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ORIGINAL ARTICLE

Evaluation of Triglyceride-Glucose Index as a Marker of Insulin Resistance in Non-Obese Young Women with Polycystic Ovary Syndrome

Polikistik Over Sendromlu Obez Olmayan Genç Kadınlarda İnsülin Direncinin Bir Belirteci Olarak Trigliserit-Glikoz İndeksinin Değerlendirilmesi

[1]Kübra GÜNDOGAN, [1]Asmar AHMADKHANLI, [1]Ali ACAR

[1]Department of Obstetrics and Gynecology, Faculty of Medicine, Necmettin Erbakan University, Konya, Turkey.

Correspondence

Kübra Gündoğan
Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Kadın Hastalıkları ve Doğum Anabilim Dalı Hocacihan Mahallesi, Abdülhamid Han Caddesi No:3, 42280 Selçuklu/Konya, Türkiye

E-Mail: kubramerdogan@gmail.com

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Highlights

- Triglyceride-glucose index (TGI) is significantly elevated in non-obese young women with PCOS, indicating metabolic alterations independent of obesity.
- TGI shows high diagnostic performance for distinguishing PCOS from healthy controls (cut-off: 8.44; sensitivity 86%, specificity 86%).
- TGI may serve as a simple, inexpensive, and practical surrogate marker for insulin resistance in non-obese patients with PCOS.

ABSTRACT

Aim: Polycystic ovary syndrome (PCOS) is frequently associated with insulin resistance (IR), even in non-obese women. The triglyceride-glucose index (TGI) has recently emerged as a potential surrogate marker of IR. This study aimed to evaluate the utility of TGI as a marker for IR in non-obese young women with PCOS.
Materials and Methods: In this retrospective study, 84 non-obese women aged 18–35 years newly diagnosed with PCOS were compared with 73 age-matched healthy controls. TGI was calculated using fasting plasma triglycerides level and fasting plasma glucose, and values were compared between groups. The ROC curve was used to calculate the optimal TGI cut-off value and the sensitivity and specificity of this value between the PCOS and control groups.
Results: No significant difference was detected between the groups in terms of age (p =0.084). TGI value was found to be 8.26 [8.14, 8.42] in the control group and 8.52 [8.46, 8.75] in the PCOS group (p<0.001). Optimal ROC cutoff value of TGI between control and PCOS groups was calculated as 8.44 with 86% sensitivity and 86% specificity (AUC: 0.904 P<0.001 95% CI 0.856-0.951).
Conclusion: TGI levels are significantly higher in young, non-obese women with PCOS, suggesting that it could be a simple, cost-effective and reliable indicator of insulin resistance in this group. These findings emphasise the importance of assessing metabolic risk in non-obese patients with PCOS and indicate a possible application for TGI in routine clinical screening.

Keywords: Insulin resistance, metabolic risk, non-obese, polycystic ovary syndrome, triglyceride-glucose index

ÖZ

Amaç: Polikistik over sendromu (PKOS), obez olmayan kadınlarda bile sıklıkla insülin direnci ile ilişkilidir. Trigliserid-glikoz indeksi (TGİ) son zamanlarda insülin direncinin potansiyel bir alternatif belirteci olarak ortaya çıkmıştır. Bu çalışma, PKOS'lu obez olmayan genç kadınlarda insülin direnci için bir belirteç olarak TGİ'nin yararını değerlendirmek amacıyla yapılmıştır.
Gereç ve Yöntem: Bu retrospektif çalışmada, 18-35 yaşları arasında yeni tanılı obez olmayan 84 PKOS'lu kadın, yaşları uyumlu 73 sağlıklı kontrol grubu ile karşılaştırıldı. TGİ, açlık plazma trigliserid düzeyi ve açlık plazma glikozu kullanılarak hesaplandı ve değerler gruplar arasında karşılaştırıldı. ROC eğrisi, optimal TGİ cut-off değerini ve bu değerin PKOS ve kontrol grupları arasındaki duyarlılık ve özgüllüğünü hesaplamak için kullanıldı.
Bulgular: Gruplar arasında yaş açısından anlamlı bir fark saptanmadı (p =0,084). TGİ değeri kontrol grubunda 8,26 [8,14, 8,42] ve PKOS grubunda 8,52 [8,46, 8,75] olarak bulundu (p<0,001). Kontrol ve PKOS grupları arasında TGİ'nın optimal ROC cutoff değeri, %86 duyarlılık ve %86 özgüllük ile 8,44 olarak hesaplandı (AUC: 0,904 P<0,001 %95 CI 0,856-0,951).
Sonuç: TGİ düzeyleri, PKOS'lu genç, obez olmayan kadınlarda anlamlı olarak daha yüksektir, bu da TGİ'nin bu grupta insülin direncinin basit, maliyet etkin ve güvenilir bir belirteci olabileceğini düşündürmektedir. Bu bulgular, PKOS'lu obez olmayan hastalarda metabolik riskin değerlendirilmesinin önemini vurgulamakta ve TGİ'nin rutin klinik taramada kullanılabileceğini göstermektedir.

Anahtar Kelimeler: İnsülin direnci, metabolik risk, obez olmayan, polikistik over sendromu, trigliserid-glikoz indeksi

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Complaints: geneltip@selcuk.edu.tr

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine and metabolic disorders affecting women of reproductive age [1]. This syndrome, often characterized by hyperandrogenism, oligo-anovulation, and a polycystic ovarian morphology on ultrasonography, also causes insulin resistance (IR), which significantly impacts long-term metabolic health [2]. It is the inability of body cells to respond adequately to the insulin hormone, and this condition is closely associated with long-term metabolic consequences in women with PCOS, including impaired glucose tolerance, type 2 diabetes, and cardiovascular and cerebrovascular diseases [3, 4]. In this condition, the ovaries are stimulated by IR and elevated insulin levels to produce more androgens [5]. Therefore, early diagnosis of IR in these patients is crucial. While IR can be observed in 50-70% of women normal body mass index (BMI) diagnosed with PCOS, this rate may be higher in those who are obese [6].

The gold standard methods for the clinical assessment of IR are complex and costly and their routine application is limited. Therefore, there is a need for alternative biomarkers that can indicate IR in a simple, affordable, and reliable manner. The triglyceride-glucose index (TGI), derived from fasting triglyceride (TG) and blood glucose levels, may be a simple and low-cost alternative for determining IR in healthy patients [7]. Clearance of triglyceride-rich lipoproteins from plasma is delayed in insulin-resistant states, resulting in hypertriglyceridemia. Compared with conventional lipid ratios, the TGI has been shown to have the strongest correlation with the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) [8]. According to a systematic review using hyperinsulinemic euglycemic clamp (HIEC) and HOMA-IR as reference tests, the TGI was found to have the highest sensitivity and specificity, with 96% and 99%, respectively [9]. In addition, this index has been confirmed in other studies to be associated with the risk of diabetes, atherosclerotic cardiovascular disease, and ischemic stroke [10, 11].

Recent studies have shown that PCOS is not a condition that only affects obese individuals but also has a significant prevalence in non-obese young women with a normal body mass index (BMI). In clinical practice, metabolic risks in this group of young patients with a normal BMI tend to be overlooked. It has been determined that women diagnosed with PCOS are more likely to develop insulin resistance, obesity, dyslipidaemia, and impaired glucose tolerance. These conditions, when combined, can lead to the development of metabolic syndrome. These metabolic risks are also evident in women with PCOS who are not obese. This demonstrates that PCOS carries a unique metabolic risk independent of obesity, and that phenotype-specific approaches are critical for early detection of these risks [12].

While there are several studies examining the relationship between TGI and PCOS, there are no studies specifically investigating this relationship in non-obese patients. Our study aimed to compare TGI values of young PCOS patients with a normal BMI with controls and determine predictive value of TGI.

Materials and Methods

This retrospective study was conducted in the Obstetrics and Gynecology Clinic of Necmettin Erbakan University Faculty of Medicine Hospital. The data of treatment-naive, non-obese patients aged 18-35 years who were newly diagnosed with PCOS between January 2024 and February 2025 were obtained by scanning the medical records and laboratory results through the hospital information system. Ethics committee approval was obtained from the Necmettin Erbakan University Ethics Committee (Decision No: 2024/5174), and the study was conducted in accordance with the principles of the Declaration of Helsinki. Eighty-four patients diagnosed with PCOS (PCOS group) by an experienced gynecologist (KG) according to the Rotterdam criteria, which include menstrual disorders (e.g., oligomenorrhea or amenorrhea), hyperandrogenism demonstrated by clinical or laboratory findings, and ultrasound findings of polycystic ovaries were included in the study [13].

Those with endocrine diseases such as diabetes, Cushing's syndrome, and congenital adrenal hyperplasia; those with other systemic diseases such as hypertension, cerebrovascular or cardiovascular diseases, and any gynecological disease other than PCOS; those with lipid metabolism disorders such as familial dyslipidemia; those who consumed alcohol or smoked; those who used any medication, including steroids, lipid-lowering drugs, or oral contraceptives; and those who had COVID-19 disease were excluded from the study. Obese patients (body mass index > 30 kg/m2) were also excluded. None of the participants in either group were pregnant. All subjects included in the study, in both the PCOS and control groups, included both normal weight (BMI <25 kg/m²) and overweight (BMI 25–29.9 kg/m²) individuals.

The control group consisted of 73 age-and gender-matched healthy women who presented for a routine gynecological examination at the Necmettin Erbakan University Faculty of Medicine Hospital Gynecology and Obstetrics Clinic and met the inclusion criteria. The patients in the control group had regular menstrual cycles and normal ovarian morphology as determined by ultrasound.

Only patients that had detailed gynecological examination findings, ultrasound findings, and concurrent laboratory data including fasting plasma glucose and fasting triglyceride levels were included in the study. TGI was calculated using Microsoft Excel using the formula Ln[fasting triglycerides (mg/dL) × fasting plasma glucose (mg/dL)/2] [7].

Statistical Analyses

IBM SPSS statistics software version 20.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis of the data. The conformity of continuous variables to normal distribution was assessed using the Kolmogorov-Smirnov test. Continuous variables with a normal distribution were expressed as mean ± standard deviation (SD), and continuous variables without a normal distribution were expressed as median [25th, 75th percentiles]. Independent

samples t-test was used to compare continuous variables with a normal distribution. Mann Whitney U test was used to compare continuous variables with non-normal distribution. Receiver operating characteristic (ROC) curve was used to calculate the optimal TGI cut-off value between the PCOS and control groups and the sensitivity and specificity of this value. The optimal cut-off value was determined using the Youden index. A two-sided p value <0.05 was considered statistically significant.

Results

There was no significant difference between the groups in terms of mean age (PCOS group 25.56±3.04 years and control group 26.55±3.94 years, p=0.084) (Table 1).

When we examined laboratory parameters, LDL values were 86.00 [70.00, 97.50] mg/dL in the control group and 89.50 [74.25, 110.00] mg/dL in the PCOS group; HDL values were 50.00 [46.00, 55.00] mg/dL in the control group and 51.00 [44.00, 56.00] mg/dL in the PCOS group, blood glucose levels were 94.00 [88.00, 99.00] mg/dL in the control group and 94.50 [92.00, 98.00] mg/dL in the PCOS group. No significant difference was found between the groups in terms of LDL, HDL and blood glucose levels (p=0.145, p=0.899, p=0.067, respectively) (Table 1).

Table 1. Comparison of age, laboratory findings, and Triglyceride-Glucose Index (TGI) between the PCOS and control groups

	PCOS Group (n=84)	Control Group (n=73)	*p value*
Age, years, mean±SD	25.56±3.04	26.55±3.94	0.084*
Glucose, mg/dl, median [25th, 75th]	94.50 [92.00, 98.00]	94.00 [88.00, 99.00]	0.067**
Triglyceride, mg/dl, median [25th, 75th]	106.00 [101.00, 123.50]	79.00 [75.00, 94.00]	**<0.001****
HDL, mg/dl, median [25th, 75th]	51.00 [44.00, 56.00]	50.00 [46.00, 55.00]	0.899**
LDL, mg/dl, median [25th, 75th]	89.50 [74.25, 110.00]	86.00 [70.00, 97.50]	0.145**
VLDL, mg/dl, median [25th, 75th]	17.00 [13.00, 23.75]	15.00 [11.00, 19.00]	**0.036****
Total Cholesterol, mg/dl, median [25th, 75th]	168.50 [148.00, 195.00]	150.00 [138.00, 165.50]	**<0.001****
TGI, median [25th, 75th]	8.52 [8.46, 8.75]	8.26 [8.14, 8.42]	**<0.001****

** Statistical significance in the Independent samples – t test*

*** Statistical significance in the Mann Whitney-U test*

HDL: *High-density lipoprotein,* **LDL:** *Low-density lipoprotein,* **VLDL:** *Very Low-density lipoprotein*

The VLDL value was 15.00 [11.00, 19.00] in the control group and 17.00 [13.00, 23.75] mg/dL in the PCOS group; total cholesterol value was 150.00 [138.00, 165.50] in the control group and 168.50 [148.00, 195.00] mg/dL in the PCOS group; triglyceride value was 79.00 [75.00, 94.00] in the control group and 106.00 [101.00, 123.50] mg/dL in the PCOS group. All three blood parameters were significantly higher in the PCOS group (p=0.036, p<0.001, p<0.001, respectively). The TGI value was 8.26 [8.14, 8.42] in the control group and 8.52 [8.46, 8.75] in the PCOS group and this difference was significant (p<0.001) (Table 1). The optimal ROC cutoff value of TGI between the control and PCOS groups was calculated as 8.44 with 86% sensitivity and 86% specificity (AUC: 0.904 P<0.001 95% CI 0.856-0.951) (Figure 1).

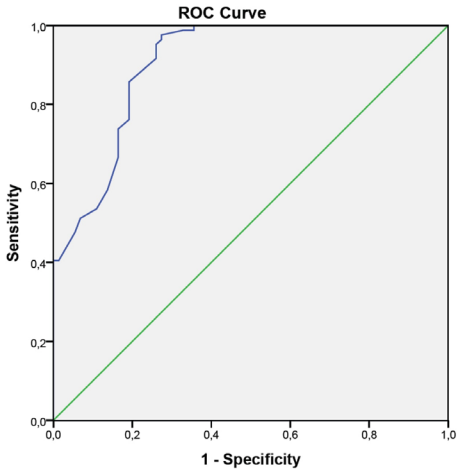

Figure 1. Receiver operating characteristics (ROC) curve analysis of Triglyceride-Glucose Index (TGI) between PCOS and control groups (Optimal ROC cutoff value: 8.44 with 86% sensitivity and 86% specificity, AUC: ~~AUC~~ 0.904 P<0.001 95%CI 0.856-0.951).

Discussion

According to the results of our study, the TGI was significantly higher in non-obese young women with PCOS compared to the control group. Sensitivity and specificity were 86% in differentiating between the PCOS and the control group, with a cut-off value of 8.44 for the TGI. The potential contribution of our findings to clinical decision-making processes is significant. These results support the hypothesis that TGI can be used as a simple, cost-effective, and reliable biomarker for assessing IR in non-obese PCOS patients particularly in primary care or gynecology outpatient clinics.

PCOS is a common health issue that affects hormone levels and fertility in women during their childbearing years. IR is a key factor in the pathogenesis and progression of long-term complications in individuals with PCOS [14]. Hyperinsulinemia, in turn, plays a significant role in exacerbating hyperandrogenism and reproductive disorders. Traditional gold standard tests used to assess IR, such as the HIEC test, are complex and costly. Therefore, there is a need to develop a simpler, practical and cost-effective method to assess IR.

In recent years, TGI has been accepted as a new biomarker used in prediction of various diseases, including diabetes mellitus, gastric malignancy, metabolism-related lung disease, cardiovascular events, and fatty liver disease due to simplicity, convenience, low cost, and accuracy [15-18]. In addition, Fernando et al. reported that TGI showed a significant correlation with HOMA-IR and HIEC test in determining IR and had high sensitivity and specificity in demonstrating IR [19]. Although many studies have demonstrated the suitability of TGI in predicting IR, very few studies have examined the capacity of TGI

to predict IR in women with PCOS [20, 21]. Yang et al. investigated the critical role of IR in the development of metabolic syndrome in women with PCOS and determined that TGI could be a new marker for early detection of metabolic problems [22]. Furthermore, Kheirollahi et al. found that the AUC levels of TGI were higher than lipid ratios such as TG/HDL-C when HOMA-IR was used as a reference [23]. In another study conducted by Kwon et al. evaluating 172 Korean PCOS patients, they reported a strong correlation between TGI and HOMA-IR (r=0.524). Their analysis determined an optimal TGI cut-off value of 8.126 with a sensitivity of 0.807 and a specificity of 0.683 for detecting IR [24]. The TGI has also been shown to correlate positively with the prevalence of metabolic syndrome, hypertension, obesity, and dyslipidaemia in women with PCOS, and exhibits strong diagnostic accuracy for identifying both metabolic syndrome and insulin resistance across different populations [25, 26]. Our study, similar to other studies, found significantly higher TGI values in the PCOS group.

One of the most important contributions of our study is its specific examination of the predictive value of TGI in young non-obese PCOS patients. While studies evaluating TGI in PCOS patients exist in the literature, no study has focused on patients with a normal BMI. Because obesity is a known risk factor for IR, it is an expected metabolic disorder in obese PCOS patients [27]. Earlier studies assessing TGI in PCOS included mixed cohorts with overweight and obese patients, making it difficult to separate the metabolic effects of obesity from those of PCOS itself. By focusing on a strictly non-obese population and applying comprehensive exclusion criteria, our study minimizes the confounding influence of adiposity and shows that TGI is elevated even in women with PCOS who have a normal BMI. However, IR and compensatory hyperinsulinemia have been reported to occur frequently in women with PCOS, independent of obesity [28]. It is also known that elevated TGI is associated with obesity [29]. The present study demonstrates that TGI could serve as a practical and cost-effective marker for assessing insulin resistance in non-obese PCOS patients. In clinical practice, TGI can be calculated from simple tests routinely requested, such as fasting blood glucose and triglycerides, thus making this method easily accessible. Metabolic risks are frequently disregarded, particularly in non-obese PCOS patients. The utilisation of TGI as a routine screening parameter in this patient group may facilitate early diagnosis of insulin resistance and timely intervention. This finding suggests a potential for contributing to the prevention of type 2 diabetes and cardiometabolic complications in the long term. The presence of IR in women with PCOS and a normal BMI suggests that this syndrome carries a unique metabolic risk, independent of obesity.

Our study has some limitations. Its retrospective and single-center design limits the generalizability of the findings and allows only associative interpretations rather than causal inferences. Moreover, because direct measures of insulin resistance such as HOMA-IR or HIEC were not available in the medical records, we were unable to validate the accuracy of TGI against gold-standard IR assessments. This may lead to an under or overestimation of TGI's true predictive performance. In addition, unmeasured lifestyle-related factors, including dietary patterns, physical activity, and family history of metabolic disease, were not captured in the database and may have influenced individual TGI levels despite our strict exclusion criteria. Future prospective, multicenter studies with comprehensive metabolic profiling and concurrent gold-standard IR measurements are needed to clarify the metabolic pathways underlying elevated TGI in PCOS and to more definitively assess its clinical utility.

Conclusion

In conclusion, our study showed that TGI levels were significantly higher in young non-obese women with PCOS compared to controls. This makes it one of the first studies to demonstrate the relationship between TGI and IR in PCOS patients with a normal BMI. The fact that TGI is easily accessible, cost-effective, and measurable with routine blood tests makes it a practical biomarker for assessing IR in non-obese PCOS patients. This may enable early identification of individuals at high risk for IR and metabolic syndrome. Early diagnosis may allow for timely implementation of appropriate interventions, contributing to the prevention of long-term complications. Prospective studies with larger sample size are needed to confirm our findings.

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