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Association between cardiometabolic index and infertility among American women aged 20–45 years: a cross-sectional analysis from 2013–2020 NHANES data

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Abstract

Background While metabolic syndrome and obesity are established risk factors for infertility, previous studies have neglected age-specific analyses and nonlinear associations, particularly in women aged 20–45 years, a critical demographic for fertility and metabolic health. Therefore, this study aimed to examine the nonlinear relationship between Cardiometabolic Index(CMI) and infertility risk in US women of reproductive age (20–45 years) using nationally representative the National Health and Nutrition Examination Survey(NHANES) data (2013–2020).

Methods Cross-sectional data from the 2013–2020 NHANES were used to analyse 3,613 women aged 20–45 years with complete CMI and infertility data. Infertility is defined as the inability to conceive after at least 12 months of regular unprotected intercourse.The CMI was calculated using waist circumference(WC), height, triglyceride(TG), and high-density lipoprotein cholesterol (HDL-C). Multivariate logistic regression analysis, supplemented by smooth curve fitting and threshold effect analysis, was used to assess the association between CMI and infertility.

Results The mean age of the subjects was (32.8 ± 7.5) years and 488 (13.51%) of them reported infertility. CMI < 0.59 were highly correlated with risk of infertility(OR = 4.47, 95%CI: 2.19–9.15, $P < 0.0001$), whereas CMI ≥ 0.59 was not significantly associated with the risk of infertility (OR = 1.01, 95%CI: 0.81–1.24, $P = 0.9621$).

Conclusion Our results show a significant positive non-linear relationship between CMI and infertility risk in US women aged 20–45, with a threshold effect.

Keywords Cardiometabolic index, Dyslipidaemia, Female infertility, NHANES

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Introduction

Infertility, defined as the inability to conceive after 12 months of regular unprotected intercourse, affects approximately 10–15% of women of reproductive age worldwide [1]. In particular, metabolic disorders, especially obesity and dyslipidaemia, have emerged as critical contributors to reproductive dysfunction [2, 3]. In the United States, the prevalence of obesity among women has risen to 41.9%, exacerbating the risk of ovulatory dysfunction and metabolic disorders associated with infertility [4]. However, conventional anthropometric indices such as body mass index (BMI) do not fully capture the heterogeneity of adiposity distribution and metabolic risk, and more accurate biomarkers are needed for risk stratification [5, 6].

The cardiometabolic index (CMI), introduced by Wakabayashi et al. in 2015, integrates waist-to-height ratio(WHtR) and triglyceride-to-high-density lipoprotein cholesterol (TG-to-HDL-C) ratio to simultaneously assess abdominal obesity and lipid metabolic abnormalities [7]. Unlike traditional measures, CMI shows superior discriminatory power for depression, metabolic syndrome, diabetes and cardiovascular disease by reflecting visceral adiposity and atherogenic lipid profiles [8–10]. Similarly, CMI has been associated with endometriosis, a condition that shares pathophysiological pathways with infertility, such as chronic inflammation and oxidative stress [11]. These findings highlight the potential of CMI as a holistic indicator of metabolic health relevant to reproductive outcomes [12].

While metabolic syndrome and obesity are established risk factors for infertility, previous studies have neglected age-specific analyses and nonlinear associations, particularly in women aged 20–45 years, a critical demographic for fertility and metabolic health. Therefore, this study aims to examine the nonlinear relationship between CMI and infertility risk in US women of reproductive age (20–45 years) using nationally representative NHANES data (2013–2020) and assess its performance in different subgroups. This will help deepen our understanding of the links between cardiometabolic health and reproductive health, and provide a scientific basis for future infertility prevention and intervention efforts.

Methods

Data source and study population

The National Health and Nutrition Examination Survey (NHANES) is a comprehensive, population-based surveillance system conducted every two years in the United States. This cross-sectional programme systematically collects multidimensional data on demographic characteristics, socioeconomic status, dietary patterns, and health-related parameters. The survey methodology integrates three main components: structured interviews, standardised physical examinations, and laboratory analyses, which together provide a robust assessment of population-level nutritional status and health indicators at the population level. Four cycles of data in the NHANES database from 2013 to 2020 data were analyzed, including women aged 20–45 years. Exclusion criteria were based on the following factors: (1) male patients, (2) individuals aged < 20 years or > 45 years, (3) lack of available information on fertility status, and (4) incomplete CMI measurements. After excluding these factors, the analysis sample consisted of 3,613 eligible individuals, as shown in the study flowchart (Fig. 1).

Assessment of infertility

Data on infertility status were collected using the NHANES Reproductive Health Questionnaire (RHQ), which was administered by certified personnel at all study sites according to established protocols [13]. The assessment included two key questions: (1) "Have you been trying to get pregnant for a year or more?" and (2) "Have you sought medical advice regarding difficulties in achieving pregnancy?". Participants who answered both questions were included in the analysis. Infertility status was operationally defined as a positive response to either question, whereas a negative response to both questions indicated fertility. Non-responses were treated as missing data and excluded from subsequent analyses.

Assessment of the cardiometabolic index

The CMI was calculated using the following formula: WHtR = WC(cm)/height(cm), CMI = WHtR ×[TG (mg/dL)/HDL-C (mg/dL)] [14]. In the analytical framework of this study, CMI was operationalised as a continuous predictor variable. For comparative analysis, Tertiles were defined for the study population according to their CMI distribution.

Covariates

For this analysis, potentially confounding variables were selected on the basis of previous studies [15, 16]. These covariates included three domains: (1) demographic characteristics, including chronological age (continuous variable), race/ethnicity category (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other), and education level (less than high school, high school diploma, college degree or higher); Poverty-Income Ratio (PIR): Calculated as the ratio of family income to the federal poverty threshold, with < 1.0 indicating poverty, 1.0–3.0 indicating low-to-middle income, and > 3.0 indicating middle-to-high income [17]. (2) behavioural factors, specifically smoking history, categorised as never smoking, former smoker, or current smoker; (3) clinical indicators, specifically hypertension and diabetes status. All covariate data were systematically

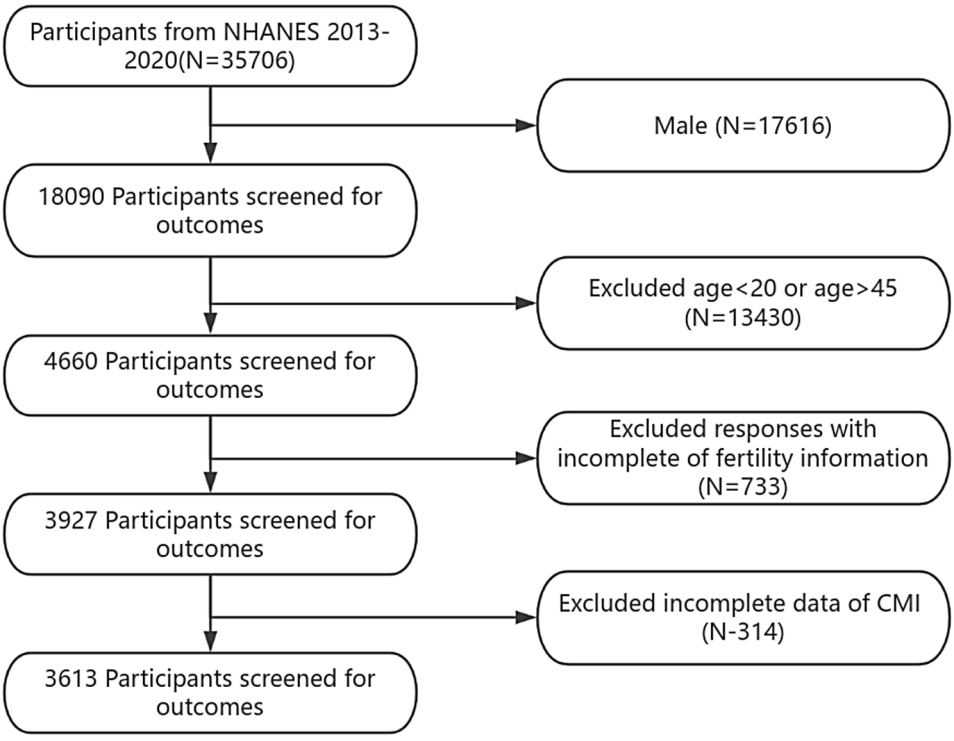

Fig. 1 Flow chart for the inclusion and exclusion of study participants.CMI: The cardiometabolic index

obtained from standardised NHANES survey instruments and corresponding laboratory assessments.

Statistical analysis

Continuous variables are described as mean ± SD or median and interquartile range (IQR). We used a generalised additive model (GAM) to investigate the dose-response relationship between CMI and risk of infertility. We used a logistic regression model to estimate the association between CMI and risk of infertility. The results are presented as odds ratios (ORs) with their 95% confidence intervals (95% CIs). Crude regression estimates and estimates adjusted for covariates are presented. After adjusting for clinical significance, we adjusted for the following covariates: Age; Race; Income ratio; Marital status; Education; Smoking; Hypertension; Diabetes.

1. As described in previous analyses [18, 19], we used threshold effect analysis to calculate 95% CIs for turning points. To test the robustness of the results, we performed subgroup analyses and examined the interaction of metabolic and demographic factors. We also performed sensitivity analyses by converting these CMIs to tertile categorical variables to assess the stability of the results. $P < 0.05$ was considered statistically significant.We performed all statistical analyses using EmpowerStats (www.empowerstats.com, X&Y Solutions, Inc., Boston, MA) and R version 4.2.2 (http://www.r-project.org).

Results

Baseline characteristics

Baseline characteristics of the study population ($N = 3613$) are shown in Table 1, participants with infertility were significantly older and had higher BMI and PIR compared to the non-infertile group (all $p < 0.001$). The infertile group also exhibited higher rates of hypertension, diabetes, and current smoking, with all differences reaching statistical significance ($p < 0.05$). Notably, the proportion of married/cohabiting individuals was substantially higher in the infertile group (71.72% vs. 55.07%, $p < 0.001$). Race, education, and menstrual regularity did not show significant differences($p > 0.05$).

Associations between cardiometabolic index and the risk of infertility

The multivariable-adjusted associations between CMI and infertility are summarized in Table 2. In Adjust I (adjusted for age, race, and education), each unit increase in CMI was associated with significantly elevated odds of infertility (OR = 1.34, 95% CI: 1.16–1.55). This association persisted in Adjust II after additional adjustment for socioeconomic and clinical confounders (OR = 1.27, 95% CI: 1.08–1.49). When categorized into tertiles, a dose-dependent increase in infertility risk was observed across

Table 1 Baseline characteristics of the study population

Variable	Total (*N* = 3613)	infertility		
		No (*N* = 3125)	Yes(*N* = 488)	*P*
Age (years)	32.80 ± 7.55	32.48 ± 7.59	34.89 ± 6.88	< 0.001
PIR	2.35 ± 1.61	2.31 ± 1.60	2.61 ± 1.66	< 0.001
BMI(kg/m^2)	29.79 ± 8.35	29.48 ± 8.20	31.79 ± 8.99	< 0.001
Race				0.258
Mexican American	594 (16.44%)	518 (16.58%)	76 (15.57%)	
Non-Hispanic White	1188 (32.88%)	1009 (32.29%)	179 (36.68%)	
Non-Hispanic Black	831 (23.00%)	721 (23.07%)	110 (22.54%)	
Other Race	1000 (27.68%)	877 (28.06%)	123 (25.20%)	
Marital status				< 0.001
Married/Living with partner	2071 (57.32%)	1721 (55.07%)	350 (71.72%)	
Separated/Widowed/Divorced	392 (10.85%)	337 (10.78%)	55 (11.27%)	
Never married	1150 (31.83%)	1067 (34.14%)	83 (17.01%)	
Education level				0.850
Less than High school	563 (15.58%)	491 (15.71%)	72 (14.75%)	
High school or equivalent	692 (19.15%)	599 (19.17%)	93 (19.06%)	
College or above	2358 (65.26%)	2035 (65.12%)	323 (66.19%)	
Smoking status				0.013
Never smoked	2542 (70.40%)	2226 (71.28%)	316 (64.75%)	
Current smoker	656 (18.17%)	551 (17.64%)	105 (21.52%)	
Former smoker	413 (11.44%)	346 (11.08%)	67 (13.73%)	
Regular menstruation in past 12 months				0.687
Yes	3232 (89.45%)	2798 (89.54%)	434 (88.93%)	
No	381 (10.55%)	327 (10.46%)	54 (11.07%)	
Hypertension				< 0.001
Yes	555 (15.37%)	451 (14.44%)	104 (21.31%)	
No	3056 (84.63%)	2672 (85.56%)	384 (78.69%)	
Diabetes				< 0.001
Yes	167 (4.62%)	125 (4.00%)	42 (8.61%)	
No	3444 (95.38%)	2998 (96.00%)	446 (91.39%)	

Notes: PIR = Poverty-Income Ratio (family income divided by the federal poverty threshold); BMI: Body Mass Index

Table 2 Associations between cardiometabolic index and the risk of infertility

Variable	Adjust I [OR(95%CI)]	Adjust II [OR(95%CI)]
CMI	1.34 (1.16, 1.55)	1.27 (1.08, 1.49)
CMI		
Low	1.0	1.0
Middle	1.49 (1.15, 1.93)	1.56 (1.19, 2.04)
High	1.95 (1.51, 2.51)	1.85 (1.41, 2.44)
P for trend	< 0.0001	< 0.0001

Notes: CMI: The cardiometabolic index

Adjust I model adjust for: Age; Race; Education

Adjust II model adjust for: Age; Race; Ratio of income; Marital status; Education; Smoke; hypertension; diabetes

ascending CMI categories (P for trend < 0.0001), with the highest tertile demonstrating nearly twofold elevated odds compared to the lowest tertile.

Smooth curve fitting (Fig. 2) revealed a pronounced non-linear association between CMI and infertility risk, with threshold analysis identifying a critical inflection point at CMI = 0.59 (Table 3). Below this threshold, each unit increase in CMI conferred a 4.47-fold elevated odds of infertility ($P < 0.001$), corresponding to a 347% risk escalation—a magnitude suggesting profound metabolic dysregulation. Beyond this threshold (CMI ≥ 0.59), the association plateaued ($P = 0.962$), implying potential saturation of obesity-driven pathological pathways.

Subgroup analyses

To assess the stability of the association between CMI and infertility after controlling for other variables, we performed subgroup analyses based on age, race, education level, marital status, diabetes, and smoking status. The results showed that none of these factors influenced the positive association between CMI and infertility, as shown in Fig. 3.

Stratified analyses showed significant effect modification by age and ethnicity. The association was markedly stronger in women aged ≥ 35 years. Non-Hispanic whites and blacks showed an increased risk compared to Mexican Americans. Married/cohabiting individuals had a lower risk than unmarried participants. Low - and

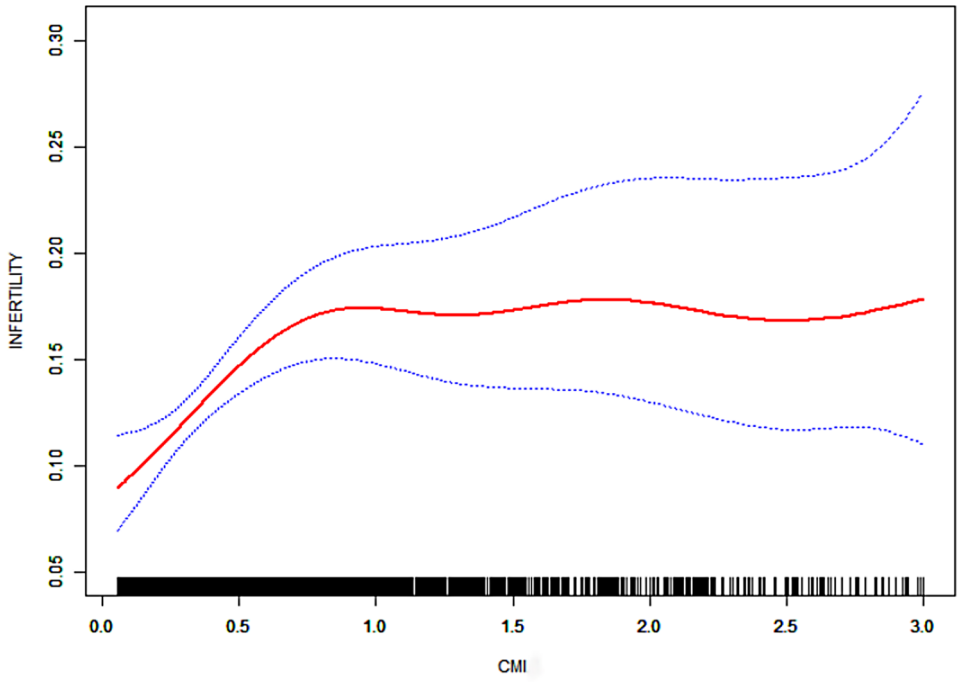

Fig. 2 Smooth curve fitting for CMI and infertility. CMI: The cardiometabolic index

Table 3 The threshold effect analysis of CMI was analyzed

	Adjusted OR (95% CI), *P*-value
Inflection point	0.59
CMI < 0.59	4.47 (2.19, 9.15) < 0.0001
CMI > 0.59	1.01 (0.81, 1.24) 0.9621
P for Log-likelihood ratio	< 0.001

Notes: CMI: The cardiometabolic index

Adjust for: Age; Race; Ratio of income; Marital status; Education; Smoke; hypertension; diabetes

middle-income participants showed a higher risk gradient. There were no significant associations with education, hypertension, diabetes or smoking status. Age, ethnicity and income emerged as important modifiers of the relationship between CMI and infertility.

Discussion

In this study, we examined the association between CMI and female infertility using NHANES data from 2013 to 2020. A total of 3613 women of childbearing age were included in the study, of which 488 cases were reported as infertility, accounting for 13.51%. Using advanced statistical methods, we found a non-linear relationship between CMI and infertility and identified a threshold effect with a CMI of around 0.59. Specifically, CMI < 0.59 was associated with a significantly increased risk of infertility (OR = 4.47, 95%CI: 2.19–9.15, $P < 0.0001$). However, when the CMI was greater than 0.59, the risk of infertility tended to remain stable (OR = 1.01, 95%CI: 0.81–1.24, $P = 0.9621$). This finding highlights the importance of early intervention in CMI, especially in individuals with low CMI, which may help to reduce the risk of infertility by improving the metabolic profile.

Several studies have explored the relationship between obesity, lipid profiles, and infertility, highlighting the role of various indices in predicting reproductive outcomes. For instance, Zhao et al. found a significant positive correlation between CMI and infertility, with an OR of 2.411 (95% CI: 1.416–4.112) after adjusting for confounding variables [15]. Similarly, Cheng et al. and Kong et al. showed that higher CMI levels were associated with an increased risk of infertility, reinforcing the idea that metabolic health is closely linked to reproductive outcomes [16, 20].Our findings advance the existing literature in three key aspects. First, this study focused specifically on women of childbearing age between 20 and 45 years to facilitate a targeted analysis. Second, our study investigated the non-linear relationship between CMI and infertility with a larger sample size and found a threshold effect of CMI at 0.59. Third, subgroup analyses and sensitivity analyses were performed to determine the stability of the results. In addition, this study focused specifically on women of childbearing age between 20 and 45 years to facilitate a targeted analysis. Clinically, the 0.59 threshold provides an actionable cutoff: women with CMI below this level-especially those in high-risk subgroups-could be prioritized for metabolic assessment (e.g., insulin sensitivity assessment, inflammatory markers) and personalized interventions (e.g., dietary adjustments targeting TG/HDL-C ratio, waist circumference reduction programs).These findings underscore the imperative for

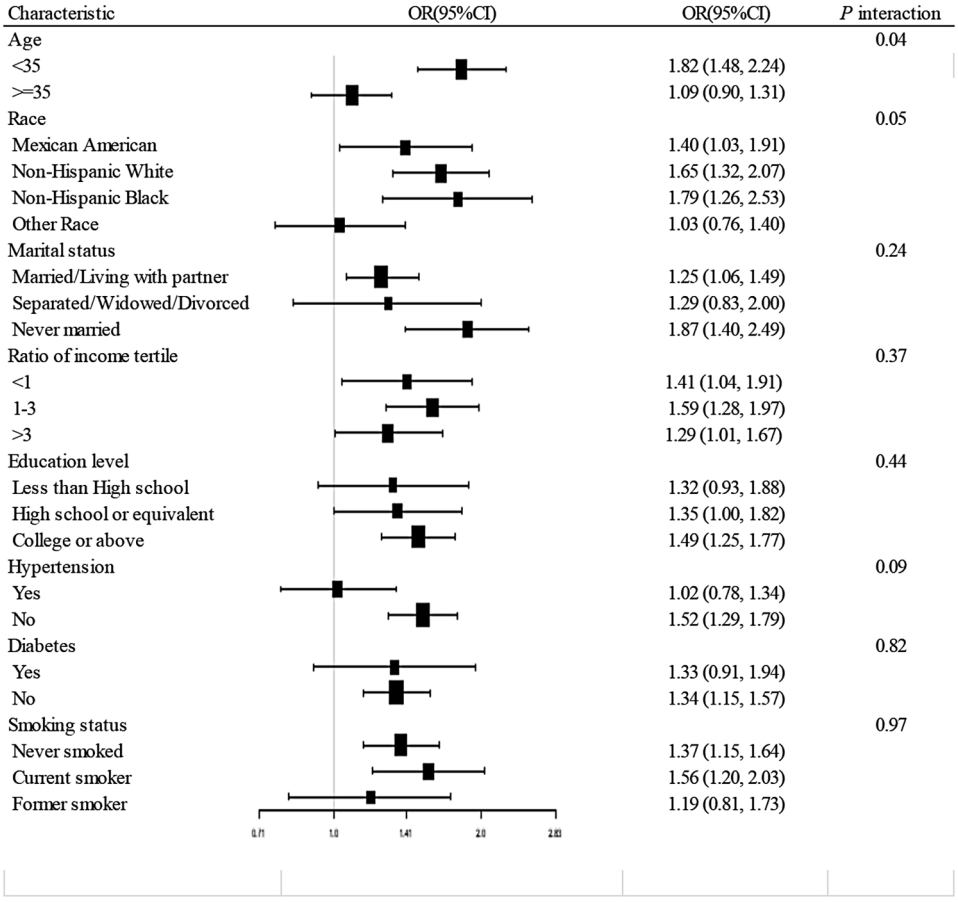

Fig. 3 Forest plots of stratified analyses of cardiometabolic index and the risk of infertility. Age, race/ethnicity, education level, PIR, smoking status, and history of hypertension or diabetes were all adjusted except the variable itself

researchers to integrate metabolic indices like CMI into fertility studies, while offering clinicians a practical tool for risk stratification and targeted interventions.

By integrating WHtR and TG-to-HDL-C ratio, CMI is a more comprehensive indicator of these metabolic disorders than traditional measures such as BMI [15, 16]. Obesity is associated with insulin resistance, which can lead to hyperinsulinemia and subsequent disruption of the hypothalamic-pituitary-ovarian axis, resulting in anovulation and infertility. In addition, dyslipidaemia, characterised by elevated TG and reduced HDL-C, can trigger systemic inflammation and endothelial dysfunction, thereby affecting ovarian function and fertility.

Several limitations should be acknowledged. First, the cross-sectional design precludes causal inference between CMI and infertility, necessitating future prospective studies. Second, the reliance on self-reported infertility may introduce recall bias, and extrapolation to other ethnic groups should be done with caution.

Conclusion

The present study reveals a nonlinear threshold relationship between the CMI and infertility risk among US women aged 20–45. Below a critical CMI threshold, the risk of infertility exhibits a marked increase, while above this threshold, the association stabilizes. By optimizing cardiometabolic health in women of reproductive age, particularly those with sub-threshold CMI, we can not only improve fertility outcomes, but also reduce the long-term risk of cardiovascular and metabolic disease.

Author contributions

Study design: [Junhui Yu]; Data analysis: [Yanyun Liu]; Manuscript drafting: [Yanyun Liu]; Critical revisions: [Gefei Ying, Zhen Chen, Hongping Liang].

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Data availability

Publicly available datasets were analyzed in this study. This data can be found here: https://wwwn.cdc.gov/nchs/nhanes/Default.aspx (assessed on January 10, 2025).

Declarations

Ethics approval and consent to participate

NHANES was approved by NCHS Ethics Review Board (https://www.cdc.gov/nchs/nhanes/irba98.htm. The patients/participants provided their written informed consent to participate in this study. Ethical approval was not provided for this study on human participants because the data were all accessed from NHANES. This study was performed in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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