International Journal of Chronic Obstructive Pulmonary Disease Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Exploring Gender Differences in the Association Between TyG Index and COPD: A Cross-Sectional Study from NHANES 1999-2018

Jun Guo[1], Jie Yang[2], Jinghua Wang[3], Wei Liu[1], Yingjie Kang[4], Zhi Li[1], Chen Hao[1], Shuai Qi[1]

[1]General Surgery, Bethune International Peace Hospital, Shijiazhuang, People's Republic of China; [2]Cadre Ward, Bethune International Peace Hospital, Shijiazhuang, People's Republic of China; [3]Nephrology, Bethune International Peace Hospital, Shijiazhuang, People's Republic of China; [4]General Surgery, Hebei Yiling Hospital, Shijiazhuang, People's Republic of China

Correspondence: Jie Yang, Cadre Ward, Bethune International Peace Hospital, Shijiazhuang, People's Republic of China, 398 West Zhongshan Road, Shijiazhuang, People's Republic of China, Tel +8615350539632, Email 270593583@qq.com

Purpose: This study examined gender differences in the association of Triglyceride-Glucose (TyG) index with the prevalence of chronic obstructive pulmonary disease (COPD), particularly in a non-diabetic population.

Methods: The study leveraged data from the National Health and Nutrition Examination Survey (NHANES), spanning from 1999 to 2018, with a cohort of 23,456 participants. Logistic regression and restricted cubic spline analyses were employed to explore the relationship between the TyG index and COPD prevalence.

Results: Statistical analyses revealed a significant positive association between the TyG index and COPD prevalence among non-diabetic women after adjustment for all covariates (OR=1.50; 95% CI, 1.08–2.08), supported by a linear relationship (P for non-linearity=0.298). No equivalent significant association was found in non-diabetic men (OR=1.00; 95% CI, 0.67–1.48). Within the diabetic group, the TyG index did not show a significant association with COPD prevalence, regardless of gender.

Conclusion: Our study reveals a significant positive correlation between the TyG index and COPD prevalence in the non-diabetic population, marked by notable gender differences.

Keywords: TyG index, insulin resistance, chronic obstructive pulmonary disease, cross-sectional study

Introduction

Chronic obstructive pulmonary disease (COPD) has emerged as a prominent global public health concern, with a surge in prevalence, mortality rates, and financial burden, especially in developing countries.[1] There has been a growing emphasis on investigating the complex origins of COPD and its established connections with various metabolic disorders.[2,3] Insulin resistance is widely acknowledged as a harbinger of diabetes and is also believed to be intricately linked to the progression of COPD.[4,5] The emerging biomarker, the Triglyceride-Glucose (TyG) index, has received considerable focus for its capacity to indicate insulin resistance within the organism.[6,7] The TyG index has been associated not only with various metabolic disorders, including diabetes, hypertension, coronary arteriosclerosis, and hepatic complications,[8–10] but also with the recent investigations that have probed its relationship with pulmonary conditions, emphasizing COPD.[11]

Earlier research has mainly concentrated on the general population,[4] neglecting the influence of gender differences on the TyG index's correlation with COPD.[12] Considering the significant role of gender differences in various physiological and pathological processes, there is a notable gap in gender-specific analysis in this field of study. This study intends to investigate gender disparities in the association between the TyG index and COPD prevalence, also taking into account the possible influence of diabetes status on this relationship.[13]

Received: 10 April 2024
Accepted: 25 August 2024
Published: 4 September 2024

Methods

Study Population

This study employed a cross-sectional design, analyzing data from NHANES participants aged 20 and older between 1999 and 2018. NHANES used a complex, multistage, stratified sampling method to accurately represent the US non-institutionalized population.[14] Demographic and medical history data were collected through comprehensive in-home interviews with participants. The Mobile Examination Centers (MEC) conducted physical examinations and collected blood samples. The Ethics Review Board of the National Center for Health Statistics approved the NHANES. All participants gave written informed consent. This study is a secondary analysis and therefore does not require ethical approval. The Bethune International Peace Hospital Ethics Committee granted an exemption, with ethics approval number 2024-KY-120.

Measurement of TyG Index

The TyG index is calculated using fasting levels of triglycerides and glucose.[15] The formula for calculating the TyG index is: TyG = ln [(fasting triglycerides (mg/dL) × fasting glucose (mg/dL)) / 2].[16]

Chronic Obstructive Pulmonary Disease

This study analyzed participants' COPD status as the dependent variable. Data collected from the NHANES questionnaire (Health Conditions section: MCQ160G, MCQ160K, MCQ170K) from 1999 to 2012 included inquiries about emphysema and current and past chronic bronchitis to determine the presence of COPD. Respondents who affirmatively indicated these conditions were categorized into the COPD group, while those who responded negatively were placed in the control group. For data from 2013 to 2018, a new questionnaire item (MCQ160O) was introduced, specifically asking participants if they had been diagnosed with COPD, using the same method for group determination.[17]

Covariates

Our investigation included various factors: age (20 years and older), gender, race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, others), marital status (married/partnered vs never married/divorced/separated/widowed), education (below high school, high school graduate, or higher), body mass index (BMI), and waist circumference. We also considered income levels (categorized as low, medium, or high poverty income ratios), smoking status (defined as over 100 cigarettes for smokers and fewer for non-smokers), alcohol consumption (defined as more than 12 drinks per year for drinkers, otherwise as non-drinkers), as well as hypertension, heart disease, diabetes, and high cholesterol. Hypertension was identified through self-reports, medication, or if blood pressure exceeded the AHA/ACC 2017 thresholds (≥130 mmHg systolic or ≥80 mmHg diastolic).[18] Cardiovascular disease and hypercholesterolemia were ascertained via questionnaire, while diabetes is considered present if one of the following conditions is met: use of insulin or diabetes medications, self-reported diabetes mellitus, glycosylated hemoglobin (HbA1c) over 6.5%, a 2-hour plasma glucose over 200 mg/dL on the Oral Glucose Tolerance Test (OGTT), or fasting blood glucose (FPG) over 126 mg/dL.[19]

Statistical Analysis

We utilized Free Statistics software version 1.9.1 and the statistical software package R version 4.2.2, employing two-tailed tests at a significance level of $P<0.05$. Considering the complex survey design of NHANES, we used appropriate weights in our analyses to derive weighted estimates representing the non-institutionalized US population from 1999 to 2018. Means ± SD were used to depict continuous data, while percentages described categorical data. The chi-square test was used to assess categorical variables, and the *t*-test was used to evaluate differences in continuous variables. To explore the correlation between the TyG index and the prevalence of COPD, we conducted both univariable and multivariable logistic regressions. We analyzed the dose-response relationship between the two using restricted cubic splines. The population was divided into tertiles (T1, T2, T3) based on the TyG index, with T1 serving as the reference group. We analyzed the relationship between the TyG index and the prevalence of COPD, presenting the results as both continuous and categorical variables, showing odds ratios (ORs) with 95% confidence intervals (CIs). To control for

confounders, we applied three multivariable logistic regression models. Model 1 adjusted for age, race/ethnicity, education level, marital status, and the poverty income ratio (PIR). Model 2 further adjusted for alcohol consumption, smoking, BMI, and waist circumference, building on Model 1. Model 3 adjusted for hypertension, cardiovascular disease, and hypercholesterolemia, adding these variables to Model 2.

Results

Baseline Characteristics

After screening and excluding missing data from the NHANES data between 1999 and 2018, a total of 23,456 participants aged 20 years or older were ultimately included in the analyses, comprising 18,985 nondiabetics and 4,471 diabetics. The study employed three different adjustment models for these two groups, each excluding missing data based on the inclusion of different covariates, which led to variations in sample size (Figure 1). The results (Table 1) indicated that among the total participants, as the TyG index increased, the proportion of females decreased, while age, BMI, and waist circumference tended to increase. There was also an observed increase in the proportion of smokers,

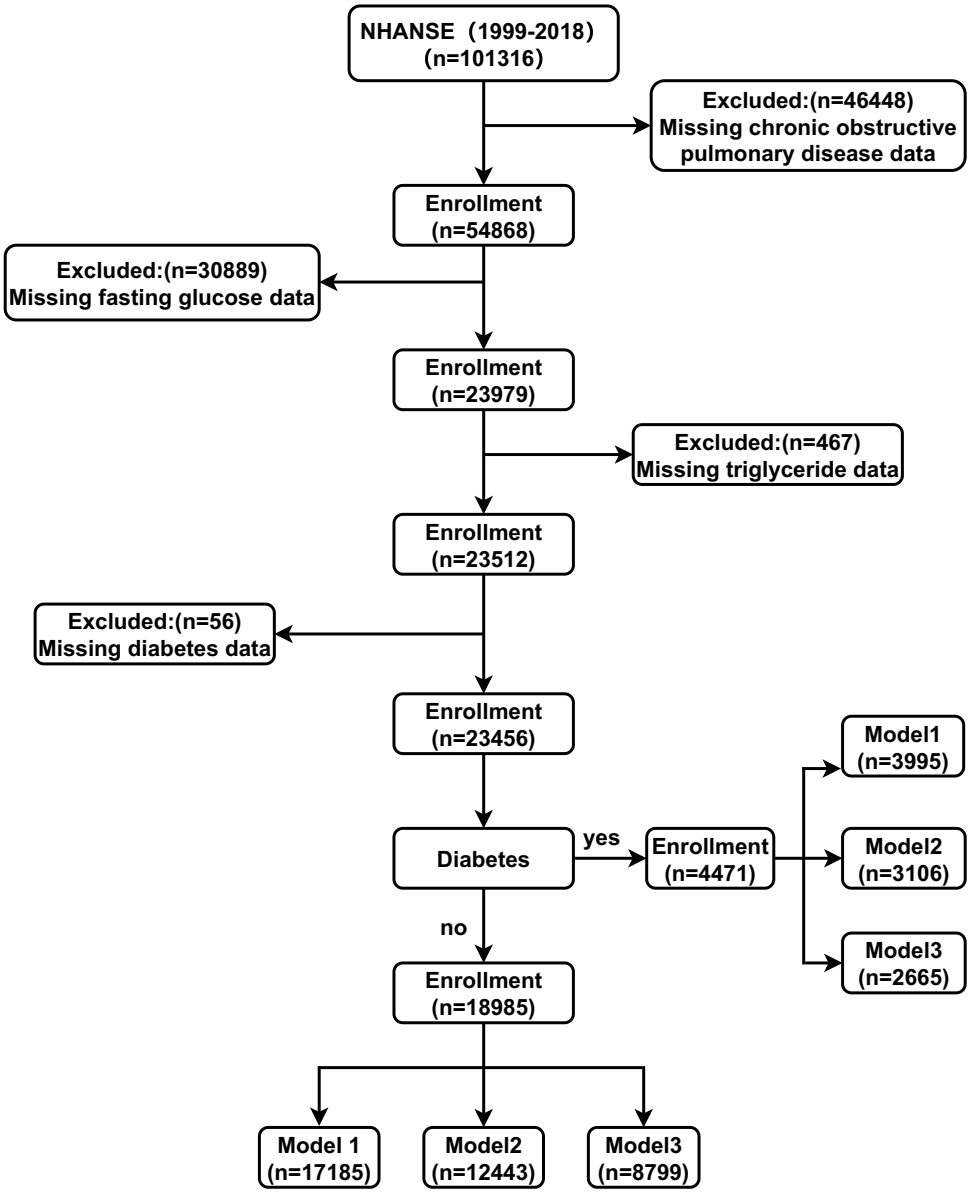

Figure 1 Flowchart of participant selection.

Table 1 Weighted Baseline Characteristics of All Participants Stratified by TyG Index Tertiles

Variables	Total (n = 23456)	T1 (n = 7818)	T2 (n=7815)	T3 (n = 7823)	P-value
Gender					< 0.0001
Male	48.37	39.96	50.06	55.91	
Female	51.63	60.04	49.94	44.09	
Age(years)	46.70±16.80	42.04±16.26	47.45±16.95	51.07±15.87	< 0.0001
Race/ethnicity					< 0.0001
Non-Hispanic White	69.04	65.18	70.75	71.72	
Non-Hispanic Black	10.96	16.67	9.33	6.38	
Mexican American	8.09	6.41	8.45	9.56	
Others	11.91	11.73	11.70	12.33	
Education					< 0.0001
Below high school	6.47	4.66	6.44	8.52	
High school graduate	35.20	30.79	35.98	39.28	
Higher	58.33	64.56	57.58	52.19	
Marital status					< 0.0001
Married/partnered	65.14	62.15	65.76	67.82	
Never married /divorced/separated/widowed	34.86	37.85	34.24	32.18	
PIR					< 0.0014
Low	21.16	20.54	20.74	22.29	
Medium	36.67	35.55	36.14	38.51	
High	42.17	43.90	43.12	39.20	
Drinking					0.0062
No	24.75	23.88	23.83	26.72	
Yes	75.25	76.12	76.17	73.28	
Smoking					< 0.0001
No	53.32	59.82	52.23	47.27	
Yes	46.68	40.18	47.77	52.73	
BMI (kg/m^2)	28.64 ± 6.9	26.34 ± 6.07	28.75 ± 6.58	30.10 ± 6.54	< 0.0001
Waist circumference (cm)	98.34±17.48	91.21±15.73	98.88±16.50	106.20±17.01	< 0.0001
Cardiovascular disease					< 0.0001
No	97.61	98.60	98.01	96.06	
Yes	2.39	1.40	1.99	3.94	
Diabetes					< 0.0001
No	86.49	95.94	90.70	71.31	
Yes	13.51	4.06	9.30	28.69	
Hypertension					< 0.0001
No	74.85	84.88	74.63	63.88	
Yes	25.15	15.12	25.37	36.12	
HCH					< 0.0001
No	55.61	73.01	54.80	38.98	
Yes	44.39	26.99	45.20	61.02	
COPD					< 0.0001
No	93.06	95.15	93.37	90.41	
Yes	6.94	4.85	6.63	9.59	
TyG index	8.64±0.67	7.97±0.29	8.62±0.16	9.39±0.47	< 0.0001

Note: The continuous variables were represented by mean ± SD. Categorical variables expressed as percentages. Absolute numbers are unweighted, observed values; Estimates were weighted.

Abbreviations: BMI, body mass index; PIR, poverty income ratio; HCH, hypercholesterolemia; COPD, chronic obstructive pulmonary disease; TyG index, Triglyceride-Glucose index.

individuals with low income, those who were married or partnered, less educated, as well as those with COPD, hypertension, cardiovascular disease, diabetes, and hypercholesterolemia. Additionally, different race groups exhibited varying trends across TyG index tertiles.

Data were analyzed for participants divided into non-diabetic and diabetic groups by gender. Among non-diabetics, age, waist circumference, BMI, COPD, hypertension, smoking, cardiovascular disease, and hypercholesterolemia

followed the same trend as the whole population as the TyG index rose. It was also observed that the proportion of low-income earners tended to increase only among non-diabetic females (Supplementary Tables S1 and S2). In patients with diabetes (Supplementary Tables S3 and S4), similar increases in BMI and waist circumference, and an increased proportion of hypercholesterolemia, were observed in both sexes, as in the non-diabetic group. In both male and female groups, no differences were found in PIR, alcohol consumption, smoking, COPD, hypertension, and cardiovascular diseases.

Association Between TyG Index and COPD Prevalence

Univariable logistic regression analyses indicated that gender, age, smoking, race/ethnicity, marital status, poverty income ratio (PIR), BMI, waist circumference, cardiovascular disease, diabetes, hypercholesterolemia, hypertension, and TyG index were associated with COPD (Table 2). In non-diabetic women, multivariate logistic regression analyses showed a positive association with the prevalence of COPD in unadjusted models when the TyG index was analyzed as a continuous variable (OR=2.09; 95% CI, 1.73–2.53). After adjusting for potential confounders using three different models, the TyG index remained associated with a higher prevalence of COPD: model 1 (OR=1.79; 95% CI, 1.43–2.23), model 2 (OR=1.43; 95% CI, 1.10–1.87), and model 3 (OR=1.50; 95% CI, 1.08–2.08). In these cases, the prevalence of COPD was higher in individuals in the highest tertile of the TyG index compared to those in the lowest tertile. No such correlation was found in non-diabetic men (Table 3), and no significant connection between the TyG index and COPD prevalence was found in diabetics, regardless of gender (Supplementary Table S5).

Table 2 Association Between Covariates and COPD Prevalence

Variables	OR (95CI%)	P-value
Gender		
Male	1(reference)	
Female	1.54 (137~1.79)	<0.001
Age	1.03 (1.03~1.03)	<0.001
Race/ethnicity		
Non-Hispanic White	1(reference)	
Non-Hispanic Black	0.65 (0.54~0.78)	<0.001
Mexican American	0.30 (0.24~0.40)	<0.001
Others	0.57 (0.44~0.73)	<0.001
Education		
Below high school	1(reference)	
High school graduate	1.05 (0.84~1.32)	0.663
Higher	0.70 (0.57~0.86)	0.001
Marital status		
Married/partnered	1(reference)	
Never married /divorced/separated/widowed	1.32 (1.14~1.53)	<0.001
PIR		
Low	1(reference)	
Medium	0.72 (0.61~0.85)	<0.001
High	0.41 (0.33~0.51)	<0.001
BMI	1.03 (1.02~1.04)	<0.001
Waist circumference	1.02 (1.01~1.02)	<0.001
Drinking		
No	1(reference)	
Yes	0.98 (0.83~1.15)	0.784
Smoking		
No	1(reference)	
Yes	2.82 (2.37~3.36)	<0.001

(*Continued*)

Table 2 (Continued).

Variables	OR (95CI%)	P-value
Cardiovascular disease		
No	1(reference)	
Yes	5.20 (4.18~6.48)	<0.001
Diabetes		
No	1(reference)	
Yes	1.76 (1.51~2.06)	<0.001
HCH		
No	1(reference)	
Yes	1.81 (1.54~2.13)	<0.001
Hypertension		
No	1(reference)	
Yes	2.44 (2.14~2.77)	<0.001
TyG index	1.50 (1.37~1.64)	<0.001

Note: Data presented are ORs and 95%CIs.
Abbreviations: BMI, body mass index; PIR, poverty income ratio; HCH, hypercholesterolemia; TyG index, Triglyceride-Glucose index.

Table 3 Gender Differences in the Association Between TyG Index and COPD in a Non-Diabetic Population

Variable	Non-Adjusted	Model 1	Model 2	Model 3
Female				
TyG	2.09(1.73–2.53)	1.79(1.43–2.23)	1.43(1.10–1.87)	1.50(1.08–2.08)
P-value	<0.001	<0.001	0.008	0.019
TyG tertile				
T1	1(Ref)	1(Ref)	1(Ref)	1(Ref)
T2	1.55(1.18–2.05)	1.35(1.00–1.82)	1.31(0.93–1.85)	1.44(0.94–2.20)
T3	2.66(2.00–3.55)	2.13(1.52–2.99)	1.58(1.04–2.38)	1.81(1.05–3.11)
P-trend	<0.001	<0.001	0.029	0.032
Male				
TyG	1.22(0.99–1.51)	1.24(0.99–1.55)	1.08(0.79–1.48)	1.00(0.67–1.48)
P-value	0.063	0.064	0.614	0.987
TyG tertile				
T1	1(Ref)	1(Ref)	1(Ref)	1(Ref)
T2	1.20(0.85–1.69)	1.14(0.78–1.65)	0.93(0.59–1.46)	1.06(0.61–1.83)
T3	1.60(1.13–2.27)	1.50(1.04–2.16)	1.37(0.92–2.04)	1.29(0.77–2.17)
P-trend	0.008	0.030	0.124	0.329

Note: Data presented are ORs and 95%CIs. Model 1: adjusted for age, race/ethnicity, education level, marital status, PIR. Model 2: adjusted for Model 1+ drinking, smoking, BMI, waist circumference. Model 3: adjusted for Model 2+ hypertension, cardiovascular disease, hypercholesterolemia.

Threshold Effect Analysis

Analysis using restricted cubic splines assessed the dose-response relationship between the TyG index and the prevalence of COPD in non-diabetic women, revealing a linear correlation (P for non-linearity = 0.298) (Figure 2).

Discussion

This study analyzed NHANES data from 1999 to 2018, involving 23,456 participants, to explore the impact of gender on the relationship between the TyG index and COPD. Findings confirmed that an elevated TyG index is associated with increased indicators of metabolic issues, such as higher BMI and waist circumference, consistent with its established role

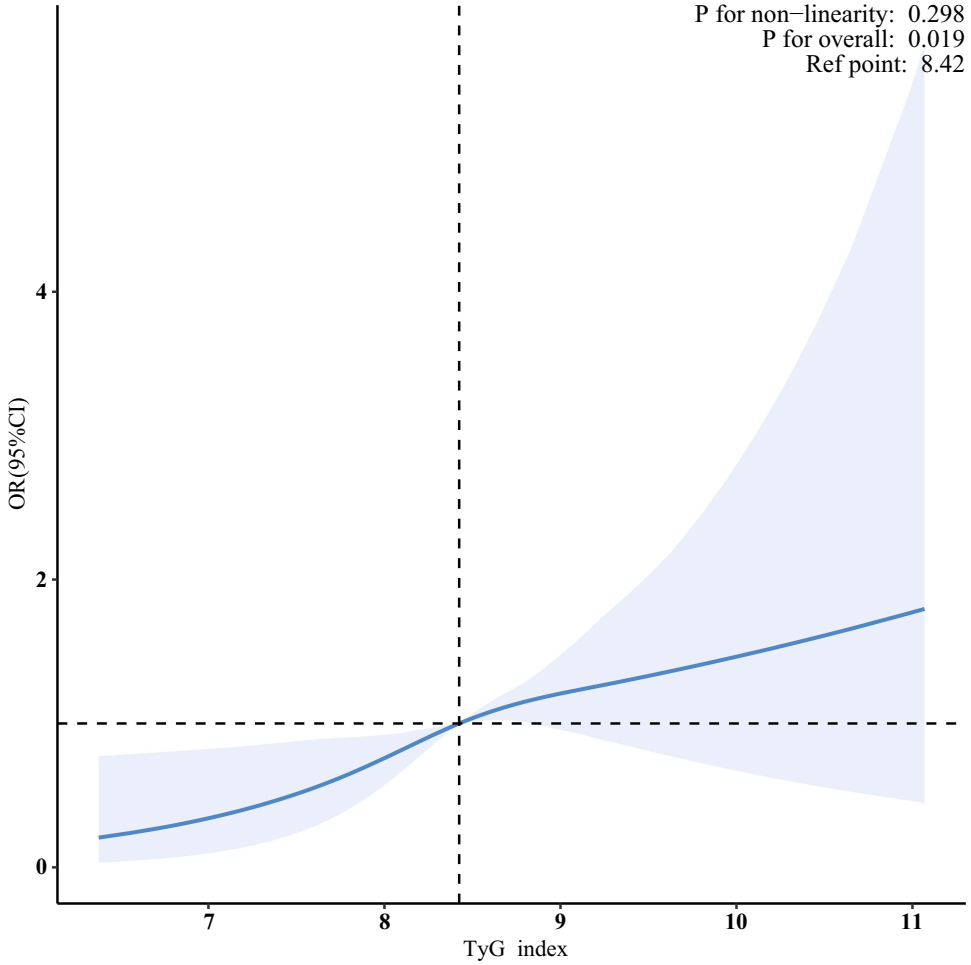

Figure 2 The association between TyG index and COPD was analyzed using restricted cubic spline curves in a population of non-diabetic women. The analysis was adjusted for all covariates. Solid lines represent multivariate-adjusted odds ratios, and the shaded areas represent 95% CIs of restricted cubic spline curves. Horizontal dashed lines represent odds ratios (reference points) of 1.0. The reference point is set at the median level of the TyG index.

as an indicator of insulin resistance and metabolic disturbances.[20] The prevalence of COPD, hypertension, cardiovascular disease, diabetes, and hypercholesterolemia increased as the TyG index increased, which may indicate an association between metabolic disorders and these diseases. Crucially, our analysis found a significant positive linear association between the TyG index and COPD prevalence in non-diabetic women, consistent across various analysis methods. Such a relationship was absent in non-diabetic men.

The TyG index may provide a simpler and more cost-effective alternative to traditional markers of insulin resistance, like the HOMA-IR,[21,22] while also offering improved predictive capabilities for insulin resistance.[12,23] Past research on the TyG index has focused on atherosclerosis, cardiovascular disease, and stroke,[24,25] but recent studies suggest its potential relevance in respiratory illnesses. Wu TD et al's research demonstrates connections between the TyG index and respiratory symptoms, chronic pulmonary diseases, and lung function. Their findings showed that the risk of chronic bronchitis increased by 21% for each unit increase in the TyG index.[10] Additionally, a Swedish longitudinal study further validates the TyG index as an effective predictor of COPD, revealing a significant risk increase in the highest TyG index quartile. The results were statistically significant only in women.[26]

Research indicates that diabetes' detrimental effects on lung function may begin in the prediabetic stage,[27–30] with approximately 31%-40% of COPD patients concurrently diagnosed with prediabetes.[31,32] In prediabetes, characteristics such as insulin resistance, hyperinsulinemia, and obesity are considered to be common risk factors leading to the decline in lung function due to COPD.[33] Chronic airway inflammation is an important feature of COPD.[34] Insulin resistance can

reduce the expression of Sfrp5 (an anti-inflammatory adipokine), activate the Wnt5a/JNK1 signaling pathway, promote macrophage activation, and thereby exacerbate airway inflammation.[35]

Research suggests that women, particularly smokers, are at a higher risk of developing COPD compared to men,[36] with their likelihood of developing the disease being approximately 50% higher than their male counterparts.[37] Even with lower smoking levels, their rate of decline in FEV1 is faster than in male smokers.[38] In this study, we divided the study population by gender and observed a gender difference in the relationship between the TyG index and the prevalence of COPD among the non-diabetic population. A study conducted by Tam A and his team, using a chronic smoke exposure mouse model, explored the influence of estrogen on COPD. The findings revealed that female mice exhibited significant increases in small airway remodeling and distal airway resistance following smoke exposure, alongside a decrease in the antioxidant gene Cyp1a1, heightened oxidative stress, and activation of TGF-β, compared to ovariectomized mice or male mice. The administration of the anti-estrogen drug tamoxifen was observed to alleviate these effects.[39] Furthermore, estrogen was found to regulate airway function by reducing Ca^{2+} influx, consequently inhibiting Ca^{2+} signaling and the stability of airway surface liquid in airway epithelial cells. Tamoxifen, an anti-estrogen medication, had the ability to either block or enhance this inhibitory effect.[40]

However, our study has some obvious limitations. Firstly, due to the cross-sectional approach, we were unable to determine the exact causal relationship between the TyG index and the prevalence of COPD, and this association needs to be further verified by more in-depth longitudinal studies. Secondly, the reliance on self-reported questionnaires could compromise data precision. Thirdly, although we accounted for many potential confounders, the influence of unidentified factors remains a possibility. Lastly, the research categorized participants only into diabetic and non-diabetic groups, omitting more detailed analyses of metabolic conditions.

Conclusion

By analyzing NHANES data from 1999 to 2018, we found a significant positive correlation between the TyG index and the prevalence of COPD among non-diabetic individuals, with observed gender differences. This suggests the importance of considering gender specificity in COPD management strategies.

Abbreviations

BMI, body mass index; PIR, poverty income ratio; HCH, hypercholesterolemia; COPD, chronic obstructive pulmonary disease; TyG index, Triglyceride-Glucose index.

Data Sharing Statement

All data in this study are available for free download in the NHANES database: National Health and Nutrition Examination Survey Homepage (cdc.gov).

Ethics Statement

The study involving human participants was reviewed and approved by the National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB). Written informed consent was obtained from all participants prior to their participation in the research.

Author Contributions

All authors made significant contributions to the conception, design, execution, and analysis of this study. JG and JY: data cleaning, statistical analysis, and initial manuscript drafting. JW and WL: data interpretation, and validation. YK, ZL, CH, and SQ: Chart layout. Each author participated in the revision process of the manuscript, provided important feedback, and approved the final version of the manuscript submitted for publication. All authors agreed to take responsibility for all aspects of the work and agreed on the journal to which the article would be submitted.

Disclosure

The authors declare no conflicts of interest in this work.

References

1. Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report. GOLD executive summary. *Am J Respir Crit Care Med*. 2017;195(5):557–582. doi:10.1164/rccm.201701-0218PP
2. van Beers M, Gosker HR, Janssen DJA, et al. Cognitive performance in relation to metabolic disturbances in patients with COPD. *Clin Nutr*. 2021;40(4):2061–2067. doi:10.1016/j.clnu.2020.09.029
3. Lambert AA, Putcha N, Drummond MB, et al. obesity is associated with increased morbidity in moderate to severe COPD. *Chest*. 2017;151 (1):68–77. doi:10.1016/j.chest.2016.08.1432
4. Su J, Li M, Wan X, et al. Associations of diabetes, prediabetes and diabetes duration with the risk of chronic obstructive pulmonary disease: a prospective UK Biobank study. *Diabetes Obes Metab*. 2023;25(9):2575–2585. doi:10.1111/dom.15142
5. Bloomgarden Z. Pulmonary disease in diabetes. *J Diabetes*. 2023;15(12):1008–1010. doi:10.1111/1753-0407.13509
6. Ren H, Yang Y, Wang F, et al. Association of the insulin resistance marker TyG index with the severity and mortality of COVID-19. *Cardiovasc Diabetol*. 2020;19(1):58. doi:10.1186/s12933-020-01035-2
7. Khan SH, Sobia F, Niazi NK, et al. Metabolic clustering of risk factors: evaluation of Triglyceride-glucose index (TyG index) for evaluation of insulin resistance. *Diabetol Metab Syndr*. 2018;10(1):74. doi:10.1186/s13098-018-0376-8
8. Jingtao X, Xu W, Chen G, et al. Association of TyG index with prehypertension or hypertension: a retrospective study in Japanese normoglycemia subjects. *Front Endocrinol*. 2023;14:1288693. doi:10.3389/fendo.2023.1288693
9. Park K, Ahn CW, Lee SB, et al. Elevated TyG index predicts progression of coronary artery calcification. *Diabetes Care*. 2019;42(8):1569–1573. doi:10.2337/dc18-1920
10. Tutunchi H, Naeini F, Mobasseri M, et al. Triglyceride glucose (TyG) index and the progression of liver fibrosis: a cross-sectional study. *Clin Nutr ESPEN*. 2021;44:483–487. doi:10.1016/j.clnesp.2021.04.025
11. Wu TD, Fawzy A, Brigham E, et al. Association of triglyceride-glucose index and lung health: a population-based study. *CHEST*. 2021;160 (3):1026–1034. doi:10.1016/j.chest.2021.03.056
12. Li M, Li L, Qin Y, et al. Elevated TyG index predicts incidence of contrast-induced nephropathy: a retrospective cohort study in NSTE-ACS patients implanted with DESs. *Front Endocrinol*. 2022;13:817176. doi:10.3389/fendo.2022.817176
13. Carstensen B, Read SH, Friis S, et al. Cancer incidence in persons with type 1 diabetes: a five-country study of 9,000 cancers in type 1 diabetic individuals. *Diabetologia*. 2016;59(5):5):980–8. doi:10.1007/s00125-016-3884-9
14. Vogtmann E, Chaturvedi AK, Blaser MJ, et al. Representative oral microbiome data for the US population: the national health and nutrition examination survey. *Lancet Microbe*. 2023;4(2):e60–e61. doi:10.1016/S2666-5247(22)00333-0
15. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F, et al. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Related Disor*. 2008;6(4):299–304. doi:10.1089/met.2008.0034
16. Zhou D, Liu XC, Kenneth L, et al. A non-linear association of triglyceride glycemic index with cardiovascular and all-cause mortality among patients with hypertension. *Front Cardiovasc Med*. 2021;8:778038. doi:10.3389/fcvm.2021.778038
17. Ibrahimou B, Azim SI, Sun N, et al. Interaction between blood lead level and chronic obstructive pulmonary disease (COPD) on risk of heart attack or stroke: USA NHANES, 2013–2014. *Pulmon Pharmacol & Therap*. 2019;58:101805. doi:10.1016/j.pupt.2019.101805
18. Whelton PK, Carey RM, Aronow WS, et al. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. *J Am Coll Cardiol*. 2017;7(1):68–74.
19. Mao Y, Li X, Zhu S, et al. Association between dietary fiber intake and risk of depression in patients with or without type 2 diabetes. *Front Neurosci*. 2022;16(920845). doi:10.3389/fnins.2022.920845
20. Fritz J, Bjørge T, Nagel G, et al. The triglyceride-glucose index as a measure of insulin resistance and risk of obesity-related cancers. *Int J Epidemiol*. 2020;49(1):193–204. doi:10.1093/ije/dyz053
21. Azzam EZ, El-Aghoury AA, Abd El-naby E-SE, et al. Studying the relation between vitamin D deficiency and glycemic state among pregnant women with gestational diabetes. *Diab Metab Syndr*. 2019;13(2):1505–1509. doi:10.1016/j.dsx.2019.03.007
22. Matli B, Schulz A, Koeck T, et al. Distribution of HOMA-IR in a population-based cohort and proposal for reference intervals. *Clin Chem Lab Med CCLM*. 2021;59(11):1844–1851. doi:10.1515/cclm-2021-0643
23. Brito ADM, Hermsdorff HHM, Filgueiras MDS, et al. Predictive capacity of triglyceride-glucose (TyG) index for insulin resistance and cardiometabolic risk in children and adolescents: a systematic review. *Crit Rev Food Sci Nutr*. 2021;61(16):2783–2792. doi:10.1080/10408398.2020.1788501
24. Li S, Guo B, Chen H, et al. The role of the triglyceride (triacylglycerol) glucose index in the development of cardiovascular events: a retrospective cohort analysis. *Sci Rep*. 2019;9(1):7320. doi:10.1038/s41598-019-43776-5
25. Wang X, Liu Q, Wang T, et al. Triglyceride–glucose index and the risk of stroke in American adults: findings from the atherosclerosis risk in communities study. *Diabetol Metab Syndr*. 2023;15(1):187. doi:10.1186/s13098-023-01161-3
26. Zaigham S, Tanash H, Nilsson PM, et al. Triglyceride-glucose index is a risk marker of incident COPD events in women. *Int J Chronic Obstr*. 2022;17:1393–1401. doi:10.2147/COPD.S360793
27. Kim JM, Kim MK, Joung KH, et al. Association between glycemic state and pulmonary function and effect of walking as a protective factor in subjects with diabetes mellitus. *Ann Translat Med*. 2019;7(20):530. doi:10.21037/atm.2019.09.139
28. Li Y, Saito M, Tobimatsu S, et al. Prediabetes and impaired lung function in asymptomatic adults. *Diabet Res Clin Pract*. 2013;100(2):e51–54. doi:10.1016/j.diabres.2013.01.021
29. Sánchez E, Gutiérrez-Carrasquilla L, Barbé F, et al. Lung function measurements in the prediabetes stage: data from the ILERVAS project. *Acta Diabetol*. 2019;56(9):1005–1012. doi:10.1007/s00592-019-01333-6
30. Kopf S, Groener JB, Kender Z, et al. Breathlessness and restrictive lung disease: an important diabetes-related feature in patients with type 2 diabetes. *Respir Int Rev Thorac Dis*. 2018;96(1):29–40. doi:10.1159/000488909
31. Rambaran K, Bhagan B, Ali A, et al. High prevalence of diabetes mellitus in a cohort of patients with chronic obstructive pulmonary disease in Trinidad, West Indies. *Turk Thorac J*. 2019;20(1):12–17. doi:10.5152/TurkThoracJ.2018.18036

32. Mekov EV, Slavova YG, Genova MP, et al. Diabetes mellitus Type 2 in hospitalized COPD patients: impact on quality of life and lung function. *Folia Med*. 2016;58(1):36–41. doi:10.1515/folmed-2016-0005
33. Katsiki N, Steiropoulos P, Papanas N, et al. Diabetes mellitus and chronic obstructive pulmonary disease: an overview. *Exper Clin Endocrinol & Diab: Off J, German Society Endocrinol German Diab Assoc*. 2021;129(10):699–704. doi:10.1055/a-1038-3883
34. Richmond BW, Du RH, Han W, et al. Bacterial-derived neutrophilic inflammation drives lung remodeling in a mouse model of chronic obstructive pulmonary disease. *Am J Respir Cell Mol Biol*. 2018;58(6):736–744. doi:10.1165/rcmb.2017-0329OC
35. Zhu Z, Yin S, Wu K, et al. Downregulation of Sfrp5 in insulin resistant rats promotes macrophage-mediated pulmonary inflammation through activation of Wnt5a/JNK1 signaling. *Biochem Biophys Res Commun*. 2018;505(2):498–504. doi:10.1016/j.bbrc.2018.09.070
36. Hardin M, Foreman M, Dransfield MT, et al. Sex-specific features of emphysema among current and former smokers with COPD. *Eur Respir J*. 2016;47(1):104–112. doi:10.1183/13993003.00996-2015
37. Barnes PJ. Sex differences in chronic obstructive pulmonary disease mechanisms. *Am J Respir Crit Care Med*. 2016;193(8):813–814. doi:10.1164/rccm.201512-2379ED
38. Gan WQ, Man SP, Postma DS, et al. Female smokers beyond the perimenopausal period are at increased risk of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Respir Res*. 2006;7(1):52. doi:10.1186/1465-9921-7-52
39. Tam A, Churg A, Wright JL, et al. Sex differences in airway remodeling in a mouse model of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2016;193(8):825–834. doi:10.1164/rccm.201503-0487OC
40. Coakley RD, Sun H, Clunes LA, et al. 17β-Estradiol inhibits Ca^{2+}-dependent homeostasis of airway surface liquid volume in human cystic fibrosis airway epithelia. *J Clin Invest*. 2008;118(12):4025–4035. doi:10.1172/JCI33893