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Relationship between triglyceride-glucose index and endometriosis: a cross-sectional analysis

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Abstract

Background The link between insulin resistance and endometriosis is not well established. The triglyceride-glucose (TyG) index serves as a straightforward and economical indicator of insulin resistance. This study examines the link between the TyG index and the prevalence of endometriosis in a U.S. cohort.

Methods This cross-sectional study analyzed data from the NHANES conducted between 1999 and 2006. Reproductive health was assessed through questionnaires, and the TyG index was derived from fasting triglyceride and glucose measurements. Weighted logistic regression models were used to analyze the relationship between the TyG index and endometriosis. Restricted cubic spline (RCS) curves explored the linear relationship, while stratified and sensitivity analyses assessed potential interactions and the robustness of the findings.

Results The study included 2,346 women, with 176 diagnosed with endometriosis and 2,170 without. Women with endometriosis exhibited an elevated TyG index compared to those without the condition. The weighted logistic regression analysis revealed that the TyG index is an independent risk factor for endometriosis (OR = 1.58, 95% CI 1.17–2.14, $p = 0.004$). RCS analysis indicated a significant positive linear association between the TyG index and endometriosis, with a turning point at 8.51. Subgroup analysis indicated a stronger association in certain populations. The post-propensity score matching analysis confirmed the robustness of these findings.

Conclusion In the U.S. population, a higher TyG index is positively and linearly associated with endometriosis prevalence. Effective management of blood glucose and lipid levels may reduce the prevalence of endometriosis.

Keywords Endometriosis, Triglyceride-glucose index, NHANES

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Background

Endometriosis is a major challenge among chronic gynecological disorders, impacting 10-15% of women in their reproductive years [1, 2]. It involves endometrial tissue growing outside the uterus, leading to chronic pelvic pain and infertility [3, 4]. Despite extensive research, early diagnosis of endometriosis remains challenging due to its diverse and nonspecific symptoms. While vaginal ultrasound is effective for detecting the disease, it struggles to identify early stages. The gold standard, laparoscopically guided biopsy [5, 6], often results in a delay of 6 to 11 years in diagnosis [7], exacerbating patient suffering and disease progression. Thus, developing novel diagnostic methods and predictive biomarkers to enhance diagnostic accuracy and sensitivity is crucial for improving patients' quality of life.

Various factors influence women's fertility, including age, lifestyle, environmental factors, and metabolic disorders like obesity and metabolic syndrome [8–10]. Among these, insulin resistance (IR) emerges as a pathophysiological condition that impairs glucose metabolism in tissue cells, potentially leading to metabolic abnormalities such as hyperglycemia, hyperlipidemia, and obesity [11–13]. Current research suggests that insulin sensitivity is reduced in endometriosis cells, which is accompanied by an increase in the glycolytic pathway, resulting in elevated lactate levels in follicular fluid. This process induces inflammation, angiogenesis, and cell proliferation [14]. Furthermore, endometriosis has been associated with an increased risk of gestational diabetes [15], highlighting metabolic dysregulation as a significant pathological feature of endometriosis. However, traditional methods for assessing IR, like the hyperinsulinemic-euglycemic clamp (HIEC), suffer from being costly and time-consuming [16]. In recent years, the triglyceride-glucose index (TyG index) has emerged as a novel indicator for IR, demonstrating advantages in evaluating IR [17–20]. Although the TyG index has been linked to adverse clinical outcomes such as cardiovascular diseases [21–23], diabetes [24, 25], atherosclerosis [26, 27], and non-alcoholic fatty liver disease [28, 29], no studies have yet examined the relationship between insulin resistance markers and endometriosis.

This study aims to examine the link between the TyG index and endometriosis in reproductive-aged women, utilizing data from the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2006. Our objective is to assess the community-level impact of the TyG index on endometriosis risk in this population, providing new insights for clinical practice and deepening our understanding of endometriosis.

Methods

Study population

NHANES is a nationally representative survey of the United States population conducted biennially. Data collection involves structured interviews at participants' homes and physical examinations with laboratory tests at mobile examination centers. This study is approved by the Ethics Review Committee of the National Center for Health Statistics (NCHS), and all participants provide written informed consent.

This cross-sectional study analyzed data from the NHANES database spanning 1999–2006. Initially, 41,474 participants were considered. Male participants (n=20,264) were excluded. Additionally, participants with missing endometriosis data (n=15,653) or those without calculable TyG index (n=3,049) and fasting weight (n=162) were excluded. The final analysis included 2,346 participants with complete data (Fig. 1).

Diagnosis of endometriosis

Self-reported endometriosis is diagnosed based on the "RHQ360" questionnaire administered in the Mobile Examination Center as part of NHANES. The structured questionnaire includes the following question: "Has a doctor or other health professional ever told you that you have endometriosis?" Individuals who answer "yes" are classified as self-reported endometriosis cases.

Evaluation of TyG index

The TyG index, the study's exposure variable, was calculated from fasting triglyceride and fasting blood glucose levels using the following formula [30, 31]: TyG index=ln[(Fasting Triglycerides (mg/dL)*Fasting Glucose (mg/dL)/2].

Covariates

The study controlled for multiple factors identified in previous research, including age, race, Body mass index (BMI), poverty-income ratio (PIR), education, smoking, drinking, marital status, menarche, pregnancy, hypertension, and diabetes. The poverty-income ratio (PIR) is calculated based on the U.S. Department of Health and Human Services Family Income Poverty Guidelines [32]. Smokers were defined as individuals who had smoked 100 or more cigarettes, while drinkers were defined as those who had consumed at least 12 drinks. Hypertension and diabetes diagnoses were based on self-report.

Statistical analysis

Data were weighted using fasting weights to provide nationally representative estimates, and multiple imputation was used to estimate missing covariates. Continuous variables were reported as means (standard errors), and categorical variables as percentages (95% confidence

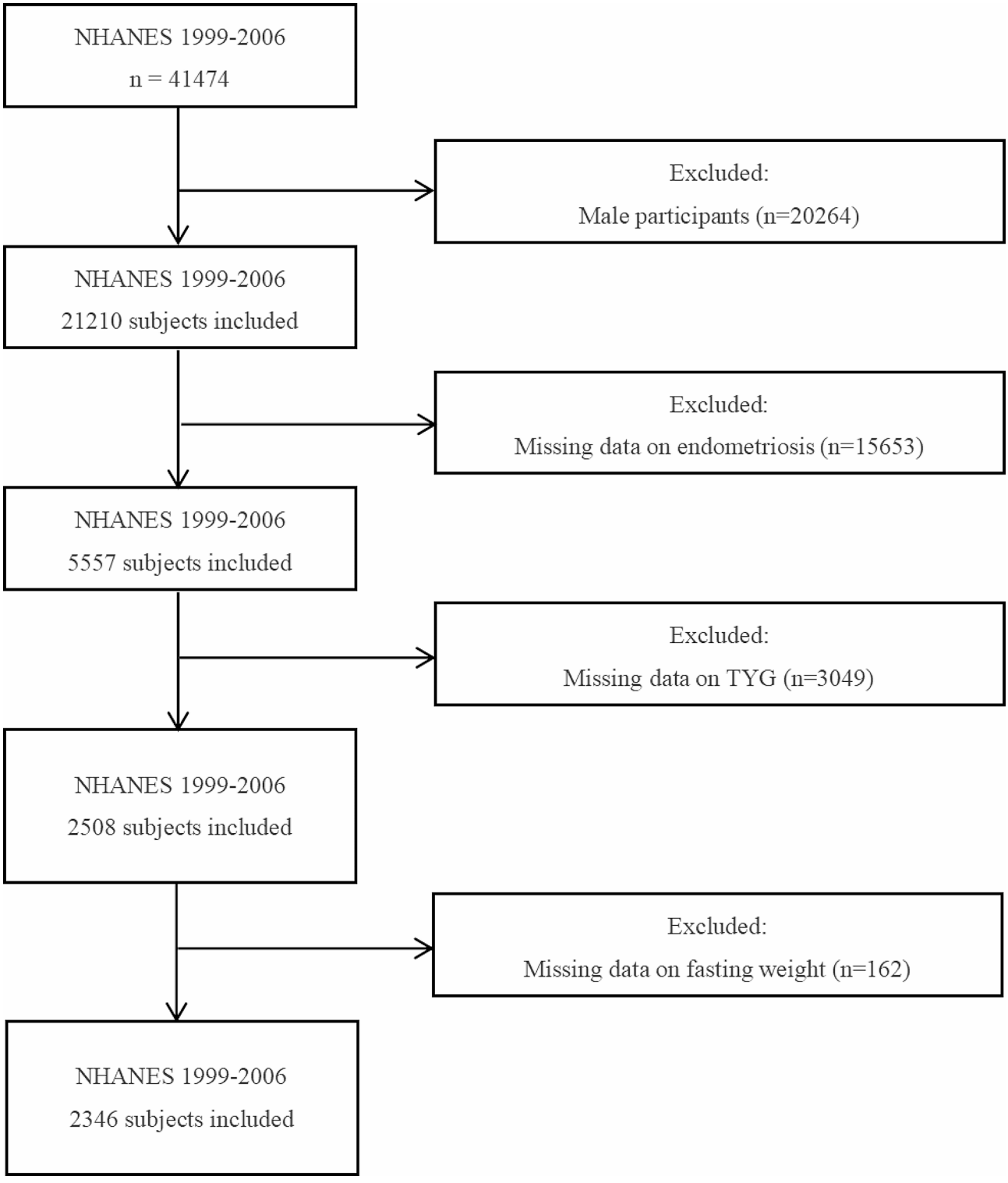

Fig. 1 Flow chart for the inclusion and exclusion criteria

intervals). Weighted logistic regression models were used to assess the relationship between the TyG index and endometriosis. Restricted cubic spline (RCS) was used to examine the non-linear relationship. Participants were stratified based on education level, race, alcohol consumption, smoking status, marital status, age at menarche, and pregnancy history. A weighted multivariate logistic regression on the post-propensity score matching

Table 1 Weighted baseline characteristics of study participants

	Controls (*n* = 2170)	Endometriosis (*n* = 176)	*P* value
Age	36.83 (0.30)	40.23 (0.63)	< 0.001
BMI	28.09 (0.20)	28.58 (0.47)	0.33
PIR	2.98 (0.05)	3.17 (0.16)	0.23
TyG	8.46 (0.02)	8.66 (0.05)	0.002
Menarche	12.67 (0.05)	12.40 (0.16)	0.11
Race			< 0.001
White	973 (67.41)	120 (83.91)	
Mexican	557 (8.57)	10 (1.41)	
Black	440 (12.69)	36 (9.09)	
Other	200 (11.33)	10 (5.59)	
Education			0.02
Less high school	548 (16.74)	22 (10.82)	
High School	453 (22.43)	45 (30.24)	
Above high school	1169 (60.83)	109 (58.95)	
Smoke			< 0.001
No	1376 (58.79)	84 (42.02)	
Yes	794 (41.21)	92 (57.98)	
Hypertension			0.29
No	1797 (82.24)	127 (79.24)	
Yes	373 (17.76)	49 (20.76)	
Diabetes			0.71
No	2088 (96.31)	169 (96.85)	
Yes	82 (3.69)	7 (3.15)	
Drinking			0.03
No	908 (39.52)	54 (28.65)	
Yes	1262 (60.48)	122 (71.35)	
Marital status			0.03
Separated	321 (15.31)	34 (16.89)	
Married	1444 (65.99)	118 (74.28)	
Never married	405 (18.71)	24 (8.83)	
Pregnancy			0.09
No	1871 (81.59)	150 (85.72)	
Yes	299 (18.41)	26 (14.28)	

BMI, body mass index; PIR, poverty-income ratio; TyG, triglyceride-glucose

(PSM) data assessed whether the TyG index and endometriosis association remained significant. Matching was performed at a 1:2 ratio with a caliper value of 0.02 using the nearest neighbor method. Covariates adjusted for in the PMS included age, race, BMI, PIR, education, smoking, drinking, marital status, menarche, pregnancy, hypertension, and diabetes. Statistical significance was set at $P<0.05$. All analyses were conducted using R software.

Results

Characteristics of study participants

Our study included 2,346 participants, of whom 176 were diagnosed with endometriosis. Table 1 presents the descriptive characteristics of the study population by endometriosis status. Compared to participants without endometriosis, those with the condition were generally older, had a higher likelihood of having a high school education, and were more likely to be non-Hispanic white. Additionally, endometriosis patients had higher rates of smoking, alcohol consumption, and marriage. Notably, they also exhibited higher TyG index levels than participants without endometriosis.

Table 2 Correlation of TyG index and endometriosis

	Model 1	Model 2	Model 3
OR (95% CI)	1.64 (1.27,2.12)	1.59 (1.17,2.15)	1.58 (1.17,2.14)
P value	< 0.001	0.003	0.004

Model 1: Non-adjusted

Model 2: Adjusted for age, race, BMI, PIR and education

Model 3: Further adjusted for marital status, menarche, pregnancy, smoke, drinking, hypertension and diabetes, based on model 2

OR: Odds ratio; CI: Confidence interval

Connections between the TyG index and endometriosis

Table 2 shows the results of the weighted logistic regression analysis. The unadjusted model indicates a

significant positive association between the TyG index and endometriosis risk (OR = 1.64; 95% CI: 1.27–2.12; $P < 0.001$). After adjusting for age, race, BMI, PIR, and education in Model 2, the TyG index remained significantly associated with a higher risk of endometriosis (OR = 1.59; 95% CI: 1.17–2.15; $P = 0.003$). This association persisted in Model 3, which adjusted for all covariates (OR = 1.58; 95% CI: 1.17–2.14; $P = 0.004$).

Linear association between the TyG index and endometriosis

A restricted cubic spline model was used to evaluate the linear relationship between the TyG index and the risk of endometriosis (Fig. 2). The analysis indicated a significant positive linear association (non-linearity $P = 0.24$; overall $P < 0.001$), with a breakpoint identified at 8.51.

Subgroup analysis

To examine the relationship between endometriosis and the TyG index among different subgroups, we conducted stratified and interaction analyses based on demographic characteristics (Fig. 3). Subgroup analysis revealed a stronger association between the TyG index and endometriosis in specific populations, including non-Hispanic white women, married individuals, smokers, drinkers, and those without a history of pregnancy. However, interaction analysis indicated that the relationship between the TyG index and endometriosis was not significantly modified by race, education, marital status, smoking, drinking, or pregnancy.

Sensitivity analysis

A sensitivity analysis was conducted to examine the association between the TyG index and endometriosis using propensity score matching (PSM). As shown in Table 3, after PSM, covariate differences between the two groups were controlled, and participants with endometriosis still had a significantly higher TyG index than the control group. Additionally, the weighted multivariate regression analysis in Table 4 demonstrated that the results post-PSM were consistent with those before matching, confirming that the TyG index is an independent risk factor for endometriosis.

Discussion

This study analyzed data from the NHANES cycles between 1999 and 2006, evaluating for the first time the relationship between the TyG index and the risk of endometriosis in 2,346 women. The results show a linear positive relationship between endometriosis risk and the TyG index. Subgroup analyses further revealed that this correlation is more pronounced in certain populations. This study underscores the importance of the TyG index in endometriosis development.

Our findings show that patients with endometriosis tend to be older and predominantly non-Hispanic white.

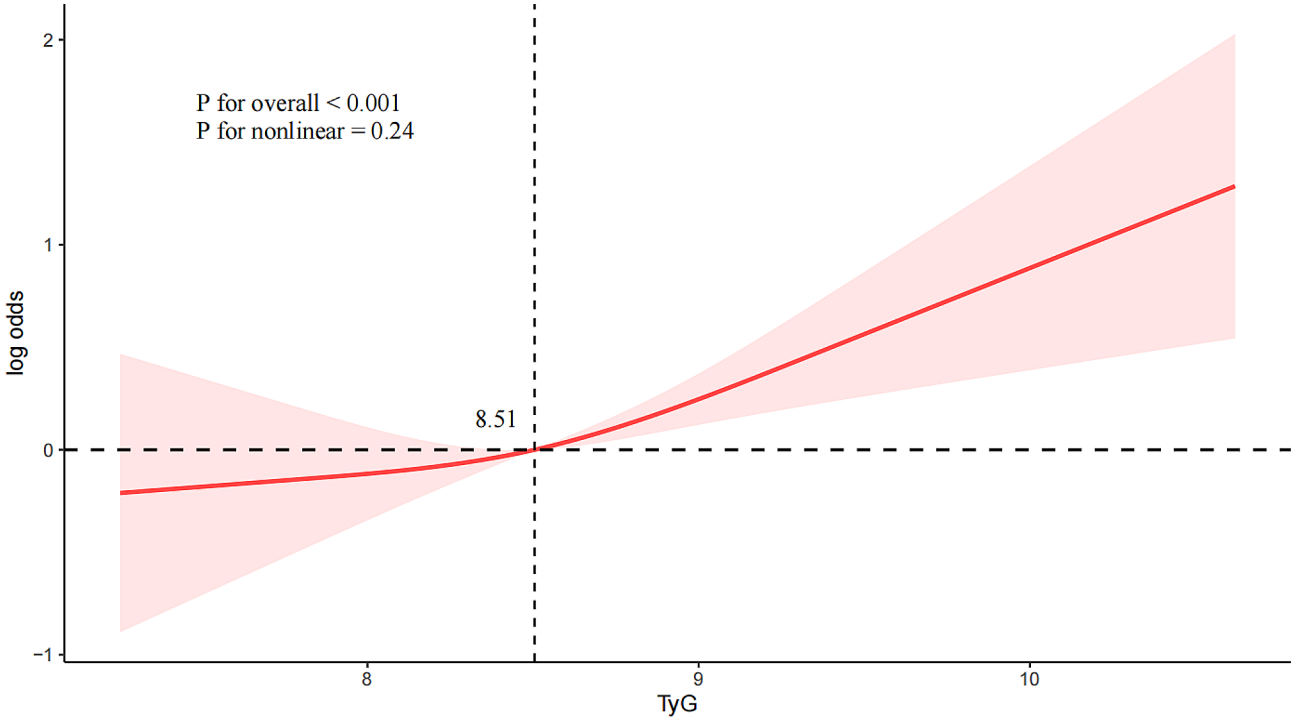

Fig. 2 The nonlinear relationship between TyG index and Endometriosis. The analysis was adjusted for age, race, BMI, PIR, education, marital status, menarche, pregnancy, smoking, drinking, hypertension, and diabetes

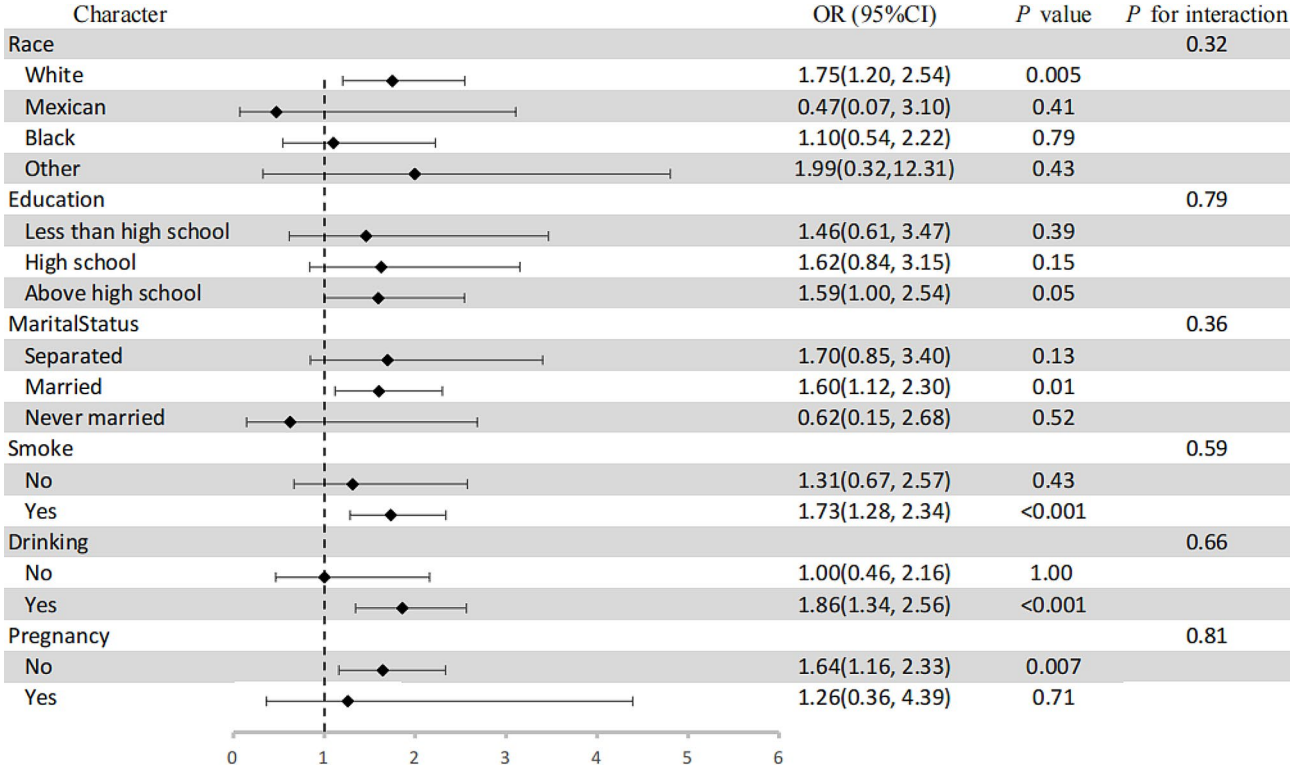

Fig. 3 Stratified analysis of the relationship between TyG index and endometriosis

Additionally, these patients are more likely to have a history of alcohol consumption and smoking. The delayed diagnosis of endometriosis, often occurring 6 to 11 years after the onset of symptoms [33, 34], likely contributes to the older age observed in these patients. The higher incidence in white individuals may be related to racial susceptibility. Furthermore, we observed increased rates of smoking and alcohol consumption among endometriosis patients, potentially due to the inflammatory responses [35–37] triggered by smoking [38, 39] and drinking [40–42], which may facilitate the development of endometriosis.

The link between endometriosis and insulin resistance remains unclear. The TyG index is a reliable and effective marker of insulin resistance [43–45] and offers significant advantages in terms of cost and convenience compared to traditional markers. Our study is the first to identify a link between the TyG index and endometriosis risk. Multivariable logistic regression analysis showed that an increase in the TyG index is significantly associated with a higher incidence of endometriosis (OR=1.58, 95% CI 1.17–2.14, p=0.004). Additionally, RCS curves indicated that the risk of endometriosis increases notably when the TyG index exceeds 8.51. Traditional metabolic markers, such as fasting glucose and triglyceride levels, may not fully capture metabolic health, and individuals with normal ranges may still have early metabolic syndrome symptoms. Therefore, a TyG index over 8.51 suggests potential metabolic abnormalities, warranting proactive management to reduce endometriosis risk.

While our study has highlighted this correlation, the exact mechanisms linking endometriosis and insulin resistance remain to be fully elucidated. Endometriosis is known to be associated with abnormally high estrogen levels [46–48]. Prolonged activation of estrogen receptors by environmental estrogens may lead to excessive insulin release, pancreatic β-cell failure, and peripheral insulin resistance [49, 50], promoting the development of ectopic endometrial tissue. This process is speculated to be closely related to inflammation. Insulin resistance may induce an inflammatory response, creating a vicious cycle that disrupts endometrial tissue function [51, 52], facilitating the attachment and spread of ectopic endometrial tissue [53, 54]. Additionally, inflammation associated with insulin resistance can cause endothelial dysfunction [55], mediating abnormal local angiogenesis and contributing to the formation and growth of ectopic endometrial lesions. Insulin resistance may also affect the balance of cell proliferation and apoptosis [56–58], influencing the colonization of ectopic cells. These mechanisms likely interact, collectively driving the onset and progression of endometriosis. Future research is needed to further investigate these potential mechanisms and their interactions to clarify the relationship between insulin resistance and endometriosis.

Table 3 Weighted baseline characteristics of study participants

	Controls (*n* = 352)	Endometriosis (*n* = 176)	*P* value
Age	40.35 (0.57)	40.23 (0.63)	0.85
BMI	28.09 (0.48)	28.58 (0.47)	0.47
PIR	3.23 (0.10)	3.17 (0.16)	0.74
TyG	8.47 (0.04)	8.66 (0.05)	0.004
Menarche	12.52 (0.07)	12.40 (0.16)	0.50
Race			0.10
White	239 (82.38)	120 (83.91)	
Mexican	7 (0.64)	10 (1.41)	
Black	84 (11.26)	36 (9.09)	
Other	22 (5.72)	10 (5.59)	
Education			0.99
Less high school	43 (9.44)	22 (10.82)	
High School	89 (26.97)	45 (30.24)	
Above high school	220 (63.59)	109 (58.95)	
Smoke			0.59
No	178 (47.76)	84 (42.02)	
Yes	174 (52.24)	92 (57.98)	
Hypertension			0.55
No	262 (75.67)	127 (79.24)	
Yes	90 (24.33)	49 (20.76)	
Diabetes			1.00
No	338 (96.44)	169 (96.85)	
Yes	14 (3.56)	7 (3.15)	
Drinking			0.96
No	107 (29.00)	54 (28.65)	
Yes	245 (71.00)	122 (71.35)	
Marital status			0.88
Separated	74 (18.84)	34 (16.89)	
Married	230 (70.06)	118 (74.28)	
Never married	48 (11.10)	24 (8.83)	
Pregnancy			0.75
No	297 (82.70)	150 (85.72)	
Yes	55 (17.30)	26 (14.28)	

Table 4 Correlation of TyG index and endometriosis

	Model 1	Model 2	Model 3
OR (95% CI)	1.55 (1.17,2.07)	1.56 (1.13,2.17)	1.65 (1.15,2.36)
P value	0.003	0.01	0.01

Model 1: Non-adjusted

Model 2: Adjusted for age, race, BMI, PIR and education

Model 3: Further adjusted for marital status, menarche, pregnancy, smoke, drinking, hypertension and diabetes, based on model 2

Subgroup analyses indicated that the association between endometriosis and the TyG index is more pronounced in certain populations, including non-Hispanic white women, married individuals, smokers, drinkers, and those without a history of pregnancy. These groups should particularly monitor their blood glucose and lipid levels, which may help reduce the risk of endometriosis. However, the underlying mechanisms require further clarification. Sensitivity analyses confirmed the robustness of our results.

The strengths of our study include the use of a large, nationally representative NHANES database, enhancing the generalizability of our findings to the U.S. population. Moreover, we were the first to explore the association between the TyG index and the risk of endometriosis. However, our study also has limitations. First, as a cross-sectional study, it cannot establish causality between the TyG index and endometriosis. Second, the diagnosis of endometriosis was based on self-reported data rather than the gold standard, which could introduce both recall bias and report bias, affecting the accuracy of the diagnosis. Despite adjusting for numerous confounding factors, the observed association between the TyG index and endometriosis may still be influenced by other unmeasured confounders. Therefore, more comprehensive prospective cohort studies are needed to verify whether the TyG index can serve as a reliable predictive or diagnostic marker for endometriosis.

Our study highlights the TyG index as a significant predictive marker for endometriosis, demonstrating a clear association between higher TyG index levels and an increased risk of endometriosis. This finding suggests that proactive management of blood glucose and lipid levels could be beneficial for patients at high risk of endometriosis. Regular monitoring of the TyG index in clinical practice may help in the early identification of high-risk women, allowing for timely interventions to reduce the incidence and severity of endometriosis, ultimately improving patient outcomes.

Conclusions

In summary, an elevated TyG index is linked to an increased incidence of endometriosis. Thus, proactive management of blood glucose and lipid levels might help reduce the prevalence of endometriosis. Future research should investigate whether interventions targeting the TyG index can improve clinical outcomes for endometriosis.

Abbreviations

TyG	Triglyceride-Glucose
NHANES	National Health and Nutrition Examination Survey
IR	Insulin Resistance
HIEC	Hyperinsulinemic-Euglycemic Clamp
BMI	Body Mass Index
RCS	Restricted Cubic Splines
NCHS	National Centre for Health Statistics
OR	Odds Ratio
PIR	Poverty-Income Ratio
CI	Confidence Interval
SE	Standard Error

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Author contributions

Y Cao & Q Yang: Draft writing, project conception and design, data acquisition, analysis, and interpretation.QQ Mai & JX Wuliu: Data acquisition and analysis. KX Deng: Manuscript review-editing and supervision.All authors have reviewed and approved the final manuscript and consent to the author order.

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Data availability

The data sets produced and/or examined in this study can be found in the NHANES repository at www.cdc.gov/nchs/nhanes.

Declarations

Ethics approval and consent to participate

This study followed the principles set forth in the Declaration of Helsinki and was approved by the Ethics Review Board of the National Center for Health Statistics (NCHS). Informed written consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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