3.62	9.49 ± 2.86	0.69
TSH (mIU/L) (P = <0.001*)	3.1 ± 0.7	2.18 ± 0.26	<0.001*
FT3 (pg/ml)	3.94 ± 0.58	3.45 ± 1.02	0.09
FT4 (ng/dL)	1.38 ± 0.18	1.31 ± 0.2	0.33
Thyroid Volume (mL)	19.84 ± 2.5	18.37 ± 2.44	0.13
Anti-TPO (IU/mL)	27.95 ± 2.32	25.1 ± 2.5	0.003
Anti-thyroglobulin (IU/mL)	22.39 ± 4.75	16.86 ± 6.34	0.01

* indicates statistically significant (P < 0.05). HTN = hypertension, DM = diabetes mellitus, IR = insulin resistance, HDL = high-density lipoprotein, LDL = low-density lipoprotein, FBG = fasting blood glucose, PPBS = postprandial blood sugar, HOMA-IR = homeostatic model assessment of insulin resistance, TSH = thyroid stimulating hormone, FT3 = free triiodothyronine, FT4 = free thyroxine. Statistical Test: Student t-test for continuous variables; Chi-square test for categorical variables.

Table 6: Thyroid Nodules and Autoantibodies by Thyroid Size in MetS (+)

Parameter	Enlarged Thyroid (n=20)	Normal Thyroid (n=12)	P value
Thyroid Nodule - Yes	15 (75%)	7 (58.3%)	0.32
Thyroid Nodule - No	5 (25%)	5 (41.7%)	
Anti-TPO (IU/mL)	28.4 ± 2.5	25.3 ± 2.6	0.002
Anti-thyroglobulin (IU/mL)	18.6 ± 6.3	14.2 ± 4.7	0.04

* indicates statistically significant (P < 0.05). Anti-TPO = anti-thyroid peroxidase.
Statistical Test: Student t-test for continuous variables; Chi-square test for categorical variables.

Table 7: Correlation Between Thyroid Volume and Clinical Markers in MetS (+)

Parameter	Correlation Coefficient (r)	P value
Weight (P = <0.001*)	0.244	<0.001*
BMI (P = <0.001*)	0.421	<0.001*
Waist circumference (P = <0.001*)	0.493	<0.001*
TSH (P = <0.001*)	0.246	<0.001*
FT3 (pg/ml)	-0.29	0.53
FT4 (ng/dL)	-0.003	0.92
Anti-TPO (P = <0.001*)	0.176	<0.001*
Anti-thyroglobulin (P = <0.001*)	0.304	<0.001*

* indicates statistically significant (P < 0.05). BMI = body mass index, TSH = thyroid stimulating hormone, FT3 = free triiodothyronine, FT4 = free thyroxine, Anti-TPO = anti-thyroid peroxidase. Statistical Method: Pearson correlation coefficient.

DISCUSSION

Prior studies have shown a strong link between MetS and its components with increased TN prevalence, especially in mild-to-moderate iodine-deficient populations. MetS(+) groups have higher thyroid volume and nodule rates, with IR as a major risk factor, regardless of age or sex [7].

In the present study, the demographic profiles, including age and sex, did not differ significantly between those with and without thyroid enlargement. However, individuals diagnosed with MetS showed markedly higher values for weight, BMI, and WC compared to healthy controls ($P < 0.001$), with no significant difference in height observed between the groups. These results align with previous research, which has consistently reported increased weight, BMI, and abdominal adiposity as prominent features among individuals with MetS [19].

The current study findings also agreed with those of Kir et al. [17], who observed non statistically significant differences in sex distribution between individuals with and without nodular thyroid disease. Furthermore, within our cohort, individuals among the enlarged thyroid group demonstrated significantly higher weight, BMI, and waist circumference compared to those with normal thyroid volume, while height remained statistically similar across groups. These findings are corroborated by Xiao et al. [20], who reported that waist circumference was a significant risk factor for thyroid enlargement, with both overweight and obese individuals showing greater thyroid volumes than those of normal weight.

Several studies have reported a positive association between insulin resistance and increased thyroid volume, suggesting a link between metabolic disturbances and thyroid structural changes. Additionally, thyroid dysfunction-including both hypo- and hyperthyroidism-has been associated with insulin resistance, which may further contribute to the observed differences between groups. Notably, HOMA-IR and fasting insulin levels were markedly elevated among those with thyroid enlargement. However, other metabolic parameters involving FBG, PPBS, and HbA1c levels didn't differ significantly between groups. These observations are in line with prior work that demonstrated a positive association between increased thyroid volume and both serum insulin levels and HOMA-IR scores [20].

Insulin resistance is considered a key driver in the development of MetS. Thyroid cells express insulin receptors, and excessive circulating insulin may bind to these receptors and activate intracellular pathways involving AMP-activated protein kinase (AMPK), ultimately promoting cellular mitosis [21]. Although the precise molecular pathways remain unclear, insulin resistance has been recognized as an independent risk factor for thyroid hypertrophy and increased nodule prevalence. It is postulated that IR contributes to thyroid cell proliferation, thereby supporting the growth and development of nodular formations [22].

In our findings, non-significant variations were revealed as regards the prevalence of hypertension, diabetes mellitus, dyslipidemia, or insulin resistance when comparing patients with and without thyroid nodules. Similarly, key laboratory markers—such as lipid profile, fasting blood glucose (FBG), postprandial blood glucose (PPBS), HbA1c, and HOMA-IR—showed no statistically significant variations between these two groups.

In contrast to the findings of previous studies, Wang and colleagues [23] proposed that hypertension may actively contribute to the pathogenesis of thyroid nodule

formation. Their research identified a positive correlation between elevated blood pressure and increased TSH levels, raising the possibility that higher TSH may play a role in the development of nodular thyroid disease. These observations suggest that hypertension, possibly through its influence on TSH, could be a modifiable risk factor for thyroid nodule formation. This is supported by other studies indicating a high prevalence of hypertension among patients with thyroid nodules and highlighting the complex interplay between cardiovascular risk factors and thyroid pathology.

In our research, we did not detect any significant variations in total cholesterol, triglycerides, HDL, or LDL levels between those with and without thyroid enlargement. This observation differs from the work of Xiao et al. [20], in which a positive association was noted between triglyceride concentrations and thyroid volume, while HDL-C levels were inversely related to thyroid size in adolescents ($P < 0.001$). These discrepancies may be attributed to differences in participant characteristics or study design. Taken together, our results indicate that thyroid enlargement is not independently associated with clinically meaningful alterations in lipid profile parameters.

Likewise, Ayturk et al. [7] identified triglycerides as an independent predictor of thyroid volume, which may reflect the influence of differing lifestyle factors across study populations.

Similarly, our findings revealed no significant differences in lipid profiles between individuals with and without thyroid nodules ($P > 0.001$). This aligns with the results of Xu et al. [25], who concluded that hyperlipidemia is not an independent risk factor for thyroid nodule development. Feng et al. [25] also reported no significant variation in HDL-C levels between subjects with and without thyroid nodules.

On the contrary, Su et al. [21] identified high HDL-C levels as a protective factor against the development of thyroid nodules. In support of a lipid-related influence, Yin et al. [14] found that elevated triglycerides were associated with a higher risk of new nodule formation, while Zou et al. [26] reported a stronger link between elevated LDL-C levels and the presence of multiple thyroid nodules.

In the current study, individuals with metabolic syndrome exhibited significantly higher thyroid-stimulating hormone levels compared to healthy controls, while free triiodothyronine and free thyroxine levels showed no significant difference between the groups. These results are consistent with findings by Ayturk et al. [7], who also observed a positive association between elevated TSH and MetS, implying a potential role of TSH in thyroid structural alterations. Similar to our findings, their study did not establish a clear association between free thyroid hormone levels and the individual components of metabolic syndrome. This is consistent with a growing body of research indicating that the relationship between thyroid function and metabolic syndrome components is complex and not always straightforward, with some studies reporting significant associations and others finding none

Liu et al. [27] similarly reported that individuals with central obesity had significantly elevated TSH levels, reinforcing the link between abdominal obesity and increased TSH concentrations.

We also observed significantly higher TSH levels in the enlarged thyroid group compared to those with normal thyroid size, while FT3 and FT4 levels remained unchanged. This aligns with Ayturk et al. [7], who identified TSH as an independent predictor of increased thyroid volume.

Moreover, among MetS patients, those with thyroid nodules demonstrated higher TSH

levels than those without nodules. These results are supported by Liu et al. [27], who also found elevated TSH significantly associated with thyroid nodules.

Our findings indicate that thyroid volume was similar in individuals with and without thyroid nodules. However, the presence of thyroid nodules was associated with significantly higher levels of anti-TPO and anti-thyroglobulin antibodies, suggesting that autoimmune mechanisms may contribute to nodule formation, particularly among patients with metabolic syndrome.

Conversely, Feng et al. [25] found larger thyroid volumes in individuals with nodules compared to controls, indicating thyroid enlargement may accompany nodule development in other populations. Supporting these findings, our study demonstrated that patients with metabolic syndrome (MetS) had significantly larger thyroid volumes and a higher prevalence of thyroid enlargement and nodules compared to controls ($P < 0.001$).

These findings are in line with results from Xiao et al. [20], Guo et al. [28], Su et al. [19], Ayturk et al. [7], Bener et al. [29], Zhang et al. [4], Shin et al. [30], Ding et al. [31], Buscemi et al. [32], Tirosh and Shimon [33], Eggo [34], Mayers et al. [35], and Anil et al. [13], highlighting a clear link between metabolic status and thyroid morphology.

Finally, our analysis demonstrated a significant positive relationship between thyroid volume and several factors, including body weight, BMI, waist circumference, TSH, anti-TPO, and anti-thyroglobulin antibody levels. These findings are consistent with those of Anil et al. [13], who identified waist circumference as an independent factor associated with increased thyroid volume, and with Su et al. [19], who confirmed waist circumference as an independent predictor of thyroid enlargement after adjusting for age and sex.

This study highlights the association that could present between metabolic syndrome and thyroid structural changes using a well-defined case–control design with age- and sex-matched groups. Strengths include the use of standardized diagnostic criteria, detailed anthropometric and biochemical assessments, and high-resolution thyroid ultrasonography.

However, limitations include the small sample size and single-center design, which may affect generalizability. The cross-sectional nature limits causal interpretation, and lifestyle factors such as diet and physical activity were not evaluated. One other limitation of this study is the absence of standardized TIRADS classification for thyroid nodules, which could have offered more precise risk stratification. Future studies are recommended to incorporate TIRADS scoring to enhance the clinical relevance of ultrasonographic findings. Future longitudinal studies are needed to confirm these findings and clarify underlying mechanisms.

Conclusions

Metabolic syndrome is significantly correlated with large thyroid volume and increased risk of development of thyroid nodules with possible underlying mechanisms such as metabolic dysregulation.

Conflict of Interest or financial disclosure

No potential conflict of interest to be reported by the authors.

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Citation

Ghanem, N., Salem, H., Arafa, M., Saeid, A. Study of Thyroid Nodules and Volume in Patients with Metabolic Syndrome. *Zagazig University Medical Journal*, 2025; (2541-2553): -. doi: 10.21608/zumj.2025.383049.3943