RESEARCH PAPER

Thyroid Dysfunction In Metabolic Syndrome: a Case-Control Study

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Abstract

Background: Metabolic syndrome (MetS) and thyroid dysfunction are prevalent endocrine disorders that mutually influence each other and synergistically increase cardiovascular morbidity and mortality. Aim: To compare serum free triiodothyronine (FT3), free thyroxine (FT4), and thyroid-stimulating hormone (TSH) levels between patients with MetS and coexisting thyroid disorder and healthy controls, and to quantify the clinical magnitude of these differences.

Methods: In this hospital-based case–control study, 100 patients with MetS (NCEP ATP III criteria) and a confirmed coexisting thyroid disorder were compared with 100 age and sex-matched healthy controls. FT3, FT4, and TSH were measured by electrochemiluminescence immunoassay. Statistical comparisons used independent t-tests (or Mann–Whitney U when appropriate); effect sizes were calculated as Cohen's d and eta squared (η^2).

Results: Compared with healthy controls, MetS patients with thyroid dysfunction had significantly lower mean FT3 (difference –0.34 pg/mL, $p = 0.0025$) and FT4 (difference –0.88 ng/dL, $p = 0.04$). TSH was markedly higher in cases (difference +26.58 µIU/mL, $p < 0.0001$), with a large effect size (Cohen's $d = 1.38$) explaining 32.4% of the variance. However, the TSH elevation is largely explained by the inclusion criterion of pre-existing thyroid disorder.

Conclusion: MetS with coexisting thyroid disorder is characterized by a distinct thyroid profile of low FT3/FT4 and markedly elevated TSH. The large effect size and substantial variance explained by TSH highlight its potential as a sensitive clinical biomarker. Study interpretations do not support routine TSH screening in all MetS patients but rather targeted testing in those with clinical features of hypothyroidism.

Keywords: Metabolic syndrome; thyroid dysfunction; TSH; free triiodothyronine; insulin resistance

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Introduction

Metabolic syndrome (MetS) represents a cluster of interconnected risk factors. The concept of metabolic syndrome (MetS) involves several interconnected risk factors like excessive abdominal fat, insulin resistance, dyslipidemia, and hypertension, increasing the risk of the development of type 2 diabetes mellitus and CVDs [1]. The prevalence of MetS has become epidemic in recent years, making it one of the major health problems because of its adverse outcomes in terms of morbidity and mortality [2]. At the same time, thyroid diseases, including subclinical hypothyroidism and hyperthyroidism, occur frequently and are known to have a significant impact on metabolic processes [3]. Thyroid hormones T3 and T4 play an important role in the regulation of basal metabolism, lipid metabolism, and heart activity [4].

Despite the clear understanding of the effects of both MetS and thyroid disorders on individuals' health, there is insufficient evidence about their interrelation. It has been shown that changes in thyroid hormones levels, particularly in TSH, could be related to some of the components of MetS, such as obesity and dyslipidemia [5, 6]. However, there is a lack of data on analysis of the complete thyroid hormone panel (FT3, FT4) among patients with MetS, as well as the quantitation of the difference between the two groups. Furthermore, the exact role of the thyroid dysfunction in MetS characteristics needs to be determined, considering other possible determinants [7]. Thus, the aim of the current research was to evaluate the relation between MetS and thyroid disorders in terms of thyroid dysfunction parameters. More precisely, it was needed to examine the pattern of thyroid dysfunction in MetS patients compared to control group members in order to facilitate timely diagnosis and treatment of thyroid dysfunction as a means to improve MetS and reduce risks of developing CVDs.

Materials And Methods

Study Design and Setting: This was a hospital-based, case-control study conducted over a specified period July 2022 to January 2026 Ethical approval was obtained from the institutional review board, and all participants provided written informed consent before enrollment.

Participants: A total of 200 subjects were enrolled in the study and assigned to two different groups. In the control group (Group 1), 100 subjects were clinically and biochemically normal without any symptoms or signs of Metabolic Syndrome (MetS) or any thyroid diseases. The experimental group (Group 2), on the other hand, had 100 subjects who were clinically confirmed to have MetS based on NCEP ATP III criteria along with coexisting thyroid disease (based on clinical evaluation and biochemistry at baseline). Subjects with other comorbid conditions such as malignancies, chronic kidney and liver disease, pregnant or lactating females, or those taking thyroid function-modifying drugs (like amiodarone, glucocorticoids, or thyroid hormones) were excluded from the study.

Data Collection and Biochemical Analysis: Variables of demographic characteristics, including age, gender, and clinical data, were recorded. Venous blood samples (5 mL) were collected from all participants fasting for 10–12 hours in the morning from 08:00 to 10:00 hours. Separated serum was stored at −80°C before analysis through centrifuging at 3000 rpm for 10 minutes. The levels of FT3, FT4, and TSH as thyroid function markers were measured using ECLIA kits based on the Cobas

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e411 analyzer (Roche Diagnostics, Germany). All analyses were performed according to the manufacturer's protocol with intra-assay and inter-assay coefficients of variation less than 5%.

Statistical Analysis: All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous data (FT3, FT4, TSH) were tested for normality using the Kolmogorov-Smirnov test. Descriptive statistics (mean, standard deviation [SD], minimum, maximum) were calculated for each parameter per group. Comparisons between the case and control groups were performed using an independent samples t-test (for normally distributed data) or Mann-Whitney U test (for non-normal data). Mean differences with 95% confidence intervals (CI), t-values, and p-values were calculated. A p-value <0.05 was considered statistically significant.

Result

The study enrolled 200 participants, comprising 100 healthy controls and 100 patients with metabolic syndrome and coexisting thyroid disorder. Age and sex distribution between the two groups are presented in Table 1.

Table 1: Baseline Demographic Characteristics

Characteristic	Group 1 (Controls) n=100	Group 2 (Cases) n=100
Gender, n (%)		
Male	30 (30%)	38 (38%)
Female	70 (70%)	62 (62%)
Age group, n (%)		
20-30 years	37 (37%)	6 (6%)
31-40 years	27 (27%)	18 (18%)
41-50 years	27 (27%)	27 (27%)
51-60 years	7 (7%)	38 (38%)
61-70 years	2 (2%)	11 (11%)

Table 2: Descriptive Statistics of Thyroid Parameters

Parameter	Group	Min	Max	Mean	SD	SEM
FT3 (pg/mL)	Control	0.86	2.49*	1.54	0.91	0.09
	Case	0.11	2.82	1.19	0.65	0.06
FT4 (ng/dL)	Control	4.98	11.0	9.05	1.52	0.15
	Case	0.8	14.0	8.17	3.95	0.39
TSH (µIU/mL)	Control	0.5	5.0	2.35	1.22	0.12
	Case	5.34	94.0	28.93	27.23	

Figure 1: Showing Thyroid parameters in Cases vs Control

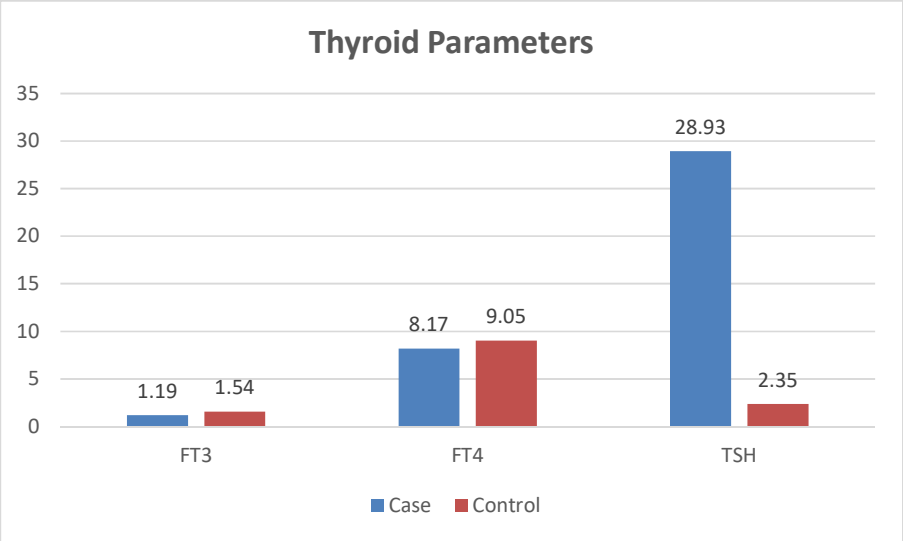

Table 3: Comparative Statistics (cases vs. controls)

Parameter	Mean Difference (Case – Control)	95% CI	t-value	p-value
FT3	–0.34	–0.56 to –0.12	–3.06	<0.0025
FT4	–0.88	–1.71 to –0.04	–2.07	<0.04
TSH	+26.58	21.20 to 31.95	9.75	<0.0001

Table 4: Effect Size and Clinical Significance

Parameter	Cohen's d	Magnitude	% Change (Case vs Control)	U3 Overlap (%)	Eta-squared (η^2)
FT3	–0.44	Small to medium	–22.7%	67%	0.045
FT4	–0.29	Small	–9.7%	61%	0.021
TSH	+1.38	Large	+1131%	92%	0.324

TSH shows a large effect size (d=1.38), a 1131% increase in cases, and explains 32.4% of the variance. FT3 and FT4 show small to medium effects.

Discussion

The interplay between metabolic syndrome and thyroid function has garnered considerable research interest, as both conditions are closely linked to cardiovascular morbidity [1, 3]. While hypothyroidism is known to induce weight gain, dyslipidemia, and insulin resistance, MetS itself may influence the hypothalamic-pituitary-thyroid axis [7]. The current study aimed to delineate the specific alterations in the thyroid hormone profile—FT3, FT4, and TSH—in patients with MetS and coexisting thyroid disorder compared to healthy controls.

FT3: The present study demonstrated a statistically significant decrease in the level of FT3 between the MetS patients (mean value 1.19 ± 0.65 pg/mL) versus the control group (mean value 1.54 ± 0.91 pg/mL). In particular, a difference of −0.34 pg/mL in favour of the control group ($p < 0.0025$) according to the data provided in Table 3. As can be seen, the obtained results agree with the findings of Alevizaki et al. (2007) and, more recently, Mehran et al. (2017), who have revealed the association of

MetS prevalence with low levels of FT3 in euthyroid subjects [8, 9]. The moderate effect size related to FT3 (Cohen's d = −0.44, Table 4) demonstrates its moderate decrease. The possible mechanism of FT3 deficiency development could be associated with the impaired action of type 1 and type 2 deiodinases in MetS patients due to insulin resistance and the development of inflammation, which characterize this disorder [4, 10]. At the same time, it is necessary to note that further confirmation of this hypothesis is required. However, the results of the research by de Almeida et al. (2024) confirm this idea since the presence of the Thr92Ala-DIO2 polymorphism that slows down the type 2 deiodinase and T4-to-T3 conversion is associated with an increase in body mass index and insulin resistance**.**

FT4: Mean FT4 levels were significantly lower in cases (8.17 ± 3.95 ng/dL) vs. controls (9.05 ± 1.52 ng/dL), difference -0.88 ng/dL ($p < 0.04$, Table 3). This finding is consistent with Park et al. (2010), who reported that subjects in the lowest FT4 quartile had a higher risk of MetS components, especially hypertriglyceridemia and abdominal obesity [11]. The small effect size (Cohen's d = -0.29, Table 4) and 9.7% reduction indicate FT4 is a less robust discriminator than TSH. The underlying mechanism may involve central regulation of the hypothalamic-pituitary-thyroid (HPT) axis; in MetS, elevated leptin (due to obesity) may stimulate the HPT axis, but the subsequent TSH rise is often unmatched by proportional T4/T3 increases due to proposed peripheral thyroid hormone resistance in MetS [12]. A recent narrative review by Badr et al. (2025) reinforces this, noting that adipose-derived leptin stimulates thyrotropin-releasing hormone (TRH) release, increasing TSH and thyroid hormones, yet resulting in relative FT4 deficiency.

TSH: TSH was markedly elevated in MetS cases (28.93 ± 27.23 μIU/mL) vs. controls (2.35 ± 1.22 μIU/mL), difference +26.58 μIU/mL ($p < 0.0001$, Table 3). This aligns with literature [13,14], though those studies examined euthyroid populations, not our selected hypothyroid cohort. The large effect size (Cohen's d=1.38, η^2=0.324) and 1131% increase suggest most cases had severe subclinical hypothyroidism. The mechanistic link is bidirectional: TSH promotes adipogenesis, increases cholesterol synthesis via HMG-CoA reductase, reduces hepatic LDL receptor expression (worsening lipid profile) [15], and induces insulin resistance by downregulating IRS-1 and GLUT4 in adipocytes [16]. A 2025 cohort study confirmed subclinical hypothyroidism in obese adults is associated with dyslipidemia, insulin resistance, and cardiovascular risk. Furthermore, Zhou et al. (2024) demonstrated in a mouse model and 3T3-L1 adipocytes that TSH directly induces insulin resistance via the ER stress–JNK pathway, providing a mechanistic basis for our findings.

Additional Findings: The baseline demographic characteristics (Table 1) reveal a higher proportion of females in both groups (70% controls, 62% cases), which is reflective of the higher prevalence of both autoimmune thyroid disease and MetS in postmenopausal women, a finding consistent with epidemiological data [17]. Furthermore, the age distribution shows a clear shift: controls were predominantly younger (37% in 20-30 years), while cases were concentrated in the 51-60 years age group (38%), indicating that the burden of combined MetS and thyroid dysfunction increases with advancing age, likely due to cumulative metabolic and endocrine insults [18].

Clinical Significance: The present study indicates that the presence of hypothyroidism, characterized by low FT3 and/or FT4 levels and significantly high levels of TSH, is quite common among MetS patients. It does not provide a basis for routine screening for TSH in all MetS patients. Instead, it suggests conducting TSH tests among MetS patients who show signs of hypothyroidism, which include unexplained fatigue, inexplicable weight gain, or difficult-to-treat dyslipidemia. Such a step would not only help in improving their lipid profile but would also lower their CVD risk, which cannot be done through universal screening at this point. Identification of thyroid dysfunction allows for effective and inexpensive treatment (levothyroxine replacement) that will lead to improvements in lipid profile and weight loss and, consequently, decrease the risk associated with CVDs. [19, 20].

Conclusion

In patients with Metabolic Syndrome and coexisting thyroid disorder, a distinct thyroid profile emerges

characterized by significantly reduced FT3 and FT4 levels alongside a dramatic, large-effect elevation in TSH. The magnitude of TSH elevation, which explains nearly one-third of the variance between cases and controls, underscores its potential as a sensitive biomarker. These findings do not support routine TSH screening in all MetS patients but rather targeted testing in those with clinical features of hypothyroidism.

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