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Evaluation of the frequency and patterns of thyroid dysfunction in patients with metabolic syndrome



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Abstract

Background: Metabolic syndrome (MetS) and thyroid dysfunction have a degree of close association, and each of them affects the other. Due to the associated cardiovascular events, MetS has increased morbidity and mortality. The study tried to detect the frequency of thyroid function in patients with MetS. This is a case control study that recruited 100 patients with MetS and 100 healthy control subjects.

Results: Patients with MetS had significantly higher body mass index and waist circumference. Also, frequency of thyroid dysfunction was significantly higher in MetS group (32% vs. 9%; $P < 0.001$). The most frequent form of thyroid dysfunction was subclinical hypothyroidism: 21% of the MetS group and 6% of the control group. Out of the studied patients with MetS, 13 (13%) patients had three criteria, 55 (55%) patients had four criteria, and 32 (32%) patients had five criteria for MetS.

Conclusion: Patients with MetS are vulnerable to develop thyroid dysfunction mainly subclinical hypothyroidism. So, it is recommended to perform regular screening for those patients as regard thyroid dysfunction.

Keywords: Thyroid dysfunction, Metabolic syndrome, Hypothyroidism

Background

Patients with thyroid dysfunction (TD) are vulnerable to cardiovascular disease (CVD). It is known that thyroid hormones have great effects on homeostasis, energy control, and metabolism. TD is known as any deviation in the level of hormones secreted by the thyroid gland [1–3]

Till now, the accurate association of TD with MetS is still a matter of controversy and clinical challenge. Increased frequency of CVD is known to be higher if both of them are present with subsequently increased risk of mortality [4].

Each of TD and MetS has common events as dyslipidemia, central obesity, and diabetes mellitus. Serious outcome may occur with bad prognosis in patients with MetS and missed TD [5]. This work was designed to assess pattern of TD in patients with MetS.

Methods

Study setting and design

A case control study was conducted in the period between 2016 and 2018. It was performed at outpatient clinics of diabetes and endocrinology unit.

Participants

The study recruited 100 patients who fulfilled criteria of MetS based on the National Cholesterol, Education Program, Adult Treatment Panel III (NCEP-ATP III revised 2005) criteria [6]. Age- and sex-matched 100 healthy subjects were enrolled who did not have full criteria of MetS as non-MetS group. Any patient with history of respiratory disease, malignancy, smoking, congestive cardiac failure, pregnant women, and patients under treatment of any thyroid related disorders were excluded.

All participants were subjected to the following:

Through clinical evaluation and examination, body mass index (BMI) and waist circumference (WC) were

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assessed. The following laboratory data were done with obtaining a blood samples after 10 h of fasting: (1) fasting blood glucose, (2) lipid profile, and (3) thyroid hormones: triiodothyronine (T3), thyroxine (T4), and thyroid-stimulating hormone (TSH). TD was classified as explained at Table 1 [7].

Statistical analysis

SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, NY) was used for data analysis. Student’s t test and Chi² test were used to compare continuous and nominal data, respectively. In case of comparison of continuous data of more than two groups, ANOVA was used. Correlation of thyroid hormones with components of metabolic syndrome was assessed by Pearson correlation. The level of confidence was kept at 95%; hence, a P value <0.05 indicated a significant association.

Results

Baseline data of enrolled groups (Table 2)

Both studied groups had no significant difference as regard age and sex distribution, but patients with MetS had significantly higher body mass index, waist circumference, and blood pressure in comparison to the control groups.

Baseline laboratory data among the studied groups (Table 3)

FBG was significantly higher among MetS group (139.51 ± 14.32 vs. 83.16 ± 6.81 mg; P< 0.001). Also, there were significant differences in all parameters of lipid profile between both studied groups. Patients with metabolic syndrome had significantly higher TSH and free T4 in comparison to control group.

State of thyroid function among enrolled groups (Tables 4 and 5)

TD was more frequent in MetS group (32% vs. 9%; P< 0.001). Subclinical hypothyroidism, subclinical hyperthyroidism, and overt hypothyroidism presented in 21%, 6%, and 5% of MetS group respectively and 6%, 2%, and 1% of the control group respectively.

Based on the number of metabolic criteria among the MetS group, those patients were further subgrouped into

Table 1 Different classes of thyroid dysfunction

	Hyperthyroidism		Hypothyroidism	
	Overt	Subclinical	Overt	Subclinical
TSH (µu/ml)	< 0.45	< 0.45	> 4.50	> 4.50
Free T4 (ng/dl)	> 0.18	0.80–1.8	< 0.80	> 1.80
Free T3 (pg/ml)	> 4.4	1.4–4.4	< 1.40	1.4–4.4

TSH, thyroid-stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine

Table 2 Baseline data of enrolled groups

	MetS group (n= 100)	Control group (n= 100)	P value
Age (years)	51.88 ± 5.86	48.86 ± 10.24	0.87
Sex			0.07
Male	40 (40%)	49 (49%)	
Female	60 (60%)	51 (51%)	
Body mass index (kg/m ²)	36.37 ± 3.98	31.07 ± 4.62	< 0.001
Waist circumference (cm)	105.25 ± 7.50	99.68 ± 11.92	< 0.001
SBP (mmHg)	165.01 ± 10.20	123.10 ± 9.067	< 0.001
DBP (mmHg)	98.05 ± 5.68	75.30 ± 10.19	< 0.001

Data was expressed in the form of frequency (percentage), mean (SD). P value was significant if < 0.05

MetS, metabolic syndrome; SBP, systolic blood pressure; DBP, diastolic blood pressure

the following: 13 (13%) patients had three criteria, 55 (55%) patients had four criteria, and 32 (32%) patients had five criteria. These subgroups had insignificant difference as regard status of thyroid function (P> 0.05) (Table 5).

Correlation of thyroid hormones with components of metabolic syndrome (Table 6)

TG level in the blood has significant positive correlation with TSH (r= 0.33; P= 0.02), and FBG has significant positive correlation with T3 (r= 0.22; P= 0.02). Also, TG level in the blood has significant positive correlation with T4 (r= 0.24; P= 0.02), and waist circumference has significant negative correlation with T4 (r= -0.26; P= 0.01). Other correlations were insignificant (Fig. 1).

Discussion

This work was designed to assess frequency of TD in patients with MetS. BMI, WC, and blood pressure were

Table 3 Baseline laboratory data among the studied groups

	MetS group (n= 100)	Control group (n= 100)	P value
Fasting blood glucose (mg/dl)	139.51 ± 14.32	83.16 ± 6.81	< 0.001
Cholesterol (mg/dl)	213.29 ± 49.82	165.66 ± 17.92	< 0.001
Triglyceride (mg/dl)	177.49 ± 39.44	122.64 ± 18.22	< 0.001
High-density lipoprotein (mg/dl)	45.20 ± 7.01	48.95 ± 4.95	0.03
Low-density lipoprotein (mg/dl)	150.41 ± 21.51	95.41 ± 16.45	< 0.001
VLDL (mg/dl)	29.31 ± 2.23	24.47 ± 3.63	0.03
TSH (µu/ml)	5.24 ± 1.80	3.24 ± 1.61	< 0.001
Free T3 (pg/ml)	3.36 ± 0.63	3.70 ± 1.01	0.39
Free T4 (ng/dl)	1.39 ± 0.33	1.12 ± 0.32	< 0.001

Data was expressed in the form of mean (SD). P value was significant if < 0.05 MetS, metabolic syndrome; VLDL, very low-density lipoprotein; TSH, thyroid-stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine

Table 4 Status of thyroid function among enrolled groups

	MetS group (n= 100)	Control group (n= 100)	P value
Thyroid dysfunction	32 (32%)	9 (9%)	< 0.001
Subclinical hypothyroidism	21 (21%)	6 (6%)	
Subclinical hyperthyroidism	6 (6%)	2 (2%)	
Overt hypothyroidism	5 (5%)	1 (1%)	

Data expressed as frequency (percentage). P value was significant if < 0.05
MetS metabolic syndrome

higher among MetS group in the current study. In line with these results, Ahmad et al. [8] stated that MetS group had significantly BMI, WC, age, and blood pressure in comparison to the control group. In the current study, 60% of MetS group was females, and this was consistent with other studies [9].

We found that MetS group had significantly higher FBG and TG. This may be due to the associated insulin resistance and impaired glucose tolerance in those patients [10]. MetS group had significantly higher TSH and free T4. These findings were similar to findings of Aljabri et al. [11].

In the current work, 13 (13%) patients of MetS group had three criteria of Mets while 55 (55%) had four criteria, and 32 (32%) had five criteria. No significant difference as regard thyroid function and TD was noticed among different groups of patients based on number of criteria. Luna-Vazquez et al. [12] found variable correlations between serum TSH, thyroid hormones, and components of the MetS.

TG level in the blood was positively correlated with TSH and T3 while FBG has positive correlation with T3. Delitala et al. [13] stated a positive correlation between TSH with TG, free thyroxine with HDL, and blood pressure with FBG while FT4 had negative correlation with WC.

Effect of thyroid hormones on the metabolism of lipid could be explained through (1) induced transcription of LDL receptor gene, expression of hydroxyl

Table 5 Frequency of thyroid dysfunction based on criteria of metabolic syndrome

	Three criteria (n= 13)	Four criteria (n= 55)	Five criteria (n= 32)
Thyroid status*			
Euthyroid	9 (69.3%)	38 (69%)	21 (65.6%)
Subclinical hyperthyroidism	1 (7.7%)	3 (5.5%)	2 (6.3%)
Subclinical hypothyroidism	3 (23%)	10 (18.2%)	8 (25%)
Overt hypothyroidism	0	4 (7.3%)	1 (3.1%)

Data was expressed in the form of frequency (percentage). P value was significant if < 0.05

*No significant difference

Table 6 Correlation of thyroid hormones with metabolic syndrome components

	TSH		Free T3		Free T4	
	r	P	r	P	r	P
Systolic blood pressure (mmHg)	0.04	0.63	0.05	0.59	0.09	0.34
Diastolic blood pressure (mmHg)	0.05	0.57	0.01	0.90	-0.17	0.08
Waist circumference (cm)	0.01	0.88	0.02	0.82	-0.26	0.01
Fasting blood glucose (mg/dl)	0.06	0.49	0.22	0.02	0.03	0.73
Triglyceride (mg/dl)	0.33	0.02	0.14	0.14	0.24	0.02
High density lipoprotein (mg/dl)	0.08	0.41	0.04	0.67	-0.06	0.51

Data was expressed in the form of r (indicates strength of correlation) and P (indicates significance of correlation). P value was significant if < 0.05

TSH, thyroid-stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine

methylglutaryl coenzyme A reductase, and finally upregulation of sterol regulatory element-binding protein-2 [13]. Also, reduction in level of FT4 is associated with visceral obesity and increased insulin resistance. In addition to, high risk of MetS was found in patients with elevated TSH levels [14–16].

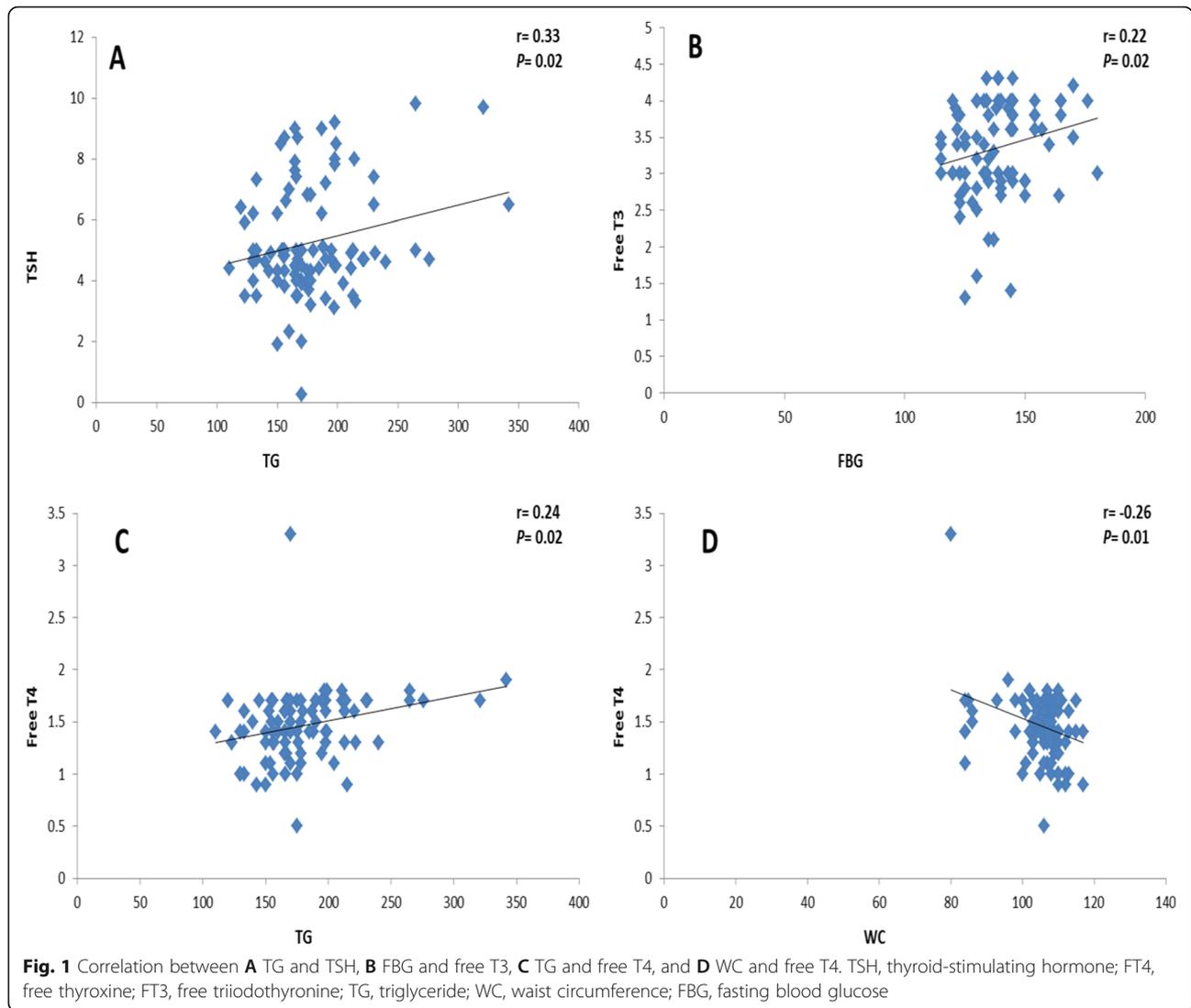
We found that patients with MetS had higher frequency of thyroid dysfunction (32% vs. 9%; $P < 0.001$) mainly in the form of subclinical hypothyroidism. Raposo et al. [17] concluded that prevalence of hypothyroidism, hyperthyroidism, and undiagnosed dysfunction was 4.9%, 2.5%, and 72.2%, respectively in MetS patients.

Khatiwada et al. [7] stated that subclinical hypothyroidism (26.6%) was the most frequent form of TD followed by overt hypothyroidism (3.5%) and subclinical hyperthyroidism (1.7%) in MetS patients. Also, Deshmukh et al. [18] found that 28% of the patients were diagnosed with TD with a higher prevalence among women compared to men. The predominance of hypothyroidism suggests that MetS could be a result of various grades of hypothyroidism during the natural course of the disease. In agreement with our findings, prevalence of hypothyroidism was 29.3% (7.4% had overt hypothyroidism and 21.9% had subclinical hypothyroidism) in previously reported study [19].

Also, Khalil et al. [20] revealed a high frequency (30.19%) of missed TD in patients with MetS. The most frequent form was hypothyroidism that affected 90.6% of those with TD. Wang et al. [21] reported that TD accounted 7.21% of MetS patients. Up to 5% had subclinical hypothyroidism, and 2.64% had subclinical hyperthyroidism.

The lesser number of subclinical hypothyroidism cases reported in such study by Wang et al. [21] could be attributed to enrolment of patients with known cases of hypothyroidism who were on levothyroxine therapy.

Yet, another study in Taiwan by Lai et al. [22] concluded the overall prevalence of TD was 7.60% with 2.10% to be subclinical hypothyroid and 5.50% to be subclinical hyperthyroid patients.



Conclusion

We concluded that TD is common with MetS. Therefore, screening for TD in patients with MetS should be done. This allows the early identification of TD with early intervention with subsequent good prognosis.

Abbreviations

TD: Thyroid dysfunction; MetS: Metabolic syndrome; TSH: Thyroid-stimulating hormone; FT4: Free thyroxine; FT3: Free triiodothyronine; TG: Triglyceride; LDL: Low-density lipoproteins; HDL: High-density lipoproteins; VLDL: Very low-density lipoproteins; BMI: Body mass index; WC: Waist circumference; FBG: Fasting blood glucose

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Authors' contributions

S.A.A. conceived and designed the research. G.A.E.A.E.H. recruited patients, and collected patients' clinical and laboratory data. N.M.M.A.M. and G.A.E.A.E.H. prepared the original draft of the manuscript and participated in data analysis and writing. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Review Board of Faculty of Medicine, Assiut University, and informed written consent was obtained from all participants according to the Declaration of Helsinki. The committee's reference number is 17100051. [Clinicaltrials.gov](https://clinicaltrials.gov) ID: NCT03214068

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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