



Research Article

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CAN WE USE THE TRIGLYCERIDE/HDL RATIO TO DETERMINE INSULIN RESISTANCE IN OBESITY SCREENING AND FOLLOW-UP IN PRIMARY CARE?

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Abstract

Objectives: Obese patients are followed up with periodic laboratory tests. Insulin resistance is also a parameter used in these tests. There is a need for parameters that can determine insulin resistance more easily and practically. The aim of our study is to investigate the discriminative power of triglyceride (Tg) and triglyceride/high-density lipoprotein cholesterol ratio (Tg/HDL) for Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) in our patient population by examining the laboratory findings.

Materials and Methods: In this retrospective study, the laboratory data of patients who applied to the Family Medicine Obesity Polyclinic of Düzce University Hospital between April 2018 and April 2019 with the desire to lose weight and/or have healthy lifestyle suggestions were examined.

Results: Of the 512 patients included in our study, 66.40% (n=340) were female and 33.59% (n=172) were male. In the examination performed on patients grouped according to their Body Mass Index (BMI), Total cholesterol, HDL, Low-density lipoprotein (LDL), Tg, HOMA-IR, Insulin and Tg/HDL ratios were significantly different between the groups. The cut-off value in the ROC analysis of the Tg/HDL parameter between patients with and without insulin resistance was found to be 2.29 with 66% sensitivity and 55% specificity (AUC: 0.634, $p < 0.001$). In Spearman's correlation analysis of Tg/HDL and HOMA-IR, both parameters were found to have a statistically significant correlation ($r: 0.248$; $p < 0.000$).

Conclusion: The significant relationship between the high Tg/HDL ratio and HOMA-IR detected in the results of our study shows that the Tg/HDL ratio can be used as a practical tool to evaluate insulin resistance in obese patients.

Keywords: Obesity, insulin resistance, HOMA-IR, Tg/HDL.

Introduction

As it is known, obesity is a disease that is common in our age and has high mortality and morbidity.¹ In the clinic, patients are evaluated by body mass index (BMI), which is expressed as body weight in kilograms divided by square meter height for obesity screening and diagnosis. According to some cut-off values patients are classified as; underweight ($<18.5 \text{ kg/m}^2$), normal weight ($18.5\text{-}24.9 \text{ kg/m}^2$), overweight ($25.0\text{-}29.9 \text{ kg/m}^2$), obese grade I ($30.0\text{-}34.9 \text{ kg/m}^2$), obese grade II ($35.0\text{-}39.9 \text{ kg/m}^2$) and obese grade III ($40.0\text{+} \text{ kg/m}^2$).² In addition to BMI and various anthropometric measurements, patients are followed up with periodic laboratory tests. HOMA-IR is also a parameter used in these examinations.³ Detection of insulin resistance can also identify individuals at high risk for diseases such as cardiovascular and diabetes.⁴ In order to measure insulin resistance, it is necessary to determine fasting insulin. However, fasting insulin is not a primary care examination, and it is a costly method in a hospital setting.⁵ Some studies have formed the idea that insulin resistance in patients can be detected by using the ratio between Tg and HDL, which can also be done in primary care.^{6,7} However, this ratio is not yet in routine use due to some conflicting results.⁸ It is interpreted that these conflicting results may be related to the variability of the study population.⁹ According to our literature search, we found that the Tg/HDL ratio of patients classified according to the BMI index was not studied in a large patient population in our country. The aim of our study is to investigate the discriminative power of the Tg/HDL ratio for HOMA-IR in our patient population by examining the examinations of patients who applied to the healthy living and obesity outpatient clinic in our university hospital.

Materials and Methods

In this retrospective study, the laboratory data of patients who applied to the Family Medicine Obesity Polyclinic of our University hospital with the desire to lose weight and/or healthy lifestyle suggestions between the dates of the year 2018-2019 were examined. Ethical permission for the study was obtained from the local ethics committee.

Study Group

During the study period, 1823 patients were admitted to the obesity outpatient clinic. Chronic diseases such as heart and kidney diseases, thyroid diseases, liver diseases, serious infections, malignancy or taking any drug known to cause discomfort in lipid metabolism were excluded from the study. Since the BMI and laboratory tests measured at the time of the first application of the patients were used for the study, recurrent applications were also excluded from the study. Finally, a total of 512 patients were included in the study (Figure 1).

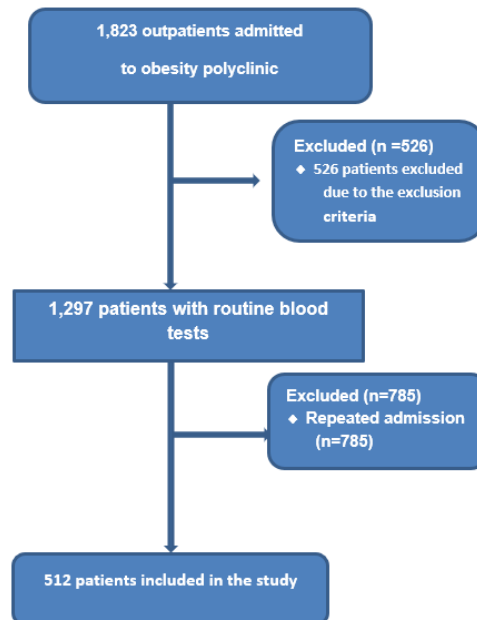


Figure 1. Study design and process

Blood samples were taken after at least 8 hours of fasting. All measurements were carried out in Düzce University Research and Application Hospital Biochemistry Laboratory. From blood tests, fasting blood glucose (FBS), insulin, total cholesterol, LDL, HDL, and Tg levels were scanned. Insulin resistance was calculated with the HOMA-IR formula (fasting glucose (mg/dl) x fasting insulin (μ IU/mL) / 405).

Statistical analysis

In descriptive statistics, quantitative data were given as mean and standard deviation, and categorical data were given as numbers and percentages. The distribution of numerical data was examined by using histogram graphics. One-way ANOVA was used for parametric data, and Kruskal Wallis tests were used for non-parametric data to compare data between groups. The cut-off value was calculated in the ROC analysis of the Tg/HDL parameter between patients with and without insulin resistance. The AUC and cut-off value (cut-off value) of each measurement were determined, and the sensitivity, specificity, and LR + cut-off values of these values were calculated and evaluated together. A value of $p < 0.05$ was accepted as statistically significant. Spearman's correlation analysis was used for the relationship between Tg/HDL and HOMA-IR. All statistics were performed by using SPSS 23.0 package program (SPSS, version 23X, IBM, Armonk, New York 10504, NY, USA).

Results

Of the 512 patients included in our study, 66.40% (n=340) were female and 33.59% (n=172) were male. According to the examination made from the routine examinations of the patients grouped according to their BMI, FBS, total cholesterol, HDL, LDL, Tg, HOMA-IR, Insulin and Tg/HDL ratio showed significant differences between groups (Table 1).

Table 1. Comparison of laboratory results of patients and BMI group

| Parameters | Group I* (n=126) | Group II* (n=158) | Group III* (n=141) | Group IV* (n= 87) | <i>p</i> ** |
|---------------------------------|---------------------|----------------------|-----------------------|----------------------|------------------|
| Gender (Female/Male) | 86/40 | 93/65 | 81/60 | 80/7 | <0.001 |
| Age | 38.21±11.42 | 40.93±9.63 | 43.82±9.55 | 43.92±11.23 | <0.001 |
| Weight | 75.23±11.21 | 86.32±10.32 | 98.34±12.34 | 112.24±15.31 | <0.001 |
| BMI | 27.91±1.61 | 32.53±1.42 | 36.93±1.46 | 44.23±4.23 | <0.001 |
| FBS | 95.82±11.14 | 95.93±10.60 | 99.21±13.24 | 102.13±17.21 | <0.001 |
| Total Cholesterol | 183.10±41.52 | 199.12±40.94 | 202.24±41.13 | 199.91±43.32 | <0.001 |
| HDL | 56.23±17.8 | 50.49±12.3 | 49.24±11 | 47.97±10 | <0.001 |
| LDL | 101.34±32.2 | 123.68±43.7 | 118.39±32 | 123.84±34 | <0.001 |
| Tg | 89 (20-412) | 118 (25-565) | 127 (38-722) | 129 (62-387) | 0.005 |
| HOMA-IR | 2.59±1.21 | 2.77±1.76 | 3.81±1.12 | 4.13±1.73 | <0.001 |
| Insulin | 9.87(1.9-31) | 10.29(2.7-61) | 12.62 (3.3-79) | 12.31 (5.4-59) | <0.001 |
| Tg/HDL | 1.61(0.3-11.9) | 2.46 (0.25-18) | 2.82 (0.56-18.8) | 2.87 (0.9-10) | <0.001 |

*The patients were grouped according to their BMI

F/M; Female/Male

BMI: Body Mass Index

FBS: Fasting blood sugar

HDL: High-density lipoprotein, LDL: Low-density lipoprotein Tg: Triglyceride

HOMA-IR: Homeostatic Model Assessment of Insulin Resistance

** One-way ANOVA and Kruskal Wallis tests were used to compare data between groups

In the ROC (Receiver Operating Characteristic) analysis of the Tg/HDL parameter between patients with and without insulin resistance; The cut-off value was 2.29 with a sensitivity of 66% and a specificity of 55% (AUC: 0.634, $p < 0.001$) (Figure 2, Table 2).

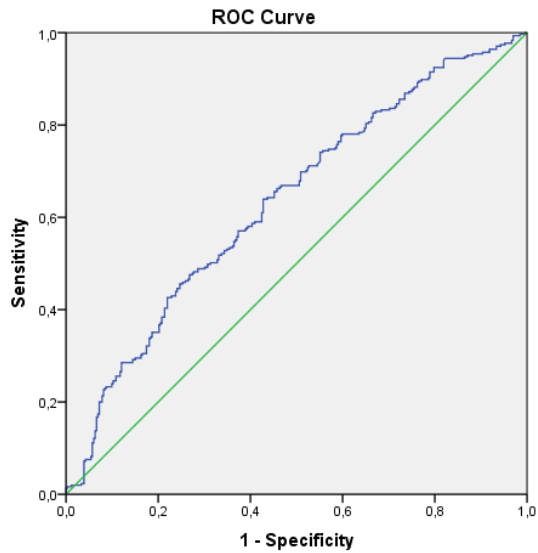


Figure 2. ROC curve of Tg/HDL variables for insulin resistance

Table 2. The cut-off value of Tg/HDL with sensitivity and specificity for insulin resistance

| Parameter | AUC (CI) | p | Sensitivity (%) | Specificity (%) | Cut-Off |
|-----------|--------------------|--------|-----------------|-----------------|---------|
| Tg/HDL | 0.634(0.591-0.677) | <0.001 | 66 | 55 | 2.29 |

AUC: Area Under the Curve, CI: Confidence Interval

In Spearman's correlation analysis of Tg/HDL and HOMA-IR, both parameters were found to have a statistically significant correlation ($r: 0.248$; $p < 0.001$) (Figure 3).

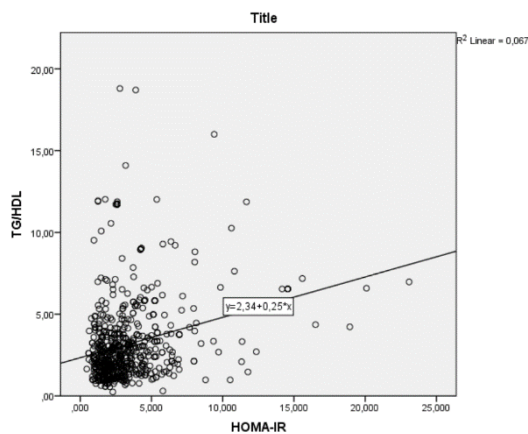


Figure 3. Spearman's correlation plot of Tg/HDL and HOMA-IR

Discussion

In our study, the laboratory findings of patients who applied to our obesity outpatient clinic at the time of their first admission were examined. In order to predict insulin resistance in primary care, it was investigated whether the Tg/HDL ratio is a practical alternative to HOMA-IR. According to our study results, as the obesity degree of the patients increased, it was determined that the FBG and Tg levels increased. Studies have revealed that as BMI increases, impaired glucose metabolism and lipid metabolism are also observed more.^{10,11} Effects of insulin on lipid metabolism; insulin suppresses lipolysis in adipose tissue by inhibiting hormone-sensitive lipase, thereby controlling the release of free fatty acids into circulation. Free fatty acids reduce insulin receptor signaling. Fat cells that are saturated with free fatty acids form the infrastructure of insulin resistance with a reverse effect.¹² This dyslipidemia caused by obesity causes permanent changes in the adipose tissue and becomes a vicious circle as a condition characterized by insulin resistance and hyperinsulinemia.¹³

In many studies, the diagnosis of health problems secondary to obesity and the possibility of early treatment in obese patients with simple hematological and biochemical tests have been suggested.^{14,15} The most important result of our study is the demonstration of a significant relationship between Tg/HDL and HOMA-IR parameters. Together with the results of ROC analysis of the Tg/HDL parameter among patients with and without insulin resistance, we can say that patients with Tg/HDL ratio above 2.29 have insulin resistance. In a large-scale study in Japan, they found that as the HOMA-IR ratio increased, the Tg/HDL ratio increased. It was also found that Tg/HDL values were lower in both men and women who exercised regularly and had high physical activity.¹⁶ Tg/HDL ratio is considered a useful and practical laboratory parameter in many studies as a predictive marker for HOMA-IR.¹⁷⁻¹⁹ Comparing the usefulness of HOMA-IR markers in the prediction of metabolic syndrome, the TG/HDL-C ratio seems to be the best and is also recommended for use in clinical practice to detect metabolic syndrome.²⁰ In studies conducted to predict insulin resistance using the Tg/HDL ratio, the cut-off value of this ratio varies between 1.1 and 3.^{6,21} In the literature, there is no standard value yet determined for these various rates. However, high Tg and low HDL levels in obese patients, and therefore high Tg/HDL ratios, may provide insight into insulin resistance.

As it is known, preventive health services are the most important component of primary care medicine. Obesity and the diseases it causes are preventable and manageable diseases in primary care. Preventing chronic diseases such as insulin resistance and metabolic syndrome before they occur provides significant advantages to the patient and the health system. Periodic follow-up of physical examination and other routine controls is recommended in obese patients.²²⁻²⁴ Being able to do these checks and scans in an easy and inexpensive way is very attractive for the primary care physician. Tg and HDL values are a test that can be

evaluated in primary care. In addition, they are tests that can be evaluated practically without sending the patient to the hospital, without any additional cost.

Limitations

Our study has some limitations. First of all, our results cannot be generalized to the whole population since our study was a single-centered study. Since it is a retrospective study, up-to-date information on the patients could not be reached. Longitudinal and large-scale studies are needed in terms of causal relationships.

Conclusion

The significant relationship between the high Tg/HDL ratio and HOMA-IR detected in the results of our study shows that the Tg/HDL ratio can be used as a practical tool to evaluate insulin resistance in obese patients. Practical and inexpensive laboratory parameters that can predict insulin resistance in primary care provide benefits to the patient in preventive health services.

Ethical considerations: Ethical approval for the study was obtained from the ethics committee of Düzce University (Approval No: 2021/228, Date: 01.10.2021).

Conflict of Interest: The authors declare no conflict of interest.

(The results of this study were presented as an oral presentation at the 20th National Family Medicine Congress.)

References

1. Albuquerque D, Nóbrega C, Manco L, et al. The contribution of genetics and environment to obesity. *Br Med Bull.* 2017;123(1):159-73.
2. Blundell JE, Dulloo AG, Salvador J, et al. EASO SAB Working Group on BMI. Beyond BMI--phenotyping the obesities. *Obes Facts.* 2014;7(5):322-8.
3. Shashaj B, Luciano R, Contoli B, et al. Reference ranges of HOMA-IR in normal-weight and obese young Caucasians. *Acta Diabetol.* 2016;53(2):251-60.
4. Tang Q, Li X, Song P, et al. Optimal cut-off values for the homeostasis model assessment of insulin resistance (HOMA-IR) and pre-diabetes screening: Developments in research and prospects for the future. *Drug Discov Ther.* 2015;9(6):380-5.
5. He J, He S, Liu K, et al. The TG/HDL-C Ratio Might Be a Surrogate for Insulin Resistance in Chinese Nonobese Women. *Int J Endocrinol.* 2014;105168.
6. Behiry EG, El Nady NM, Abdel Haie OM, et al. Evaluation of TG-HDL Ratio Instead of HOMA Ratio as Insulin Resistance Marker in Overweight and Children with Obesity. *Endocr Metab Immune Disord Drug Targets.* 2019;19(5):676-82.
7. Ren X, Chen ZA, Zheng S, et al. Association between Triglyceride to HDL-C Ratio (TG/HDL-C) and Insulin Resistance in Chinese Patients with Newly Diagnosed Type 2 Diabetes Mellitus. *PLoS One.* 2016;11(4):e0154345.
8. Sumner AE, Finley KB, Genovese DJ, et al. Fasting triglyceride and the triglyceride-HDL cholesterol ratio are not markers of insulin resistance in African Americans. *Arch Intern Med.* 2005;165(12):1395-400.
9. Borrayo G, Basurto L, González-Escudero E, et al. Tg/Hdl-C Ratio As Cardio-Metabolic Biomarker Even In Normal Weight Women. *Acta Endocrinol (Buchar).* 2018;14(2):261-7.
10. Qian Y, Lin Y, Zhang T, et al. The characteristics of impaired fasting glucose associated with obesity and dyslipidaemia in a Chinese population. *BMC Public Health.* 2010;10:139.
11. Berings M, Wehlou C, Verrijken A, et al. Glucose intolerance and the amount of visceral adipose tissue contribute to an increase in circulating triglyceride concentrations in Caucasian obese females. *PLoS One.* 2012;7(9):e45145.
12. M Blüher. Adipose tissue dysfunction contributes to obesity related metabolic diseases. *Best Pract Res Clin Endocrinol Metab.* 2013;27(2):163-77
13. Dimitriadis G, Mitrou P, Lambadiari V, et al. Insulin effects in muscle and adipose tissue. *Diabetes Res Clin Pract.* 2011;93 Suppl 1:S52-9.
14. Çağlar Şimşek CE, Çelik N, Aygüneş U, et al. Obez Çocuk ve Adolesanlarda Hematolojik Parametreler ve Demir Düzeyinin Değerlendirilmesi. *Ankara Med J.* 2019; 19(3): 479-87.

15. Doğan Ş, Sönmez CI, Başer DA. Evaluation of Anthropometric and Biochemical Properties of Patients who Applied to Obesity Polyclinics. *Ankara Med J.* 2020;20(2):407-15.
16. Moriyama K. Associations Between the Triglyceride to High-Density Lipoprotein Cholesterol Ratio and Metabolic Syndrome, Insulin Resistance, and Lifestyle Habits in Healthy Japanese. *Metab Syndr Relat Disord.* 2020;18(5):260-6.
17. Gong R, Liu Y, Luo G, et al. Associations of TG/HDL Ratio with the Risk of Prediabetes and Diabetes in Chinese Adults: A Chinese Population Cohort Study Based on Open Data. *Int J Endocrinol.* 2021;9949579.
18. Nur Zati Iwani AK, Jalaludin MY, Wan Mohd Zin RM, et al. TG : HDL-C Ratio Is a Good Marker to Identify Children Affected by Obesity with Increased Cardiometabolic Risk and Insulin Resistance. *Int J Endocrinol.* 2019;8586167.
19. Kheirollahi A, Teimouri M, Karimi M, et al. Evaluation of lipid ratios and triglyceride-glucose index as risk markers of insulin resistance in Iranian polycystic ovary syndrome women. *Lipids Health Dis.* 2020;19(1):235.
20. Krawczyk M, Rumińska M, Witkowska-Sędek E, et al. Usefulness of the Triglycerides to High-Density Lipoprotein Cholesterol ratio (TG/HDL-C) in prediction of metabolic syndrome in Polish obese children and adolescents. *Acta Biochim Pol.* 2018;65(4):605-11.
21. Pantoja-Torres B, Toro-Huamanchumo CJ, Urrunaga-Pastor D, et al. Insulin Resistance and Metabolic Syndrome Research Group. High triglycerides to HDL-cholesterol ratio is associated with insulin resistance in normal-weight healthy adults. *Diabetes Metab Syndr.* 2019;13(1):382-8.
22. Lemieux I, Després JP. Metabolic Syndrome: Past, Present and Future. *Nutrients.* 2020;12(11):3501.
23. Gluvic Z, Zaric B, Resanovic I, et al. Link between Metabolic Syndrome and Insulin Resistance. *Curr Vasc Pharmacol.* 2017;15(1):30-9.
24. Ardiç C, Şahin A, Yazan Arslan A, et al. Changes in Early Childhood Obesity from 2016 to 2019 and Effective Factors. *Konuralp Medical Journal.* 2020;12(3):435-42.