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Predictive role of triglyceride-glucose index in assessing endometriosis risk

Endometriozis riskini değerlendirmede trigliserid-glikoz indeksinin öngörücü rolü

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ABSTRACT

Aim: The aim of our study was to evaluate the predictive role of triglyceride-glucose index in assessing the risk of endometriosis.

Materials and Methods: Our study included 91 patients who were admitted to our gynecology clinic between february 2018 and 2024 and diagnosed with endometriosis and 260 patients in the control group. Body masss index (BMI), total ccholesterol (TC), triglyceriide (TG), high-density lippoprotein cholesterol (HDL-C), low-density lip,oprotein cholesterol (LDL-C), triglyceride-glucose index (TyG), luteinizing hormonne (LH), follicle-stimulating hormonne (FSH), fasting blood glucose (FBG) levels of all patients were retrospectively evaluated in the hospital database.

Results: The combine oral contraceptive use rate and smoking rate was significantly higher in the endometriosis group compared withh the controls group ($p<0.001$, $p=0.046$ respectively). The gravidity and parity value was significantly lower in the endometriosis group compared withh the controls group ($p=0.024$, $p=0.032$ respectively). The FSH value was significantly higher in the endometriosis group compared withh the controls group ($p=0.008$). The TyG index was significantly higher in the endometriosis group compared withh the controls group ($p=0.038$).

Conclusion: Our findings suggest that the TyG index may serve as an alternative tool to predict endometriosis risk and potentially guide future prevention strategies. Larger prospective cohort studiess are needed to confirm these findingss and elucidate the underlyingg mechanismss.

Keywords: Endometriosis, insulin resistance, triglyceride-glucose index

ÖZ

Amaç: Çalışmamızın amacı endometriozis riskini değerlendirmede trigliserid-glikoz indeksinin öngörücü rolünü değerlendirmektir.

Gereç ve Yöntemler: Çalışmamıza Şubat 2018-2024 tarihleri arasında kadın doğum kliniğimize başvuran ve endometriozis tanısı konulan 91 hasta ve kontrol grubundaki 260 hasta dahil edildi. Tüm hastaların vücut kitle indeksi, toplam kolesteroll, trigliserid, yüksek yoğunluklu lippoprotein kolesterol, düşük yoğunluklu lippoprotein kolesterol, trigliserid-glikoz indeksi, luteinize edici hormon, folikül uyarıcı hormon , açlık kan şekeri düzeyleri hastane veri tabanında retrospektif olarak değerlendirildi.

Bulgular: Endometriozis grubunda oral kontraseptif kullanım oranı ve sigara içme oranı, kontrol grubuna göre anlamlı yüksek saptandı ($p<0.001$, $p=0.046$ sırasıyla). Endometriozis grubunda gravida ve parite sayısı kontrol grubuna göre anlamlı düşük saptandı ($p=0.024$, $p=0.032$ sırasıyla). FSH değeri endometriozis grubunda kontrol grubuna göre anlamlı yüksek saptandı ($p=0.008$). Endometriozis grubunda TyG indeksi kontrol grubuna göre anlamlı yüksek saptandı ($p=0.038$).

Sonuç: Bulgularımız TyG indeksinin endometriozis riskini tahmin etmek ve potansiyel olarak gelecekteki önleme stratejilerine rehberlik etmek için alternatif bir araç olarak hizmet edebileceğini göstermektedir. Bu bulguları doğrulamak ve altta yatan mekanizmaları açıklamak için daha büyük prospektif kohort çalışmalarına ihtiyaç vardır.

Anahtar Kelimeler: Endometriozis, insülin direnci, trigliserid-glikoz indeksi

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INTRODUCTION

Endometriosis is a chronic, inflammatory, gynecological disease characcterized by the presence of endometrium-like tisssue outside the uteruss, affecting approximately 10% of women of reproductive age (1-4). Endometrial tissue growing outside the uterus leads to chronic pelvic pain and infertility (5). Endometriosis can cause negative physical, emotional and social effects on women's daily lives (6). Laparoscopic imaging and histopathological confirmation of endometriosis lesions has long been considered the gold standard for diagnosis, although recent published guidelines advocate a nonsurgical diagnosis based on physical examination and imaging and symptoms (7,8). This evolution in the diagnosis of endometriosis is based on the view that surgery is not fully curative and has risks, but also on the recognition that surgical diagnosis can lead to a considerable delay between the onset of sympptoms and the initiation of effective treatment (9-11).

The high incidence and recurrence rates of endometriosis in society have made it necessary to evaluate new options for the long-term management of the disease. Developing new diagnostic methods and predictive biomarkers to increase sensitivity in the diagnosis of endometriosis can make significant contributions to improving the quality of life of patients. It has been reported that endometriosis may be associated with metabolism-related diseases (12,13). Endometriosis has been associated with dysregulation of glucose and lipid metabolism in women (14-18). Women with laparoscopically confirmed endometriosis have been shown to have an increased relative risk of hypercholesterolemia and hypertension (12). The presence of endometriosis has been associated with a higher risk of type 2 diabetes (13). Endometriosis has been associated with an increased risk of gestational diabetes, highlighting that metabolic dysregulation is an important pathological feature of endometriosis (19).

Evidence from recent studies has suggested that a calculated measurement incorporating triglycerides and glucose, called the "Fasting triglyceride-glucose index" or simply the "TyG index," may be helpful as a surrogate marker for assessing insulin resistance (20). The TyG index has even been shown to predict insulin resistance better than surrogate markers such as HOMA-IR when compared to direct measures such as the hyperglycemic clamp method (21). Considering the potential role of metabolic disorders in the pathogenesis of endometriosis, it seems reasonable to investigate the association of insulin resistance with the risk of endometriosis.

The aim of our study was to evaluate the predictive role of triglyceride-glucose index in assessing the risk of endometriosis.

MATERIALS AND METHODS

The present study had a retrospective observational case-control design. The study was designed in line with the Declaration of Helsinki Principles. Informed consent forms were obtained from the patients. This study was started after receiving ethics committee approval from our hospital (Date: 27/11/24, Number: 2024/353). Our study included 91 patients who were admitted to our gynecology clinic between february 2018 and 2024 and diagnosed with endometriosis and 260 patients in the control group. Laparoscopic visualization and histopathological confirmation of endometriosis lesions was used as the gold standard (7,8). Age, body mass index (BMI), parity, combined oral contraceptive (COC) use, smoking and alcohol use history of all patients were evaluated retrospectively. All patients; luteinizing hormonne (LH), follicle-stimulating hormonne (FSH), fasting blood glucose (FBG) TyG index, TyG-BMI index, total cholesterol (TC) level, TC/HDL-C level, triglyceride level, TG/HDL-C level, LDL-C/HDL-C level were evaluated. TyG index: ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL) / 2]; TyG-BMI: TyG index × BMI; TC/HDL-C: TC (mg/dL) / HDL-C (mg/dL); TG/HDL-C: TG (mg/dL) / HDL-C (mg/dL) method was used to calculate. Patients with known diabetes mellitus, chronic hypertension, familial or acquired hyperlipidemia, autoimmune disease, and those using regular corticosteroids secondary to any chronic inflammatory process were excluded from the study. Statistical analysis was performed using the SPSSx version 26.0 statistics software (IBM Incc., Chicago, ILı, USA). The normality of the distribution was evaluated using the Kolmogorov-Smirnov test. Normal variables were expressed as mean ± standard deviation. Quantitative data of all patients are presented as median (minimum-maximum). Student's t-test or the Mann Whitney-U test was used to compare differences between groups. Non-normally distributed parameters were analyzed using the Mann-Whitney U test. Results were evaluated at a 95% confidencee interval (CI). The p-value considered statistically significant was <0.05.

RESULTS

The COC use rate was significantly higher in the endometriosis group compared with the controls group ($p<0.001$). The smoking rate was significantly higher in the endometriosis group compared with the controls group ($p=0.046$). The gravidity value was significantly lower in the endometriosis group compared with the controls group ($p=0.024$). The parity value was significantly lower in the endometriosis group compared with the controls group ($p=0.032$) (Table 1).

The FSH value was significantly higher (8.24±3.46 mIU/mL) in the endometriosis group compared with the controls group (6.68±3.86

Table 1. Comparison of demographic and obstetric data according to the presence of Endometriosis

	Endometriosis n=91	Controls n=260	p
	median (min-max)		
Age (years)	32 (18-41)	31 (18-40)	0.16
BMI (kg/m²)	24.4 (18.9-35.3)	24.2 (18.6-34.7)	0.22
COC, n (%)	19 (20.8%)	12 (4.6%)	<0.001
Smoking, n (%)	18 (19.7%)	39 (15%)	0.046
Alcohol, n (%)	12 (13.1%)	35 (13.4%)	0.42
Gravidity	1.3 (1-3)	1.8 (1-4)	0.024
Parity	1.1 (1-3)	1.6 (1-4)	0.032

BMI: Body mass index, COC: Combined oral contraceptive

Table 2. Comparison of lipid parameters according to the presence of Endometriosis

	Endometriosis n=91	Controls n=260	p
	mean ± SD		
FSH (mIU/mL)	8.24±3.46	6.68±3.86	0.008
LH (mIU/mL)	8.08±1.92	7.68±1.86	0.48
TC (mg/dL)	198.7±44.82	188.58±36.4	0.046
TG (mg/dL)	140.44±63.58	121.52±46.54	0.018
TC/HDL-C	4.30±1.32	4.02±1.44	0.044
TG/HDL-C	3.04±1.22	2.57±1.2	0.012
HDL-C (mg/dL)	46.61±18.4	47.18±17.8	0.56
LDL-C (mg/dL)	123.34±22.8	116.84±20.48	0.026
LDL-C/HDL-C	2.67±1.11	2.46±1.13	0.042
FBG (mg/dL)	94.9±15.22	90.3±13.54	0.022
TyG	8.44±0.51	8.34±0.38	0.038
TyG-BMI	205.94±44.1	200.16±41.8	0.061

FSH: Follicle-stimulating hormone, LH: luteinizing hormone, TC: Total cholesterol, TG: Triglyceride, HDL: High density lipoprotein, LDL: Low density lipoprotein, FBG: Fasting blood glucose, TyG: Triglyceride glucose, TyG-BMI: Triglyceride glucose-body mass index

mIU/mL) (p=0.008). The TC value was significantly higher (198.7±44.82 mg/dL) in the endometriosis group compared with the controls group (188.58±36.4 mg/dL) (p=0.046). The TG value was significantly higher (140.44±63.58 mg/dL) in the endometriosis group compared with the controls group (121.52±46.54) (p=0.018). The TC/HDL-C ratio was significantly higher (4.30±1.32) in the endometriosis group compared with the controls group (4.02±1.44) (p=0.044). The TG/HDL-C ratio was significantly higher (3.04±1.22) in the endometriosis group compared with the controls group (2.57±1.2) (p=0.012). The LDL-C value was significantly higher (123.34±22.8 mg/dL) in the endometriosis group compared with the controls group (116.84±20.48 mg/dL) (p=0.026). The LDL-Cx/HDL-Cx ratio was significantly higher (2.67±1.11) in the endometriosis group compared with the controls group (2.46±1.13) (p=0.042). The FBG value was significantly higher (94.9±15.22 mg/dL) in the endometriosis group compared with the controls group (90.3±13.54 mg/dL) (p=0.022). The TyG index was significantly higher (8.44±0.51) in the endometriosis group compared with the controls group (8.34±0.38) (p=0.038) (Table 2).

DISCUSSION

Although there are many studies in the literature evaluating the relationship between the Tyg index and systemic diseases, data on the predictive role of the TyG index and accompanying lipid parameters in predicting the risk of endometriosis are quite limited. When endometriosis patients were compared with the control group, COC use rate, smoking rate, FSH, TC, TG, TC/HDL-C, TG/HDL-C, LDL-C, LDL-C/HDL-C, TyG and FBG levels were higher, and gravidity and parity values were lower.

Endometriosis is a multifactorial and systemic disease caused by many factors and the exact pathogenesis has not been clearly elucidated (1). Recently, metabolic abnormalities, including dyslipidemia and glucose metabolism dysfunction, have been increasingly reported as an etiology of endometriosis (14,23). Endometriosis is known to be associated with abnormally high estrogen levels (24,25). Additionally, hyperinsulinemia may promote androgen production, leading to hormonal imbalances

between estrogen and progesterone, which may further facilitate the formation and growth of ectopic endometrial lesions (26,27). Prolonged activation of estrogen receptors by environmental estrogens can lead to excessive insulin secretion, pancreatic β-cell failure, and peripheral insulin resistance, and may promote the development of ectopic endometrial tissue (28,29). Insulin resistance is associated with chronic systemic inflammation, which plays a role in the development and progression of endometriosis (30). Insulin resistance can cause an inflammatory response, creating a vicious cycle that impairs endometrial tissue function (31). Accordingly, ectopic endometrial tissue may become more easily attached and spread (32). Inflammation associated with insulin resistance may cause endothelial dysfunction (33). The resulting abnormal local angiogenesis contributes to the formation and growth of ectopic endometrial lesions (34,35). Insulin resistance may also affect the balance of cell proliferation and apoptosis and affect the colonization of ectopic cells (34,35). These mechanisms likely interact to collectively drive the onset and progression of endometriosis. Numerous studies have demonstrated the potential of the TyG index in predicting the risk of various metabolism-related disorders (36–40).

There are studies indicating that the TyG index is a reliable and effective marker of insulin resistance and offers significant advantages in terms of cost and convenience compared to traditional markers (41,43). There are several views on the possible underlying mechanisms linking the TyG index to endometriosis. Insulin resistance may lead to hyperinsulinemia and elevated levels of insulin-like growth factor-1 (IGF-1), potentially promoting the growth and proliferation of endometrial tissue outside the uterus (44,45).

In the study by Brito et al., the TyG index, measured based on blood fasting triglycerides and glucose, was suggested as an effective surrogate marker for insulin resistance and indicated that it could integrate the effect of both triglycerides and glucose on endometriosis (46). In the study conducted by Liu et al. using the National Health and Nutrition Examination Survey data, a significant positive association was found between the TyG index and the risk of endometriosis in the US adult population, and it was emphasized that the TyG index may have a clinical role in the prevention and treatment strategies of endometriosis. After adjusting for several covariates, they found that participants in the highhest quartile of the TyG index had a 104% higher risk of endometriosis compared with participants in the lowest quartile (47). In the study by Cao et al., multivariate logistic regression analysis showed that an increase in the TyG index was significantly associated with a higher incidence of endometriosis. They revealed that the risk of endometriosis increased significantly when the TyG index exceeded 8.51 (48). In the study conducted by Yavuzcan et al., it was revealed that TyG, TyG-BMI and LAP indices may not serve as reliable markers for PCOS screening but may be useful in defining insulin resistance in Turkish women diagnosed with PCOS (49). In the study of Verit et al., positive associations were found between unexplained infertility and hs-CRP, TG, TC and LDL and a negative association was found with HDL. Of these markers, TG, HDL and hs-CRP were expressed as independent predictors associated with unexplained infertility (50). In the study by Yilmaz et al., it was revealed that patients with endometriosis had a high risk of developing a proatherogenic lipid profile and an elevated atherogenic plasma index. Among serum lipid parameters, triglyceride levels were found to be significantly higher in endometriosis patients than in the control group (51).

In our study, consistent with the results of related publications in the literature, lipid parameters, especially TyG index, were found to be significantly higher in the endometriosis group compared to the control group. Our findings provide new insights into the relationship between insulin resistance and associated changes in lipid parameters and the development of endometriosis, suggesting that the TyG index may serve as a valuable clinical tool to predict and assess the risk of endometriosis. It is well known that pregnancy can cause significant metabolic and hormonal changes, which may mediate the effect on the progression of endometriosis through insulin resistance (52). However, parity is considered an important protective factor for endometriosis (53).

In our study, consistent with the literature, the parity number in the endometriosis group was found to be significantly lower than in the control group. It is emphasized that there is an increase in cigarette and alcohol consumption in patients with endometriosis, and that inflammatory responses triggered by cigarette and alcohol consumption may facilitate the development of endometriosis (54-58). Potentially attributable to the hypothesis that smoking and alcohol consumption may exacerbate the negative impact of insulin resistance on endometrial tissue, ultimately resulting in an increased susceptibility to the development of endometriosis (59,60).

In our study, the smoking rate in the endometriosis group was found to be significantly higher than in the control group. In the study by Vercellini et al., regarding the stratified analysis according to the use of oral contraceptives, it was reported that the use of oral contraceptives may reduce the risk of endometriosis, indicating that the use of oral contraceptives may serve as a protective factor against the development of endometriosis (61). In our study, the rate of COC use in the endometriosis group was found to be significantly higher than in the control group. The reason for this may be that COC was recommended to patients as a medical treatment option in various centers in the preoperative period.

There are some limitations to our study. The retrospective cross-sectional nature of our study limits the establishment of a causal relationship between the TyG index and endometriosis. However, the small sample size of the study can be considered another limitation. Despite adjusting for multiple confounding factors, the observed relationship between the TyG index and endometriosis may still be affected by other unmeasured confounding factors. The fact that endometriosis was diagnosed surgically, independent of self-reporting, can be considered a strength of the study as it eliminates recall bias.

CONCLUSION

Our findings suggest that the TyG index may serve as an alternative tool to estimate the risk of endometriosis and potentially guide future prevention strategies. Routine calculation and listing of the TyG index in laboratory biochemical tests may help gynecologists effectively identify individuals at higher risk and facilitate early intervention and treatment. Additionally, targeting metabolic dysfunctions such as insulin resistance through lifestyle changes and pharmacological interventions may offer a new therapeutic approach for the management of endometriosis. Larger prospective cohort studies are needed to confirm these findingss and elucidate the underlying mechanisms.

Conflict of Interest: Authors declared that there is no conflict of interest.

Author Contribution: Idea: UA. Design:OY, AB; Literature search: TBB, Aİ; Materials: AA, CA. Statistical analysis: SE; Writing: UA; Critical Review: ACÖ, FA

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