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ORIGINAL PAPER

Comparison of triglyceride-glucose index and HOMA-IR as indicators of insulin resistance in obese women with subclinical hypothyroidism

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ABSTRACT

Introduction and aim. Thyroid hormones play an important role in glucose metabolism as in many metabolic events. The aim of our study is to evaluate the relationship between subclinical hypothyroidism (SCH) and insulin resistance, especially in obese women.

Material and methods. Newly diagnosed SCH patients with body mass index (BMI) ≥30 who applied to our outpatient clinic between March 2021 and October 2021, and euthyroid obese women who applied for routine control were included in the study. In this study, we used homeostasis model assessment of insulin resistance (HOMA-IR) and triglyceride glucose (TyG) indexes, which are noninvasive, simple and useful methods for evaluating insulin sensitivity.

Results. The study included 78 female patients between the ages of 19 and 64. A correlational analysis was performed between thyroid stimulating hormone (TSH) and HOMA-IR, TyG, and BMI. The results showed that TSH levels were positively correlated with HOMA-IR (R=0.297, p=0.008), TyG (R=0.316, p=0.005) and BMI (R=0.307, p=0.006). This relationship was stronger for TyG compared to the other variables. As another finding, BMI was positively correlated with HOMA-IR (R=0.359, p=0.001) and TyG (R=0.404, p<0.001). This relationship was stronger for TyG than HOMA-IR.

Conclusion. These results show that patients with SCH are at risk of developing diseases that accompany insulin resistance, such as metabolic syndrome and cardiovascular disorders. The most important finding of our study is that the TyG index gives more significant results than HOMA-IR, especially in obese women.

Keywords. HOMA-IR, insulin resistance, subclinical hypothyroidism, triglyceride-glucose index

Introduction

Subclinical hypothyroidism (SCH) is defined as a serum thyroid-stimulating hormone (TSH) level above the upper limit of normal despite normal levels of serum free thyroxine.[1] Its incidence in general population surveys varies between 3% and 8%.[2] It is likely to go undiagnosed for a long time, as it usually does not cause significant symptoms in patients. Even if SCH does not cause significant discomfort in patients, it is metabolically associated with many conditions. It has been shown that it may increase the risk of obesity and SCH can cause cardiovascular diseases due to hyperuricemia, and heart failure may develop due to decreased myocardial contractility.[3,4] In addition, previous studies suggest that SCH raises blood pressure and cholesterol levels, impairs insulin secretion, and increases the risk of peripheral neuropathy, peripheral arterial disease, and diabetic

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nephropathy by damaging both micro and macrovascular function.[5]

Thyroid hormones play an important role in glucose metabolism as in many metabolic events. In animal studies performed during the fetal period, it has been shown that free T3 levels have a significant effect on hepatic and cardiac glycogen stores.[6] Increased T3 concentrations are associated with an increase in glucose turnover and an increase in insulin-mediated glucose flux into skeletal muscle and adipocytes, through the insulin-sensitive glucose transporter-4.[7]

Many studies have shown that there is a strong relationship between overt hypothyroidism and metabolic syndrome, type 2 diabetes mellitus and obesity.[8,9] Although most of the studies show that SCH also increases the risk of these disorders, there are also publications suggesting that there is less relationship between SCH and these diseases.[10] Insulin resistance is defined as a decreased response to insulin at normal concentrations in the circulation. Insulin resistance can be seen in non-diabetic obese individuals and in type 2 diabetic patients.[11] The pathophysiological reasons underlying insulin resistance have not been adequately clarified yet. Generally, insulin resistance is seen as a result of insulin activity defect.

Aim

The aim of our study is to evaluate the relationship between SCH and insulin resistance, especially in obese women who are in the risk group for metabolic diseases. In this study, we used Homeostasis model assessment of insulin resistance (HOMA-IR) and triglyceride glucose (TyG) indexes, which are noninvasive, simple and useful methods for evaluating insulin sensitivity. This is the first study showing the relationship between newly diagnosed SCH obese women and insulin resistance evaluated with TyG in our knowledge.

Material and methods

Study was approved by the institutional review board, and a waiver of authorization was given (Ethics Committee decision no: 02, date: 26.08.2022).

This retrospective study included 78 subjects as a patient group of 48 females and control group of 30 females. Newly diagnosed SCH patients with body mass index (BMI) ≥30 who applied to our outpatient clinic between March 2021 and October 2021, and euthyroid obese women who applied for routine control were included in the study. Demographic data and assay results of the patients were evaluated retrospectively. Patients with diabetes mellitus, dyslipidemia, hypertension, rheumatological disease, malignancy, pregnancy and known thyroid disease were excluded from the study. Patients with infection, high acute phase markers, and patients using drugs such as corticosteroids with known effects on insulin resistance were not included in the study. The TyG index was calculated as ln[fasting triglycerides (mg/dL) × fasting glucose (mg/dL)/2]. The HOMA-IR index was calculated using the following formula: HOMA-IR = fasting insulin (μU/mL) × fasting glucose (mg/dL)/405.

Statistical analyses of the data obtained in the study were made using SPSS version 26.0 software (IBM, Armonk, NY, USA). Conformity of the data to normal distribution was examined visually (histogram and probability graphs) and with the analytical method of the Kolmogorov-Smirnov test. Results for quantitative variables are expressed as mean ± SD for normally distributed data; and mean (interquartile range) for non-parametric data. Comparisons of quantitative variables between the groups were made using the Student's t-test or the Mann Whitney U-test according to the conformity of the data to normal distribution. The Spearman's correlation coefficient was applied to measure the correlation between various parameters. A two-sided value < 0.05 was considered statistically significant.

Results

The study included 78 female patients between the ages of 19 and 64. The mean age of the patients was 40.2±10.7. Both groups were similar in terms of age (p=0.087). Patients compared to HOMA-IR and TyG index scores, the median HOMA-IR (p=0.044) and TyG index scores (p=0.016) were higher in the SCH group. When the groups were compared in terms of BMI levels, SCHs had higher BMI levels than controls (p=0.037). According to the laboratory parameters, the mean values of Triglyceride (Tg) were higher in the SCH group (p=0.029), and no difference was determined in respect of fasting glucose (p=0.078), insulin (p=0.062), and LDL (p=0.223) levels. The demographic and clinical characteristics of all study patients are shown in Table 1.

Table 1. Characteristics of the study sample: study group vs. control group*

	Total, n=78	Control group, n=30	Study group, n=48	p
Age (Years)	40.2±10.7	37.6±10.0	41.8±10.9	0.087
BMI (kg/m^2)	33 (32–35)	32 (31–34)	34 (32–36)	0.037
Fasting glucose	96 (89–104)	93 (87–100)	98 (91–105)	0.078
Insulin (uIU/mL)	9.3 (6.4–15)	8.4 (5.2–11.6)	10.9 (7.1–15.6)	0.062
HOMA-IR	2.3 (1.5–3.4)	1.8 (1.1–2.7)	2.6 (1.7–3.9)	0.044
TyG index	4.7 (4.5–4.9)	4.6 (4.4–4.7)	4.8 (4.5–5)	0.016
LDL (mg/dL)	93 (68–113)	88 (66–109)	100 (69–116)	0.223
Tg (mg/dL)	122 (92–164)	109 (81–140)	140 (96–197)	0.029
TSH (mIU/L)	6.3 (2.3–7.8)	2 (1.6–4)	7.5 (6.5–8)	<0.001

*LDL – low-density lipoprotein; BMI – body mass index, TyG – triglyceride-glucose; Tg – triglyceride; TSH – thyroid stimulating hormone

A correlational analysis was performed between TSH and HOMA-IR, TyG, and BMI. The results showed

that TSH levels were positively correlated with HOMA-IR (R=0.297, p=0.008), TyG (R=0.316, p=0.005) and BMI (R=0.307, p=0.006). This relationship was stronger for TyG compared to the other variables. As another finding, BMI was positively correlated with HOMA-IR (R=0.359, p=0.001) and TyG (R=0.404, p<0.001). This relationship was stronger for TyG than HOMA-IR. Correlations for study variables are shown in Table 2.

Table 2. Correlation matrix of study variables[a]

		HOMA-IR		TyG index		TSH		BMI
HOMA-IR	R	—						
	p	—						
TyG index	R	0.274	*	—				
	p	0.015		—				
TSH	R	0.297	**	0.316	**	—		
	p	0.008		0.005		—		
BMI	R	0.359	**	0.404	***	0.307	**	—
	p	0.001		<0.001		0.006		—

* p<0.05, ** p<0.01, *** p<0.001; TyG – triglyceride-glucose; BMI – body mass index; TSH – thyroid stimulating hormone

Discussion

Hyperinsulinemic euglycemic clamp technique is the gold standard method for determining insulin sensitivity, but this method is an expensive and invasive procedure and can only be used for research purposes.[11] Therefore, non-invasive methods have been developed to measure insulin resistance. One of the most commonly used methods for this purpose is HOMA-IR. Recently, TyG index, which is calculated by Tg level and fasting glucose level, has been proposed as a reliable and simple indicator of insulin resistance in many studies. It has been shown in some studies that the TyG index is more significant than HOMA-IR and even correlates with the hyperinsulinemic euglycemic clamp method.[12,13] In this study, we evaluated the relationship between SCH and insulin resistance using both these methods.

Pergola et al., in their study on euthyroid obese women, progressive central fat accumulation is associated with a parallel increase in FT3 levels, and it was thought that this might be due to a thermogenic phenomenon.[14] In the same study, it is stated that as the BMI level increases, the feedback effect of free thyroid hormones on TSH may be impaired.[14] In the study by Singh et al., the BMI values of patients with both SCH and overt hypothyroidism were found to be higher than the control group.[15] In our study, a significant positive correlation was found between TSH level and BMI.

Overt hypothyroidism has been shown to be associated with glucose intolerance and insulin resistance in many studies, and it has been found that these disorders ameliorate as a result of conversion to euthyroid state with levothyroxine treatment.[16,17] There are studies showing that the mechanism of development of insulin resistance in hypothyroidism occurs as a result of decreased sensitivity to insulin in skeletal muscle and adipose tissue.[18] However, this relationship could not be revealed so clearly in SCH. Conflicting results have been observed in previous studies. While Shanta et al. found a significant relationship between TSH and insulin resistance in female patients with SCH, another study by Owecki et al. found no significant relationship between TSH level and HOMA-IR.[19,20]

Choi et al. study on 5727 patients showed that the association between SCH and TyG index was only statistically significant in females with hypothyroidism. In female patients, association is evident with subclinical thyroid dysfunction.[21] In the same study, the authors also evaluated the relationship between SCH and the HOMA-IR and they found that TSH was not significantly correlated with HOMA-IR.[21] In our study, we found that both HOMA-IR and TyG indices were statistically correlated with TSH values. However, this relationship was more significant for TyG. We think that the difference between the HOMA-IR values in these two studies is due to the inclusion of only obese patients in our study. Both Choi et al.'s study and our study suggest that the TyG index is more significant than HOMA-IR in demonstrating insulin resistance in SCH patients. The TyG index is a better indicator of peripheral IR as it mainly reflects the IR in the muscle. In contrast, HOMA-IR reflects IR mainly in the liver and is a better indicator for hepatic IR. Therefore, these differences can be observed.[22,23]

The relationship between SCH and lipid parameters has been evaluated in many studies before. Although there are conflicting results in studies between SCH and LDL, it is seen that SCH increases the Tg level in many studies. While no significant relationship was found between TSH level and LDL in the study by Pergola et al., a statistically significant relationship was found between SCH and LDL in the study conducted by Ebrahimpour et al.[9,14] In the review published by Fatourechi, it was stated that levothyroxine replacement in SCH patients did not have a significant effect on LDL.[2] Since the Tg value, which is also used in the calculation of the TyG index, shows a positive correlation with TSH, it is statistically significant as a result of our study. This correlation seems to be compatible with previous studies.

This work had some limitations. First, this study was a retrospective and single-centre analysis with a limited sample size. In addition, due to the retrospective nature of the study, free T3 levels of many patients could not be reached.

Conclusion

As a result, it was observed that patients with SCH had increased insulin resistance and Tg levels. BMI levels of SCH patients were also found to be higher than the con-

trol group. These results show that patients with SCH are at risk of developing diseases that accompany insulin resistance, such as metabolic syndrome and cardiovascular disorders. In our opinion, the most important finding of our study is that the TyG index gives more significant results than HOMA-IR, especially in obese women. Initiation of levothyroxine replacement therapy may be considered in patients with SCH in order to reduce the risk of metabolic diseases mentioned above. More comprehensive prospective studies are needed in this regard.

Declarations

Funding

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Author contributions

Conceptualization, C.O.K. and H.A.F.; Methodology, C.O.K.; Software, H.A.F.; Validation, V.S. and C.O.K.; Formal Analysis, H.A.F.; Investigation, C.O.K. and V.S.; Resources, C.O.K.; Data Curation, H.A.F.; Writing – Original Draft Preparation, C.O.K. and V.S.; Writing – Review & Editing, C.O.K. and H.A.F.; Visualization, V.S.; Supervision, H.A.F.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

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

Ethics approval

Study was approved by the institutional review board, and a waiver of authorization was given (Ethics Committee decision no: 02, date: 26.08.2022).

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