Original Article / Özgün Araştırma

The Role of Triglyceride-HDL Ratio and Triglyceride-glucose Index in Estimating Glycemic Control in Patients with Type 2 Diabetes Mellitus

Tip 2 Diabetes Mellitus Hastalarında Glisemik Kontrol Tahmininde Trigliserit-HDL Oranı ve Trigliserit-glukoz İndeksinin Rolü

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Abstract

Objective: Our aim is to evaluate blood glucose regulation in patients with diabetes using the triglyceride glucose index and the triglyceride to high density lipoprotein (HDL) ratio.

Materials and Methods: The data of our retrospective study were obtained from the database of our hospital. The study was conducted with 340 type 2 patients with diabetes. Demographic data of the patients, glucose, hemoglobin A1c (HbA1c), high density lipoproteine-cholesterol (HDL-C), triglyceride, alanine aminotransferase (ALT) and creatinine values were recorded. The value obtained from the study was evaluated with the SPSS 21 version program.

Results: Of the participants, 202 were female and 138 were male. Patients were divided into groups according to the percentage of HbA1cs. In the group with HbA1c ≥7%, triglyceride/HDL value, triglyceride-glucose index, fasting glucose, diabetes age, triglyceride values were statistically significantly higher, while HDL cholesterol was lower. We found a significant correlation between Triglyceride/HDL value, triglyceride glucose index with both glucose and HbA1c. The cut-off value of triglyceride-glucose (TyG) was 9.38.

Conclusion: TG/HDL and TyG index values are related with HbA1c. In particular, the TyG index, whose cut-off value determined between these two parameters, is a parameter that can be used to evaluate good glycemic control instead of HbA1c in cases where HbA1c cannot be measured.

Öz

Amaç: Amacımız, diyabetli hastalarda kan şekeri regülasyonunu trigliserit glikoz indeksi ve trigliseritin yüksek yoğunluklu lipoprotein'e (HDL) oranını temel alarak değerlendirmektir.

Gereç ve Yöntemler: Retrospektif çalışmamızın verileri hastanemizin veri tabanından elde edilmiştir. Çalışma 340 tip 2 diyabet hastası ile yapılmıştır. Hastaların demografik verileri, glukoz, hemoglobin A1c (HbA1c), HDL-kolesterol, trigliserit, alanin aminotransferaz (ALT), kreatinin değerleri kayıt edildi. Çalışmadan elde edilen veriler SPSS 21 versiyon program ile değerlendirildi.

Bulgular: Katılımcıların 202'si kadın, 138'i erkekti. Hastalar HbA1c yüzdelerine göre gruplara ayrıldı. HbA1c ≥%7 olan grupta trigliserit/HDL değeri, trigliserit-glukoz indeksi, açlık glukozu, diyabet yaşı, trigliserit değerleri istatistiksel olarak anlamlı daha yüksek iken HDL kolesterol daha düşüktü. Trigliserit/HDL değeri ve trigliserit

glukoz indeksi ile hem glukoz ve hem HbA1c arasında anlamlı bir ilişki saptandı. Kötü glisemik kontrollü (HbA1c ≥%7) hastalar için trigliserit-glukoz indeksi için cut-off değer 9,38 olarak saptandı.
Sonuç: Trigliserit/HDL ve trigliserit-glikoz (TyG) indeks değerleri HbA1c ile ilişkilidir. Özellikle bu iki parametre arasından cut-off değeri belirlenen TyG indeksi, HbA1c bakılamayan durumlarda HbA1c yerine iyi glisemik kontrolü değerlendirmek için kullanılabilecek bir parametredir.

Introduction

In type 2 diabetes (T2DM) insulin resistance occurs in peripheral tissues. Insulin resistance occurs in peripheral tissues. Insulin levels decrease due to decreased pancreatic beta cell function over time (1). In the presence of insulin resistance, glucose and free fatty acid levels rise. This causes an increase in very low density lipoprotein (VLDL), the triglyceride (TG) transporter. The increase in VLDL levels is also due to decreased clearance owing to the decreased lipoprotein lipase activity and decreased hepatic uptake. An increase in hypertriglyceridemia increases cholesterol ester transfer protein enzyme activity, resulting in decreased high density lipoprotein-cholesterol (HDL-C) and increased Low Density Lipoprotein-cholesterol (LDL-C) levels (1).

The decrease in pancreatic beta cell reserve may develop due to many factors, and exposure of beta cells to increased free fatty acids is one of these reasons. Increasing free fatty acids may cause insulin resistance via oxidative pathways (2).

The complications of diabetes can be microvascular or macrovascular and due to these complications, diabetes is an increasing cause of morbidity and mortality. Prevention of these complications of diabetes is only possible with intense treatment. The most important laboratory test used to evaluate the success of treatment is hemoglobin A1c (HbA1c), which is the level of glycosylated hemoglobin over 3 months. Keeping HbA1c below 7% is necessary to prevent complications (3).

However, since HbA1c analysis cannot be performed in every hospital laboratory and it can be affected by anemia, kidney failure, and some drugs, a requirement has arisen to find an indicator that shows glycemic control well, can be easily performed in every laboratory, is cheaper, and that will not be affected by other variables (4).

Diabetes mellitus is accompanied by an increase in TG. In addition, low HDL-C levels have highlighted these two parameters in previous years. As a matter of fact, previous studies in the literature have shown that TG/HDL ratio very well reflects atherogenicity due to endothelial dysfunction, which poses a risk for metabolic syndrome and cardiovascular diseases (5-7). It has been revealed that the TG/HDL ratio also reflects insulin resistance (8). It has been determined by studies that the triglyceride-glucose (TyG) index also shows insulin resistance well (9,10). It has also been previously shown that the TyG index may indicate an increased risk of cardiovascular disease in Type 2 diabetics without symptoms (11). Studies have reported a strong correlation between the TyG index and the development of diabetes (12,13).

In previous studies, we found only one study on the relationship between diabetes mellitus, TG-HDL ratio and TyG index (14). Our study aims to decide whether the TG/HDL and TyG index in our patient population are useful in predicting glycemic control in diabetic patients.

Materials and Methods

Research permission was taken from the Ethics Committee of our hospital before starting the study with the approval number 259, dated 01.07.2021. İndividual with a diagnosis of T2DM who applied to the internal medicine outpatient clinic of our hospital were retrospectively searched from our hospital database.

All patients over 18 years of age followed up with T2DM participated in the study. First of all, those younger than eighteen years of age, those with chronic kidney failure and/or chronic liver disease, pregnant or breastfeeding women, those using statins, fenofibrate or fish oil, those with malignancy and thyroid disease were excluded from the study. In the second elimination stage, the patients with the missing data were excluded. The fasting blood glucose, HbA1c, lipid profile, alanine aminotransferase (ALT), and creatinine values were simultaneously checked with the body mass index (BMI). The remaining 340 patients after two eliminations were accepted as the study group.

Glucose, HbA1c, ALT, creatinine, and lipid values were studied using the colorimetric method in an auto-analyzer (Beckman Coulter Brand, AU5800, USA).

The TG-HDL formula: TG/HDL (15)

Calculated in BMI kg/m^2 (16).

For the TyG index, previous studies were guided, and values were obtained with the formula Ln [fasting triglyceride value (mg/mL) X fasting glucose value (mg/mL)/2] (16).

Patients were defined as two groups according to their HbA1c values as those with diabetes under control (<7%) and those with uncontrolled diabetes (<7%) (17).

Statistical Analysis

SPSS version 21 program was used. Normally distributed data were given as mean ± standard deviation, non-normally distributed data as median and interquartile range (25th and 75th percentiles). Compliance of quantitative data with normal distribution was determined by Kolmogorov-Smirnov test. Chi-square test was performed to compare categorical data If the distribution was homogeneous, Student t-test was performed. If not, the Mann-Withney U test was used. Pearson was used if the distribution was homogeneous in the correlation analysis. If not homogeneous, Spearman was applied. P<0.05 is significant.

Results

Two hundred two women and 138 men took part in the study. There were 153 patients with HbA1c levels <7 and 187 patients with ≥7. In the group with HbA1c ≥7, TG/HDL value and TyG index were statistically higher than the group with HbA1c <7 (p=0.010, p<0.001). In the group with HbA1c ≥7, glucose, diabetes duration, and triglyceride levels were statistically higher than the group with HbA1c <7 (Table 1).

We found a significant correlation between triglyceride/HDL value and both glucose and HbA1c. (r=0.207, p<0.001; r=0.261 p<0.001). There was positive correlation between TyG index and HbA1c and glucose levels (r=0.576, p<0.001; r=0.710 p<0.001). TyG index had a negative correlation with HDL (r=-0.356 p< 0.001). TyG index was positively correlated with LDL (r=0.134 p=0.016) (Table 2).

Cases with HbA1c ≥7% were considered poorly controlled diabetic. The receiver operating characteristic (ROC) curve was made. The cut-off value of the TyG index was 9.38 (sensitivity 69%, specificity 73%, AUC= 0.759) (Table 3) (Figure 1). However, a cut-off value could not be determined for TG/HDL.

Table 1. Comparison of demographic and laboratory data

	HbA1c <%7 (n=153)	HbA1c ≥%7 (n=187)	p-value
Age (year)	59.50±10.50	60.40±10.5	0.407
BMI (kg/m^2)	30.70±4.79	30.50±5.25	0.685
Female, n (%)	90 (59)	112 (60)	0.842[a]
Male, n (%)	63 (41)	75 (40)	
HbA1c (%)	6.30±0.44	9±1.72	<0.001
Glucose (mg/dL)	117(103-117)	198(143-242)	<0.001[b]
Diabetes duration	7.50±5	10±6.90	<0.001
HDL-C (mg/dL)	47±11	45±11	0.034
TG (mg/dL)	159 (111.5-201)	168 (121-249)	0.046[b]
LDL-C (mg/dL)	121 (101-121)	125 (106-147)	0.307[b]
ALT (IU/mL)	19 (15-25)	22 (16-27)	0.055[b]
Creatinine (mg/dL)	0.75±0.20	0.72±0.20	0.271
TG/HDL	3.42 (2.2-4.9)	3.9 (2.5-6.4)	0.010[b]
TyG index	9.09±0.54	9.73±0.75	<0.001

BMI: Body mass index, HbA1c: Hemoglobin A1c, HDL-C: High density lipoprotein cholesterol, TG: Triglyceride, LDL-C: Low density lipoprotein cholesterol, ALT: Alanine aminotransferase, Student t-test, [a]Chi-square test, [b]Mann Whitney-U test

Table 2. Correlation between indexes values and data

		Age (years)	Diabetes duration (years)	BMI (kg/m²)	Glucose (mg/dL)	HbA1c (%)	TG (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)
TGA/HDL	r	-0.084	-0.070	0.069	0.261	0.207	0.916	-0.667	0.032
	p	0.123	0.203	0.207	<0.001	<0.001	<0.001	<0.001	0.567
TyG index	r	-0.069	0.026	0.028	0.710	0.576	0.824	-0.356	0.134
	p	0.207	0.639	0.609	<0.001	<0.001	<0.001	<0.001	0.016

TGA: Thermal degradation, HDL: High density lipoprotein, TyG: Triglyceride-glucose, *Pearson and Spearman correlation tests were applied according to the distribution

Table 3. Cut-off data for TyG index value according to HbA1c <7 and ≥7

	AUC (95%)	Cut-off	Sensitivity (%)	Specificity (%)	p-value
TyG index	0.759 (0.709-0.810)	9.38	69	73	0.001

TyG: Triglyceride-glucose

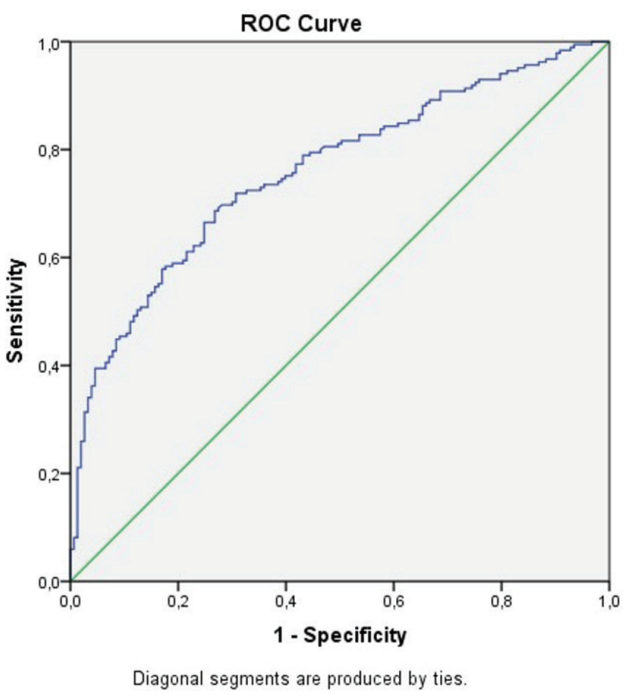

Figure 1. ROC curve of TyG index
ROC: Receiver operating characteristic, TyG: Triglyceride-glucose

Discussion

T2DM is espacially related with increased cardiovascular complications. Diabetes, hyperlipidemia, and obesity are among the metabolic syndrome parameters and each of them should be dealt with a separate treatment and follow-up program.

In our study, we found that the patients with poorly controlled diabetes (HbA1c ≥7) had higher TG-HDL ratio and TyG index. At the same time, both TG-HDL and TyG index were correlated with glucose and HbA1c. It is known that high TG and low HDL-C levels are related with insulin resistance and T2DM and atherosclerotic diseases (18,19). Since triglycerides and HDL cholesterol levels are affected by hyperinsulinemia, their levels may be affected by glycemici control in patients with diabetes (1). When we examine the previous studies in the literature; similar to our study, TG/HDL and TyG index were found to be correlated with HbA1c (14,20). Additionally, Babic et al. (14) It was concluded that TG/HDL and TyG index values are useful as an indicator of glycemic control. Zonszein et al. (21) They found that the triglyceride-HDL ratio is an easily predictable and practical biomarker in determining insulin-resistant patients and glycemic control in diabetic patients. T2DM patients have dyslipidemia characterized by predominance of LDL-C particles, increased triglyceride and decreased HDL-C levels (1). Dyslipidemia together with type 2 DM constitute the main risk factors for cardiovascular diseases. It has been reported that TG/HDL value and TyG index are related with atherosclerotic diseases (11,15). In our study, TyG index showed a positive correlation with LDL-C and an opposite correlation with HDL-C. Similar to our findings, the TyG index was found to be related with dyslipidemia in T2DM (14). Therefore, we can say that the TyG index predicts dyslipidemia.

Possible potential mechanisms to explain the relationship between TG/HDL and TyG index and

Hba1c could be; First, islet beta cell failure and insulin resistance are the main pathological features of T2DM. Increased glucose and free fatty acid levels have toxic effects on beta cells (2,22). Increased triglyceride levels can cause free fatty acids to rise, thereby increasing the flow of free fatty acids to the tissues. This may affect insulin resistance and glucose metabolism. Studies have shown that high triglyceride levels affect glucose metabolism in the liver and muscle (23). Second; recently, it has been shown that HDL can also directly affect glucose metabolism (24). Recombinant HDL infusion has been reported to be beneficial on glucose metabolism in T2DM (25). All these mechanisms point to the role of triglycerides and HDL-cholesterol in the pathogenesis of Type 2 DM. Therefore, TG/HDL value and TyG index are good options that can be used in the evaluation of regulation in T2DM.

In our study, when we performed ROC analysis, we found that the TyG index had a larger AUC than TG/HDL to identify poor diabetics. Accordingly, if the TyG index is above 9.38, which we assume as the cut-off value, the probability of the patient's HbA1c being over 7 is high.

The study has limitations. First of all, our study is retrospective and cross-sectional. Secondly, the relationship of TG/HDL ratio and TyG index with poor and well-controlled diabetes was examined, but their relationship with insulin resistance was not examined. Studies evaluated with the HOMA-IR levels may provide further information.

Conclusion

According to the results of our study, we can say the following; TG/HDL value and TyG index may be useful both in predicting dyslipidemia in Type 2 DM and in predicting diabetes regulation due to a positive relationship with HbA1c. Especially in cases where TyG index hba1c is not performed, it can be preferred instead of Hba1c Our study will shed light on similar studies to be done in the future.

Ethics

Ethics Committee Approval: The present cohort study was designed as a survey and was approved by the local Ethical Committee of İstanbul Prof. Dr. Cemil Taşçıoğlu City Hospital (decision no: 259, date: 02.07.2021)

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.A., S.K., Concept: Ö.A., Design: Ö.A., S.K., Data Collection or Processing: Ö.A., Analysis or Interpretation: Ö.A., S.K., Literature Search: Ö.A., S.K., Writing: Ö.A.

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