# The relationship between thyroid hormone and lipid metabolism/body fat content in euthyroid male patients with type 2 diabetes mellitus in China: A cross-sectional study

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# Abstract

Background: This study compared the relationship between thyroid hormones and lipid metabolism/body fat content in euthyroid male patients with type 2 diabetes mellitus (T2DM) in China. Methods: A total of 64 male patients who were diagnosed as T2DM and 64 non-diabetic males who underwent health examination were matched according to age at a 1:1 ratio. Results: The 32 subjects in each sub-group showed differences in age, body mass index (BMI), mean arterial pressure, waist circumference, visceral fat content, body fat percentage, HbA1c, HOMA-IR, FT3, TSH, HDL-c, adiponectin, leptin, visfatin and TNF-α (all $P < 0.05$). In the overall population, FT3 was positively correlated with body fat percentage ($r=0.21$, $P=0.02$), and negatively correlated with HOMA-IR ($r=-0.18$, $P=0.04$) and visfatin ($r=-0.47$, $P <0.01$); TSH was positively correlated with body fat percentage ($r=0.23$, $P=0.01$). In the T2DM-OB group FT3 was positively correlated with BMI ($r=0.45$, $P <0.05$), visceral fat content ($r=0.50$, $P <0.05$), and body fat percentage ($r=0.44$, $P <0.05$); FT4 was positively correlated with visceral fat content ($r=0.38$, $P <0.05$); and TSH was positively correlated with HOMA-IR ($r=0.39$, $P <0.05$). Conclusion: TSH increased in obese people and FT3 was lower in patients with T2DM.


# Background

In recent years, the prevalence of diabetes mellitus (DM) has been rising rapidly and it has become a prominent global public health problem. Currently, around 415 million people worldwide have diabetes, this accounts for 9% of the population, and this number is predicted to increase even further [1].

Insulin resistance is common in the pathogenesis of type 2 diabetes mellitus (T2DM) and metabolic syndrome [2, 3]. Metabolic syndrome is an accumulation of factors that increase the risk of disease, approximately 2-fold for cardiovascular disease and 5-fold or more for T2DM [4]. Insulin resistance is also a risk factor for stroke and other diseases such as end-stage renal disease [5]. Obesity is the basis of insulin resistance because of the destructive effects of excess fat accumulation on glucose metabolism, which causes functional impairments in metabolic pathways of several areas such as adipose tissue and peripheral organs, like liver, heart, pancreas and muscle [6].

Thyroid hormones, including thyroxine and triiodothyronine, regulate the synthesis, mobilization, and breakdown of lipids. Therefore, thyroid hormones are closely related to obesity, and slight changes of serum thyroid hormone level can cause local fat accumulation and increased body mass [7, 8]. The thyrotropin receptor (TSHR) has long been considered as a key regulator of thyroid function [9]. Recent studies have shown that thyroid stimulating hormone (TSH) can also directly bind to TSHR in tissues outside the thyroid to exert external effects, such as in the adipose tissue and liver [10].

The role of thyroid function in energy metabolism has been extensively studied, but traditional viewpoints only emphasize the role of hypothyroidism or subclinical hypothyroidism in obesity. Among patients with obesity but normal thyroid function, thyroid hormones, especially TSH, are significantly different from that of people of healthy weight. This manifests as the TSH, free triiodothyronine (FT3), and free thyroxine (FT4) of obese patients being higher than that of healthy people [11, 12]. The incidence of thyroid diseases in patients with T2DM is significantly increased, especially subclinical hypothyroidism (SCH), and is more common in women than men [13, 14]. However, the relationship between TSH, FT3, FT4 and adipocytokines and lipid metabolism in T2DM patients with normal thyroid function and people with normal blood glucose has not been reported.

The purpose of this study was to explore the changes in thyroid hormones in patients with T2DM and normal thyroid function, compared with people with normal blood glucose. We then studied the correlation between thyroid hormone

and lipid metabolism/body fat content.

## Methods

# Study design and subjects

This study was a prospective cross-sectional study, which included T2DM patients hospitalized in Lishui Central Hospital from January 2017 to June 2017. The inclusion criteria were: 1) older than 17 years old; 2) male; 3) normal thyroid function; 4) the diagnosis of diabetes met the WHO diagnostic criteria of 1999. The exclusion criteria were: 1) acute complications of diabetes mellitus; 2) pulmonary and heart diseases; 3) liver and kidney dysfunction; 4) clinical and subclinical thyroid diseases. Non-diabetic males who underwent a health examination from January 2017 to May 2017 in the physical examination center of our hospital were selected and matched according to age with the T2DM group at a 1:1 ratio. Diabetes mellitus, impaired glucose tolerance (IGT) and impaired fasting blood glucose (IFG) were excluded in the control group by oral glucose tolerance test (OGTT).

According to body mass index (BMI), the patients were divided into normal control group (NC, BMI < 25 kg/$m^2$), pure obesity group (SOB, BMI 25 kg/$m^2$), non-obesity diabetic group (T2DM-NOB), and diabetic obesity group (T2DM-OB).

This study was approved by the Ethics Committee of Lishui Central Hospital (Ethics No. 2016-26). All patients provided informed consent for inclusion in the study.

# Data collection

Baseline data was collected from all participants, including age, T2DM disease course, anthropometric, and laboratory measurements.

# Anthropometric measurements

Height (m), weight (kg), waist circumference and BMI (kg/$m^2$) were measured by uniformly trained nurses for all subjects. Body fat percentage and visceral fat content were measured by direct segmental-impedance measurement (InBody 720 human body composition analyzer, Shanghai baisibeisi medical equipment trading co., LTD. China). Blood pressure was recorded, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured at sitting position, and mean blood pressure (MBP) was calculated.

# Laboratory tests

After 12 hours of fasting overnight, blood from the elbow vein was collected into two sample tubes. The serum was centrifuged from one tube within 2 hours, and hematological parameters were determined immediately. Fasting blood glucose was detected by hexokinase (Abbott, USA), total cholesterol (TC) by CHOD-PAP (Zhongya Company, China), triglyceride (TG) by GPO-PAP (Zhongya Company), high density lipoprotein (HDL-C) and low density lipoprotein (LDL-C) by homogeneous direct method (Zhongya Company), fasting insulin (FIns) by chemiluminescence method (Abbott, USA), and glycosylated hemoglobin (HbA1C) by ion chromatography (TOSOH, Japan). Blood TSH, FT3 and FT4 were detected by chemiluminescence (Abbott, USA), and the normal reference ranges of TSH were 0.34–5.60 uIU/ml, FT3 1.71–3.71 pg/ml and FT4 0.70–1.48 ng/dl, respectively.

After adding anticoagulant to the other tube, the plasma was centrifuged and preserved at − 70 °C for the determination of adiponectin, leptin, visfatin and tumor necrosis factor alpha (TNF-α). The laboratory determination was by Shanghai Enzyme-linked Biotechnology Co., Ltd., China. The standard curve of plasma adiponectin was 0.156-10 ng/ml, leptin was 0–50 ng/ml, visfatin was 0.1–1000 ng/ml, and plasma TNF-α was 2.5–80 pg/mL.

The insulin resistance index (HOMA-IR) was calculated by the minimum homeostasis model. The formula was FPG*FINS/22.5.

## Statistical analysis

All data were processed by SPSS 21.0 (IBM Corp., Armonk, NY, USA) statistical software. Continuous variables were first tested for normality. Normally distributed continuous variables were expressed by mean ± SD and multi-group comparison was conducted by analysis of variance (ANOVA) and post-test (SNK-q). Non-normally distributed continuous variables were expressed by median (range) and multi-group comparison was conducted by Kruskal-Wallis H test. Linear correlation analysis was used for univariate analysis and multiple linear regression analysis was used for multivariate analysis. $P < 0.05$ was considered statistically significant.

# Results

## Baseline characteristics

A total of 128 male patients were enrolled, including NC, SOB, T2DM-NOB and T2DM-OB groups with 32 subjects in each group. There were statistical differences in age, BMI, mean arterial pressure (MAP), waist circumference, visceral fat content and body fat percentage among the four groups (all $P < 0.05$). Post-hoc comparison between pairs of groups showed that the SOB group was significantly different to the NC group in BMI, MAP, waist circumference, visceral fat content and body fat percentage (all $P < 0.05$). The T2DM-NOB group was significantly different to the NC and SOB groups in age, BMI, waist circumference and visceral fat content (all $P < 0.05$)., but only significantly different to the NC group in MAP and the SOB group in body fat percentage. BMI, waist circumference, visceral fat content and body fat percentage were significantly different between the T2DM-NOB group and T2DM-OB group (all $P < 0.05$). There was no statistically significant difference in age, course of diabetes mellitus ($P = 0.49$) and MAP between the T2DM-NOB and T2DM-OB group (Table 1).

Table 1
Baseline characteristics

| | NC group | SOB group | T2DM-NOB group | T2DM-OB group | P |
|---|---|---|---|---|---|
| No. | 32 | 32 | 32 | 32 | |
| Age, years, mean ± SD | 44.34 ± 7.53 | 43.41 ± 6.94 | 51.47 ± 10.32 [a,b] | 47.81 ± 8.36 | < 0.05 |
| Course of diabetes mellitus, years, mean ± SD | - | - | 4.59 ± 4.58 | 5.37 ± 4.36 | 0.49 |
| BMI, $Kg/m^2$, mean ± SD | 21.42 ± 1.90 | 27.15 ± 1.76 [a] | 22.58 ± 1.78 [a,b] | 27.89 ± 2.51 [a,c] | < 0.05 |
| MAP, mmHg, mean ± SD | 88.21 ± 10.00 | 94.21 ± 9.05 [a] | 96.15 ± 11.81 [a] | 99.06 ± 13.75 [a] | < 0.05 |
| Waist circumference, mm | 79.59 ± 6.13 | 91.42 ± 5.67 [a] | 84.23 ± 6.16 [a,b] | 94.44 ± 8.23 [a,c] | < 0.05 |
| Visceral fat content, %, mean ± SD | 78.41 ± 20.00 | 118.09 ± 14.39 [a] | 96.52 ± 21.08 [a,b] | 123.56 ± 25.29 [a,c] | < 0.05 |
| Body fat percentage, %, mean ± SD | 18.31 ± 5.08 | 28.41 ± 3.37 [a] | 20.36 ± 4.74 [b] | 26.42 ± 6.09 [a,c] | < 0.05 |
| NC: normal weight control group; SOB: simple obesity group; T2DM-NOB: non-obesity diabetic group; T2DM-OB: diabetic obesity group; SD: standard deviation; BMI: body mass index; MAP: mean arterial pressure. | | | | | |
| [a]Vs NC group, P < 0.05 | | | | | |
| [b]Vs SOB group, P < 0.05 | | | | | |
| [c]Vs T2DM-NOB, P < 0.05 | | | | | |

# Laboratory test results

There were significant differences in HbA1c, HOMA-IR, FT3, TSH, HDL-c, adiponectin, leptin, visfatin and TNF-α (all P < 0.05) and no significant difference in FT4, TC, TG, and LDL-C (all P > 0.05) among the four groups. Post-hoc comparison between the two groups showed that the SOB group was significantly different from the NC group in HOMA-IR, TSH, leptin, visfatin and TNF-α (all P < 0.05). The two T2DM groups were significantly different from the NC group in HBA1c%, HOMA-IR, FT3 HDL-C and visfatin; while only the T2DM-NOB group was significantly different to the NC group in terms of TNF-α and only the T2DM-OB group was significantly different in terms of leptin and adiponectin (all P < 0.05). The T2DM groups were significantly different from the SOB group in HbA1c%, FT3, leptin, visfatin and TNF-α, while only the T2DM-NOB group was significantly different in terms of TSH and only the T2DM-OB group was significantly different in HDL-C and adiponectin (all P < 0.05). FT3, TSH, adiponectin, leptin and TNF-α were significantly different in the T2DM-NOB and T2DM-OB groups (all P < 0.05). There was no significant difference in fasting blood glucose (P = 0.61) and fasting insulin (P = 0.81) between the T2DM-NOB and T2DM-OB group (Table 2).

Table 2
Comparison of laboratory tests in four groups

| | NC | SOB | T2DM-NOB | T2DM-OB | P |
|---|---|---|---|---|---|
| No. | 32 | 32 | 32 | 32 | |
| Fasting blood glucose | | | 10.21 ± 5.17 | 9.57 ± 4.64 | 0.61 |
| Fasting Insulin | | | 8.22 ± 7.05 | 8,61 ± 5.32 | 0.81 |
| HbA1c% | 5.44 ± 0.28 | 5.45 ± 0.32 | 9.05 ± 3.82 [a,b] | 9.54 ± 1.95 [a,b] | < 0.05 |
| HOMA-IR | 1.42 ± 0.79 | 2.70 ± 1.23 [a] | 3.02 ± 1.86 [a] | 3.43 ± 2.11 [a] | < 0.05 |
| FT3, pg/ml | 3.05 ± 0.37 | 3.15 ± 0.20 | 2.40 ± 0.42 [a,b] | 2.71 ± 0.38 [a,b,c] | < 0.05 |
| FT4, ng/dl | 1.07 ± 0.09 | 1.19 ± 0.84 | 1.00 ± 0.14 | 1.04 ± 0.13 | 0.35 |
| TSH, uiu/m | 1.55 ± 0.45 | 1.95 ± 0.74 [a] | 1.29 ± 0.58 [b] | 1.80 ± 0.57 [c] | < 0.05 |
| TC, mmol/L | 4.85 ± 0.83 | 5.18 ± 0.82 | 4.69 ± 1.39 | 4.84 ± 1.18 | 0.33 |
| TG, mmol/L | 1.59 ± 0.89 | 2.16 ± 1.28 | 1.68 ± 1.42 | 2.39 ± 1.68 | 0.06 |
| HDL-c, mmol/L | 1.26 ± 0.24 | 1.17 ± 0.28 | 1.06 ± 0.27 [a] | 1.00 ± 0.23 [a,b] | < 0.05 |
| LDL-c, mmol/L | 2.83 ± 0.58 | 3.12 ± 0.64 | 2.81 ± 1.18 | 2.68 ± 0.69 | 0.18 |
| Adiponectin, ug/mL | 4.92 ± 0.62 | 5.11 ± 0.63 | 4.89 ± 0.60 | 5.77 ± 0.54 [a,b,c] | < 0.05 |
| Leptin, ng/mL | 2.92 ± 0.27 | 3.12 ± 0.30 [a] | 2.91 ± 0.24 [b] | 3.40 ± 0.29 [a,b,c] | < 0.05 |
| Visfatin, ng/mL | 23.71 ± 2.58 | 19.89 ± 2.86 [a] | 29.71 ± 3.65 [a,b] | 28.60 ± 2.55 [a,b] | < 0.05 |
| TNF-α, pg/mL | 20.48 ± 1.70 | 14.43 ± 1.72 [a] | 16.10 ± 1.85 [a,b] | 19.76 ± 1.62 [b,c] | < 0.05 |

NC: normal weight control group; SOB: simple obesity group; T2DM-NOB: non-obesity diabetic group; T2DM-OB: diabetic obesity group; TSH: thyroid stimulating hormone; FT3: free triiodothyronine; FT4: free thyroxine; TC: total cholesterol; TG: triglyceride; HDL-C: high density lipoprotein; LDL-C: low density lipoprotein; HbA1C: glycosylated hemoglobin; HOMA-IR: insulin resistance index; TNF-α: tumor necrosis factor-alpha.

[a]Vs NC group, P < 0.05

[b]Vs SOB group, P < 0.05

[c]Vs T2DM-NOB, P < 0.05

# Correlation analysis

In the overall population, after adjustment for age, MAP, and waist circumference, FT3 was positively correlated with body fat percentage (r = 0.21, P = 0.02), and negatively correlated with HOMA-IR (r=-0.18, P = 0.04) and visfatin (r=-0.47, P < 0.01). There was no significant correlation between FT4 and fat distribution/metabolism. TSH was positively correlated with body fat percentage (r = 0.23, P = 0.01). (Table 3)

Table 3

Partial correlation analysis of thyroid hormone and fat metabolism/distribution in the whole population

| | FT3 | | FT4 | | TSH | |
|---|---|---|---|---|---|---|
| | r | P value | r | P value | r | P value |
| BMI | 0.06 | 0.50 | 0.11 | 0.21 | 0.12 | 0.15 |
| Visceral fat content | 0.16 | 0.07 | 0.06 | 0.51 | 0.10 | 0.26 |
| Body fat percentage | 0.21 | 0.02 | 0.11 | 0.23 | 0.23 | 0.01 |
| HOMA-IR | -0.18 | 0.04 | -0.05 | 0.57 | 0.10 | 0.24 |
| Adiponectin | -0.07 | 0.40 | 0.04 | 0.67 | 0.04 | 0.65 |
| Leptin | -0.04 | 0.61 | 0.11 | 0.21 | 0.11 | 0.23 |
| Visfatin | -0.47 | < 0.01 | -0.06 | 0.49 | -0.17 | 0.06 |
| TNF-α | 0.13 | 0.15 | 0.02 | 0.86 | 0.09 | 0.31 |
| Adjusted for age, MAP and waist circumference | | | | | | |
| TSH: thyroid stimulating hormone; FT3: free triiodothyronine; FT4: free thyroxine; HOMA-IR: insulin resistance index; TNF-α: tumor necrosis factor-alpha; BMI: body mass index; MAP: mean arterial pressure. | | | | | | |

Subgroup analysis showed that in the T2DM-OB group FT3 was positively correlated with BMI ($r = 0.45$, $P < 0.05$), visceral fat content ($r = 0.50$, $P < 0.05$), and body fat percentage ($r = 0.44$, $P < 0.05$); FT4 was positively correlated with visceral fat content ($r = 0.38$, $P < 0.05$); and TSH was positively correlated with HOMA-IR ($r = 0.39$, $P < 0.05$) (Table 4).

Table 4

Partial correlation analysis of thyroid hormone and fat metabolism/distribution in each subgroup

| | NC | | | SOB | | | T2DM- NOB | | | T2DM- OB | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | FT3 | FT4 | TSH | FT3 | FT4 | TSH | FT3 | FT4 | TSH | FT3 | FT4 | TSH |
| | r | r | r | r | r | r | r | r | r | r | r | r |
| BMI | -0.18 | -0.24 | 0.21 | 0.19 | 0.23 | -0.03 | 0.04 | -0.09 | -0.18 | 0.45* | 0.36 | -0.12 |
| Visceral fat content | -0.10 | -0.03 | 0.13 | 0.19 | 0.06 | 0.02 | -0.24 | -0.04 | 0.11 | 0.50* | 0.38* | -0.24 |
| Body fat percentage | -0.06 | -0.09 | 0.30 | 0.36 | 0.11 | 0.24 | -0.26 | 0.14 | 0.22 | 0.44* | 0.33 | -0.12 |
| HOMA-IR | 0.14 | -0.35 | 0.26 | -0.21 | 0.11 | 0.27 | -0.09 | -0.03 | -0.09 | 0.16 | 0.11 | 0.39* |
| Adiponectin | -0.08 | 0.24 | -0.01 | -0.05 | -0.09 | -0.13 | -0.02 | 0.27 | 0.01 | 0.18 | 0.26 | 0.08 |
| Leptin | 0.24 | -0.01 | -0.21 | -0.01 | 0.14 | 0.03 | -0.02 | 0.28 | 0.30 | -0.23 | -0.06 | 0.12 |
| Visfatin | -0.01 | -0.11 | 0.08 | -0.05 | 0.07 | -0.08 | -0.19 | -0.05 | -0.05 | 0.13 | 0.14 | 0.25 |
| TNF-α | 0.05 | 0.24 | 0.16 | 0.06 | 0.23 | 0.32 | 0.34 | 0.11 | 0.24 | 0.31 | 0.21 | -0.05 |
| Adjusted for age, MAP and waist circumference | | | | | | | | | | | | |
| * the correlation was significant (P < 0.05). | | | | | | | | | | | | |
| TSH: thyroid stimulating hormone; FT3: free triiodothyronine; FT4: free thyroxine; HOMA-IR: insulin resistance index; TNF-α: tumor necrosis factor-alpha; BMI: body mass index; MAP: mean arterial pressure. | | | | | | | | | | | | |

# Discussion

The aim of this study was to investigate the relationship between thyroid hormones and lipid metabolism/body fat content in patients with T2DM. We enrolled male patients with T2DM and matched them with control subjects with normal blood glucose, and then subdivided both populations into those with and without obesity according to their BMI. The results showed that HbA1c, HOMA-IR, FT3, TSH, HDL-c, adiponectin, leptin, visfatin and TNF-α were significantly different between the four groups, and pairwise comparison showed many of the measures were different between groups. Overall, FT3 was positively correlated with body fat percentage, and negatively correlated with HOMA-IR and visfatin; TSH was positively correlated with body fat percentage. In the T2DM-OB group FT3 was positively correlated with BMI, visceral fat content, and body fat percentage; FT4 was positively correlated with visceral fat content; and TSH was positively correlated with HOMA-IR.

Previous studies have shown that thyroid metabolism is closely related to obesity and T2DM even in euthyroid patients [11–14]. However, the complexity of the mechanism is highlighted by different results depending on the populations studied. A previous study from China in patients with diabetes showed that TSH was higher in females than males and that TSH was positively associated with serum TC and LDL-C in women with T2DM [15]. In this study, all the subjects were males, and the interference of sex hormones on thyroid function and lipid metabolism could be excluded. Javed A [7] et al. found hyperthyrotrophin (TSH) in obese adolescents with normal thyroid function. In this study, TSH was positively correlated with body fat percentage in a normal thyroid function population; but there was no correlation between TSH and lipid metabolism. The results of this study also suggest that in the total population

FT3 was positively correlated with body fat percentage and negatively correlated with HOMA-IR and visfatin. A previous study showed that progressive central fat accumulation was associated with an increase in both FT3 and TSH serum levels in women, but this was independent of insulin resistance [16]. This result merits further examination in men.

TSHR expression on adipocyte surface is positively correlated with obesity and elevated serum TSH is an important risk factor for metabolic syndrome and positively correlated with insulin resistance [17, 18]. It has been reported that thyroid microstructure disorder exists in T2DM patients with normal thyroid hormone levels, and the degree of disorder is related to blood glucose level and insulin resistance index [19]. In this study, there was a positive correlation between TSH and HOMA-IR in the T2DM-OB group, which also supported the above opinion, suggesting that TSH may be involved in the early onset of T2DM, and the increase of TSH may be part of the pathogenesis of metabolic disorders in the development of early T2DM. However, another study found no significant difference in HOMA-IR and BMI values among a population including patients with subclinical hypothyroidism who were classified according to TSH levels [20]. A larger study of 2758 male subjects also suggested a negative association of T4 with insulin resistance in Iranians [21]. We did not see this association in this study, but a larger sample size may be needed.

Adipose tissue is an organ that actively participates in the balance of energy metabolism. Adipose tissue can secrete many adipocytokines to regulate the functions of itself and other tissues, such as adiponectin, leptin, and visfatin. Lu et al. [18] believed that TSHR was an important regulator of adipocyte differentiation and TSH may act on adipocytes expressing TSHR, thus changing the growth and differentiation of adipocytes and regulating the secretion of various adipokines in adipocytes. However, in this study, TSH was not correlated with adipokines, which may be related to the limitations of the study such as the small number of samples. A larger sample size would allow further quartile analysis can be conducted.

## Conclusions

In conclusion, thyroid hormone is closely related to lipid metabolism and may also be involved in the early onset of T2DM with normal thyroid function. Changes in thyroid hormone levels, such as increased TSH in obese people and lower FT3 in T2DM, may be part of the pathogenesis of metabolic disorders. FT3 may be involved in the pathogenesis of diabetes through adipocytokine mediation and may be involved in the regulation of blood glucose.

## List Of Abbreviations

T2DM : Type 2 diabetes mellitus

TSH: Thyroid stimulating hormone

FT3: Free triiodothyronine

FT4 : Free thyroxine

SCH: Subclinical hypothyroidism

BMI: Body mass index

MBP: Mean blood pressure

HDL-C: High density lipoprotein

LDL-C: Low density lipoprotein

HOMA-IR: Insulin resistance index

NC: Normal control group

SOB: Obesity group

T2DM-NOB: Non-obesity diabetic group

T2DM-OB: Diabetic obesity group

# Declarations

**Ethics approval and consent to participate:** This study was approved by the Ethics Committee of Lishui Central Hospital (Ethics No. 2016-26). All patients provided informed consent for inclusion in the study.

**Consent for publication:** Written informed consent was obtained from the patients.

**Availability of data and materials:** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors have no conflict of interest to declare

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**Authors' contributions:** XS conceived of the study and designed the study RW , DZ and YH collected the data. XS and LC did the analyses, XS wrote the paper.

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# References

1. Jaacks LM, Siegel KR, Gujral UP, Narayan KM. Type 2 diabetes: A 21st century epidemic. Best Pract Res Clin Endocrinol Metab. 2016;30(3):331-43.
2. DeFronzo RA. Pathogenesis of type 2 diabetes mellitus. Med Clin North Am. 2004;88(4):787-835, ix.
3. Guo S. Insulin signaling, resistance, and the metabolic syndrome: insights from mouse models into disease mechanisms. J Endocrinol. 2014;220(2):T1-t23.
4. Samson SL, Garber AJ. Metabolic syndrome. Endocrinol Metab Clin North Am. 2014;43(1):1-23.
5. Maffi P, Secchi A. The Burden of Diabetes: Emerging Data. Dev Ophthalmol. 2017;60:1-5.
6. Yazici D, Sezer H. Insulin Resistance, Obesity and Lipotoxicity. Adv Exp Med Biol. 2017;960:277-304.
7. Javed A, Balagopal PB, Vella A, Fischer PR, Piccinini F, Dalla Man C, et al. Association between thyrotropin levels and insulin sensitivity in euthyroid obese adolescents. Thyroid. 2015;25(5):478-84.
8. Iwen KA, Schroder E, Brabant G. Thyroid hormones and the metabolic syndrome. Eur Thyroid J. 2013;2(2):83-92.

9. Kleinau G, Biebermann H. Constitutive activities in the thyrotropin receptor: regulation and significance. Adv Pharmacol. 2014;70:81-119.
10. Williams GR. Extrathyroidal expression of TSH receptor. Ann Endocrinol (Paris). 2011;72(2):68-73.
11. Muscogiuri G, Sorice GP, Mezza T, Prioletta A, Lassandro AP, Pirronti T, et al. High-normal TSH values in obesity: is it insulin resistance or adipose tissue's guilt? Obesity (Silver Spring). 2013;21(1):101-6.
12. Erdogan M, Canataroglu A, Ganidagli S, Kulaksizoglu M. Metabolic syndrome prevalence in subclinic and overt hypothyroid patients and the relation among metabolic syndrome parameters. J Endocrinol Invest. 2011;34(7):488-92.
13. Ozair M, Noor S, Raghav A, Siddiqi SS, Chugtai AM, Ahmad J. Prevalence of thyroid disorders in North Indian Type 2 diabetic subjects: A cross sectional study. Diabetes Metab Syndr. 2018;12(3):301-4.
14. Zhou CP. Study on the relationship between subclinical hypothyroidism and diabetic vascular complications in type 2 diabetes mellitus. New World of Diabetes. 2017;20(14):69-70.
15. Zhang Y, Lu P, Zhang L, Xiao X. Association between lipids profile and thyroid parameters in euthyroid diabetic subjects: a cross-sectional study. BMC Endocr Disord. 2015;15:12.
16. De Pergola G, Ciampolillo A, Paolotti S, Trerotoli P, Giorgino R. Free triiodothyronine and thyroid stimulating hormone are directly associated with waist circumference, independently of insulin resistance, metabolic parameters and blood pressure in overweight and obese women. Clin Endocrinol (Oxf). 2007;67(2):265-9.
17. Lai Y, Wang J, Jiang F, Wang B, Chen Y, Li M, et al. The relationship between serum thyrotropin and components of metabolic syndrome. Endocr J. 2011;58(1):23-30.
18. Lu S, Guan Q, Liu Y, Wang H, Xu W, Li X, et al. Role of extrathyroidal TSHR expression in adipocyte differentiation and its association with obesity. Lipids Health Dis. 2012;11:17.
19. Liu Z, Liu Q, Wu L. A study of thyroid axis microdisorders in type 2 diabetes mellitus patients with normal thyroid function. Hebei Medicine. 2017;39(14):2109-12.
20. Aksoy N, Yeler MT, Ayan NN, Ozkeskin A, Ozkan Z, Serin NO. Association between thyroid hormone levels and insulin resistance and body mass index. Pak J Med Sci. 2015;31(6):1417-20.
21. Amouzegar A, Kazemian E, Gharibzadeh S, Mehran L, Tohidi M, Azizi F. Association between thyroid hormones, thyroid antibodies and insulin resistance in euthyroid individuals: A population-based cohort. Diabetes Metab. 2015;41(6):480-8.