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The nonlinear association between body roundness index and infertility in married women

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Infertility is increasingly linked to obesity, especially visceral fat accumulation. The Body Roundness Index (BRI) provides a precise quantification of body and visceral fat but its implications for infertility risks and diagnostic value are yet to be fully determined. This study analyzed data from 1,305 married women aged 20–45 years, drawn from the National Health and Nutrition Examination Survey (NHANES). Logistic regression was utilized to examine the relationship between BRI and infertility, incorporating univariate and multivariate regression analyses, smooth curve fittings, and subgroup analyses. Additionally, Receiver Operating Characteristic (ROC) analysis assessed the predictive capability of BRI for infertility. An increase in one unit of BRI correlated with a 13% higher prevalence of infertility after adjusting for covariates (OR = 1.13; 95% CI: 1.05, 1.21). Women with higher BRI exhibited greater infertility odds compared to the reference group (OR: 2.20, 95% CI: 1.42, 3.42). Smooth curve fitting analysis revealed a positive, nonlinear relationship, with an inflection point observed at a BRI value of 7.95. Subgroup analyses upheld the robustness of this association across varied demographic segments. ROC curves indicated significant diagnostic potential of BRI in younger women, whereas its predictive relevance diminished in those over 35, akin to other obesity markers. This study is the first to rigorously affirm a strong link between increased BRI and the higher prevalence of infertility among married women aged 20–45. To optimize fertility, maintaining a healthy weight and waist circumference is recommended. The integration of BRI into clinical practice could assist in early intervention for women at risk of infertility. However, further research is required to identify effective predictive markers for infertility in women aged 36–45.

Infertility is medically defined as the inability to conceive after 12 months of regular, unprotected sexual intercourse[1]. This condition is a major global reproductive health issue, affecting an estimated 186 million people worldwide[2]. In the United States, infertility impacts approximately 6.7–15.5% of women of reproductive age[3]. Given its significant impact on human development, the US Centers for Disease Control and Prevention (CDC) emphasizes the importance of prioritizing the diagnosis and treatment of infertility[4]. Despite increasing international attention to infertility as a public health concern, the underlying factors contributing to it require further exploration[5–7].

Obesity has become a global epidemic, with reliable estimates indicating that over 1.1 billion people are affected worldwide[8]. The negative effects of obesity on reproductive health are well-documented, as obese women often experience irregular menstruation, impaired ovulation, and endometriosis[9]. However, much of the existing research on the relationship between obesity and infertility has relied primarily on body mass index (BMI) as an indicator. While BMI is a common measure of obesity, it is limited in its ability to differentiate between lean and fat tissues[10,11]. Recently, more precise measures have been developed to assess visceral fat accumulation, which is closely linked to reproductive dysfunction[12]. For instance, the weight-adjusted waist circumference index (WWI) shows a positive association with infertility among U.S. women[13]. Similarly, the Visceral Adiposity Index (VAI), which reflects dysfunction and accumulation of visceral adipose tissue, has been positively correlated with increased infertility incidence[14]. Introduced in 2013, the Body Roundness Index (BRI) offers a superior estimation of body fat distribution and visceral adiposity than other traditional anthropometric measures[15,16]. Unlike the BMI, which is based solely on height and weight, the BRI incorporates waist circumference, offering a more comprehensive perspective on body shape[17].This feature enhances the BRI's ability to identify abdominal obesity, particularly in individuals with excess visceral fat, providing a more accurate assessment of this condition[18]. Furthermore, the BRI is less influenced by muscle mass, making it a more reliable indicator of fat-related health risks in individuals with higher muscle mass[19]. Additionally, the inclusion of height in the BRI formula distinguishes it from other obesity indices such as WWI or VAI, allowing

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it to more thoroughly reflect an individual's body composition and fat distribution[14,20,21]. Despite its promising advantages, the significance of the BRI in relation to infertility among married women has yet to be explored. This study aims to fill this gap by examining the association between BRI and infertility. Furthermore, this research will evaluate and compare four obesity indices—BRI, BMI, WWI, and the VAI—as screening tools for identifying American married women at heightened odds of infertility. By pinpointing individuals at increased risk, targeted preventive interventions can be devised to mitigate the incidence of infertility.

Methods

Study design and population

This study utilizes data from the ongoing National Health and Nutrition Examination Survey (NHANES), managed by the National Center for Health Statistics under the Centers for Disease Control and Prevention. Further details on NHANES are accessible via the CDC's dedicated website (http://www.cdc.gov/nchs/nhanes/). NHANES employs a multistage probability sampling technique to collect detailed data from a representative sample of the non-institutionalized, civilian U.S. population. The original collection of NHANES data received ethical approval from the Institutional Review Board of the National Center for Health Statistics (NCHS), and informed consent was obtained from all participants. Following ethical guidelines, de-identified data from the NHANES program are publicly available. For this study, researchers not involved with the initial NHANES program accessed and analyzed these data; therefore, no further ethics approval was required for this secondary analysis.

The dataset from 2013 to 2018 was chosen for analysis to include responses from a detailed questionnaire on infertility. The initial dataset consisted of 29,400 participants who had completed assessments regarding demographics, health conditions, and laboratory tests. We systematically excluded participants for several reasons: male participants ($n = 14{,}452$), individuals with marital status other than married ($n = 10{,}875$), those outside the 20–45 age range ($n = 2{,}368$), and individuals lacking data on BMI, WWI, VAI, BRI, or fertility status ($n = 384$). Additionally, extreme values of BRI were identified and excluded based on a threshold of mean ± 3 standard deviations ($n = 16$). After these exclusions, the final sample consisted of 1,305 participants. Figure 1 illustrates the sample selection flowchart.

Definition of infertility and BRI, BMI, WWI, VAI

Infertility was assessed using self-reported data from the Reproductive Health Questionnaire, specifically question RHQ074, which asked if the participant had attempted to conceive for over a year. Answers affirming this were categorized as 'infertile', and all others as 'fertile'. Anthropometric measurements, including body height, body weight, and waist circumference (WC), were collected by trained examiners at a mobile examination center equipped with standardized instruments. Body weight was measured using calibrated platform scales with a precision of 0.1 kg, and height was assessed with stadiometers to the nearest 0.1 cm, with participants standing upright. These measurements were taken while participants wore light clothing and no shoes. Triglycerides (TG) were measured using the Wahlefeld method, while high-density lipoprotein cholesterol (HDL) was quantified using the magnesium sulfate/glucan method. Both TG and HDL measurements were performed on serum samples, and participants were instructed to fast for at least 9 h prior to blood collection. BMI was calculated by dividing weight in kilograms by the square of height in meters[22]. BRI was computed by $364.2\text{-}365.5*(1\text{-}[WC(m)/2\pi]^2/[0.5*height(m)]^2)^{[½}$ [23]. The WWI, indicating obesity levels by normalizing WC to body weight, is determined by the square root of the WC divided by body weight[24]. For females, the VAI is calculated as WC/(36.58 + (1.89*BMI))*(TG/0.81)*(1.52/HDL-C), where TG and HDL-C are measured in mmol/L and WC in cm[12].

Covariates

Our analyses adjusted for a range of covariates identified from prior research[12,24,25]: age, race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, and Other), poverty-to-income ratio (PIR), educational level (below high school, at least high school), diabetes status, hyperlipidemia, hypertension, smoking status (defined as having smoked 100 or more cigarettes lifetime), ,menstrual regularity over the past 12 months, history of pelvic infection or pelvic inflammatory disease treatment, hormone usage, physical activity level, and alcohol consumption (categorized as drinking at least once a month or not). Diagnoses of diabetes, hyperlipidemia, and hypertension were verified through medical records, current medication use, or if fasting plasma glucose levels exceeded 7.0 mmol/L. Information on these variables was obtained from the NHANES database (https://www.cdc.gov/nchs/nhanes/).

Statistical analysis

In adherence to guidelines set by the NCHS, we applied sample weights in our statistical estimates to accurately represent the noninstitutionalized civilian U.S. population. Participant demographics and baseline characteristics were summarized using means ± standard deviations for continuous variables and percentages for categorical variables. To assess differences between participants with and without infertility, we compared means and proportions.

Initially, relationships were explored univariately. The link between BRI and infertility was further analyzed through multivariate logistic regression. We utilized four models: Model 1 was unadjusted; Model 2 adjusted for age and race; Model 3 further adjusted for health behaviors and comorbidities; and Model 4 adjusted for a comprehensive set of variables including age, race, educational level, PIR, smoking status, alcohol consumption, diabetes, hyperlipidemia, hypertension, physical activity level, menstrual regularity in the past 12 months, history of pelvic infection treatment, and hormone use.

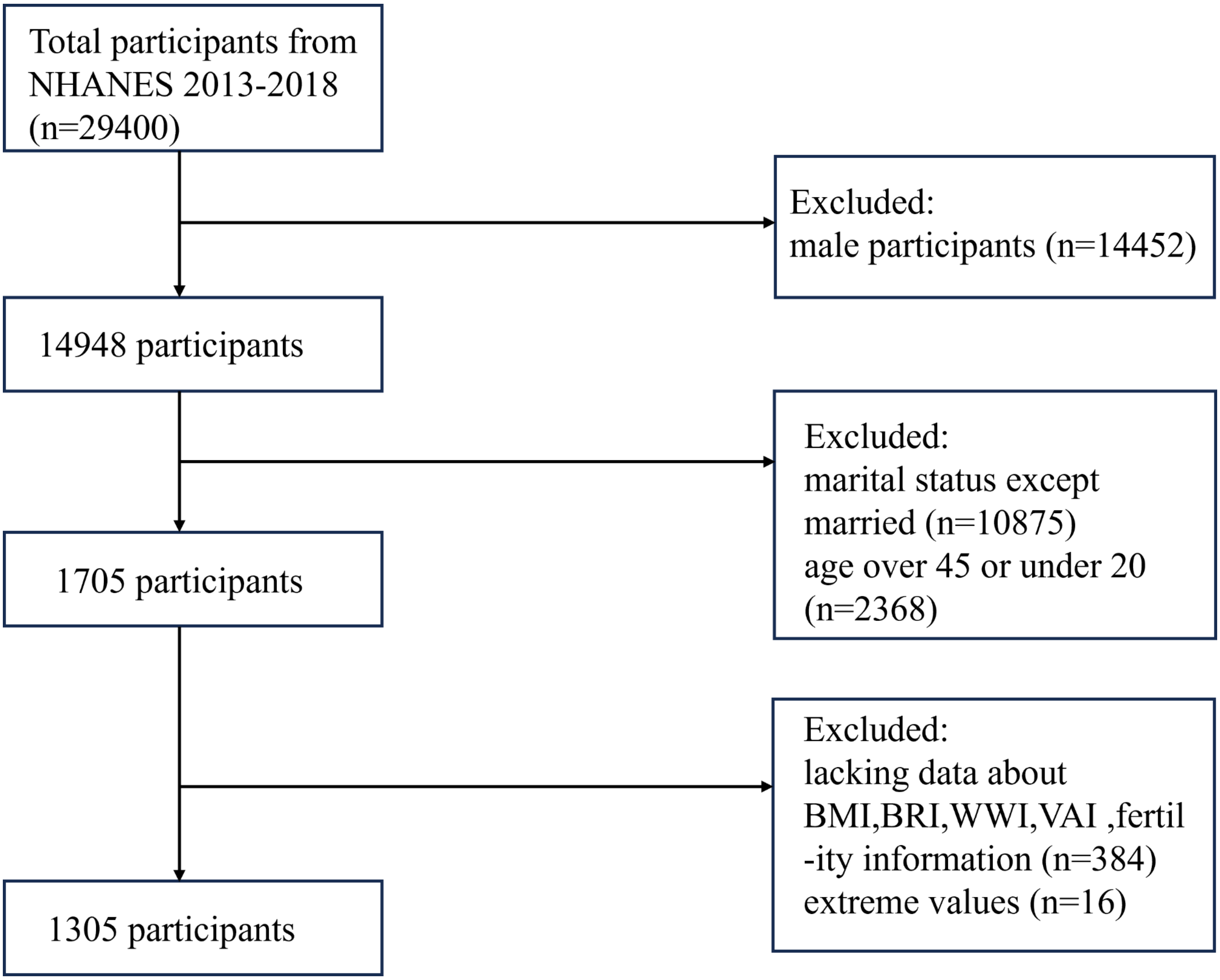

Fig. 1. Sample selection flowchart from NHANES 2013–2018.

To investigate potential nonlinear relationships, we employed generalized additive models (GAM) and smooth curve fitting techniques. Nonlinear associations prompted the use of a recursive method to pinpoint the inflection point, followed by a two-piecewise linear regression to analyze segments on either side of this point. Subgroup analyses were performed using stratified multivariate regression, incorporating interaction terms to explore variability across different subgroups. The predictive capacity of obesity indices for identifying infertility was evaluated using receiver operating characteristic (ROC) analysis and area under the curve (AUC) values. A p-value of 0.05 or less was considered statistically significant. All analyses were conducted using R (http://www.Rproject.org) and EmpowerStats (http://www.empowerstats.com).

Results

Baseline characteristics of participants

Our analysis included 1,305 participants. Table 1 outlines the clinical characteristics stratified by the presence of infertility. Compared to controls, individuals with infertility were generally older, exhibited higher BMI values, a greater prevalence of diabetes, and a higher BRI level. No significant differences were observed between the groups in other baseline characteristics, including race, PIR, education level, physical activity, smoking status, alcohol consumption, menstrual regularity in the past 12 months, history of pelvic infection treatment, and hormone use, hypertension, and hyperlipidemia ($p > 0.05$).

Associations between BRI and the prevalence of infertility

Table 2 details the results from our multivariate logistic regression analyses. In Model 1, which was unadjusted, BRI demonstrated a positive association with the prevalence of infertility [Odds Ratio (OR) = 1.13; 95% Confidence Interval (CI): 1.06, 1.20; $p < 0.0001$]. This association persisted in Model 2, which adjusted for age and race (OR = 1.13; 95% CI: 1.06, 1.20; $p < 0.0001$). When further adjusted for health behaviors and comorbidities in Model 3, the positive association was still evident (OR = 1.10; 95% CI: 1.03, 1.18; $p = 0.0038$). The fully adjusted Model 4 confirmed a significant positive association (OR = 1.13; 95% CI: 1.05, 1.21; $p = 0.0009$), indicating a

Variables	Control (n = 1101)	Infertility(n = 204)	P-value
Age(years)	34.71 ± 6.67	36.58 ± 6.07	0.0011
BMI (kg/m^2)	28.88 ± 7.67	31.81 ± 8.63	0.0021
PIR	3.13 ± 1.61	3.22 ± 1.56	0.5483
Race (%)			0.8540
Mexican American	13.04	8.58	
Other hispanic	7.71	4.17	
Non-hispanic white	60.17	71.30	
Non-hispanic black	6.18	7.15	
Other	12.90	8.80	
Education level (%)			0.8473
Less than high school	25.30	24.63	
High school or high diploma	74.70	75.37	
Moderate physical activity (%)			0.6410
No	47.19	49.80	
Yes	52.81	50.20	
Hypertension (%)			0.7601
No	88.39	79.41	
Yes	11.61	20.59	
Diabetes (%)			< 0.0001
No	93.39	85.69	
Yes	6.61	14.31	
Hyperlipidemia (%)			0.0751
No	85.48	79.81	
Yes	14.52	20.19	
Alcohol consumption (%)			0.8311
No	36.83	36.10	
Yes	63.17	63.90	
Smoking status (%)			0.2992
No	75.17	71.02	
Yes	24.83	28.98	
Regular periods in past 12 month (%)			0.2802
No	11.90	15.07	
Yes	88.10	84.93	
History of pelvic infection treatment (%)			0.1099
No	96.71	94.11	
Yes	3.29	5.89	
Ever use female hormones (%)			0.7271
No	93.32	92.36	
Yes	6.68	7.64	
BRI	5.22 ± 2.35	6.11 ± 2.52	0.0016

Table 1. Baseline characteristics of participants, weighted. Mean ± SD for continuous variables: the P value was calculated by the weighted linear regression model. (%) for categorical variables: the P value was calculated by the weighted chi-square test.

13% increase in the prevalence of infertility per unit increase in BRI. Furthermore, the highest tertile of BRI was associated with an 120% increased prevalence of infertility compared to the lowest tertile in Model 4, underscoring a significant trend (p for trend = 0.0004).

The generalized additive models and smooth curve fits employed to delineate the nonlinear relationship between BRI and the prevalence of infertility. Notably, an inflection point was identified, as shown in Fig. 2. A subsequent threshold effect analysis employing a two-piecewise linear regression model pinpointed the inflection point at 7.95 (Table 3). The likelihood ratio tests comparing the piecewise models to standard linear models revealed a significant improvement ($p = 0.038$), suggesting that the piecewise model more accurately represented the data.

The area between the upper and lower dashed lines is represented as 95% CI. Each point shows the magnitude of the BRI and is connected to form a continuous line. age, race, educational level, poverty-to-income ratio, smoking status, alcohol consumption, diabetes, hyperlipidemia, hypertension, physical activity level, menstrual regularity in the past 12 months, history of pelvic infection treatment, and hormone use were adjusted.

Exposure	Model 1 OR (95%CI), *P* value	Model 2 OR (95%CI), *P* value	Model 3 OR (95%CI), *P* value	Model 4 OR (95%CI), *P* value
BRI	1.13 (1.06, 1.20) < 0.0001	1.13 (1.06, 1.20) < 0.0001	1.10 (1.03, 1.18) 0.0038	1.13 (1.05, 1.21) 0.0009
BRI tertiles				
Low	Reference	Reference	Reference	Reference
Middle	1.28 (0.86, 1.91) 0.2252	1.36 (0.90, 2.03) 0.1409	1.24 (0.82, 1.88) 0.3130	1.33 (0.86, 2.05) 0.1957
High	2.07 (1.42, 3.00) 0.0001	2.19 (1.48, 3.24) < 0.0001	1.90 (1.25, 2.88) 0.0026	2.20 (1.42, 3.42) 0.0004
P for trend	0.0001	< 0.0001	0.0022	0.0004

Table 2. Association between BRI and the prevalence of infertility. Data are presented as OR, 95% CI and P-value. Model 1: adjusted for nothing. Model 2: adjusted for age and race. Model 3: adjusted for age, race, smoking status, alcohol consumption, diabetes, hyperlipidemia, hypertension. Model 4: adjusted for age, race, educational level, PIR, marital status, smoking status, alcohol consumption, diabetes, hyperlipidemia, hypertension, physical activity level, menstrual regularity in the past 12 months, history of pelvic infection treatment, and hormone use.

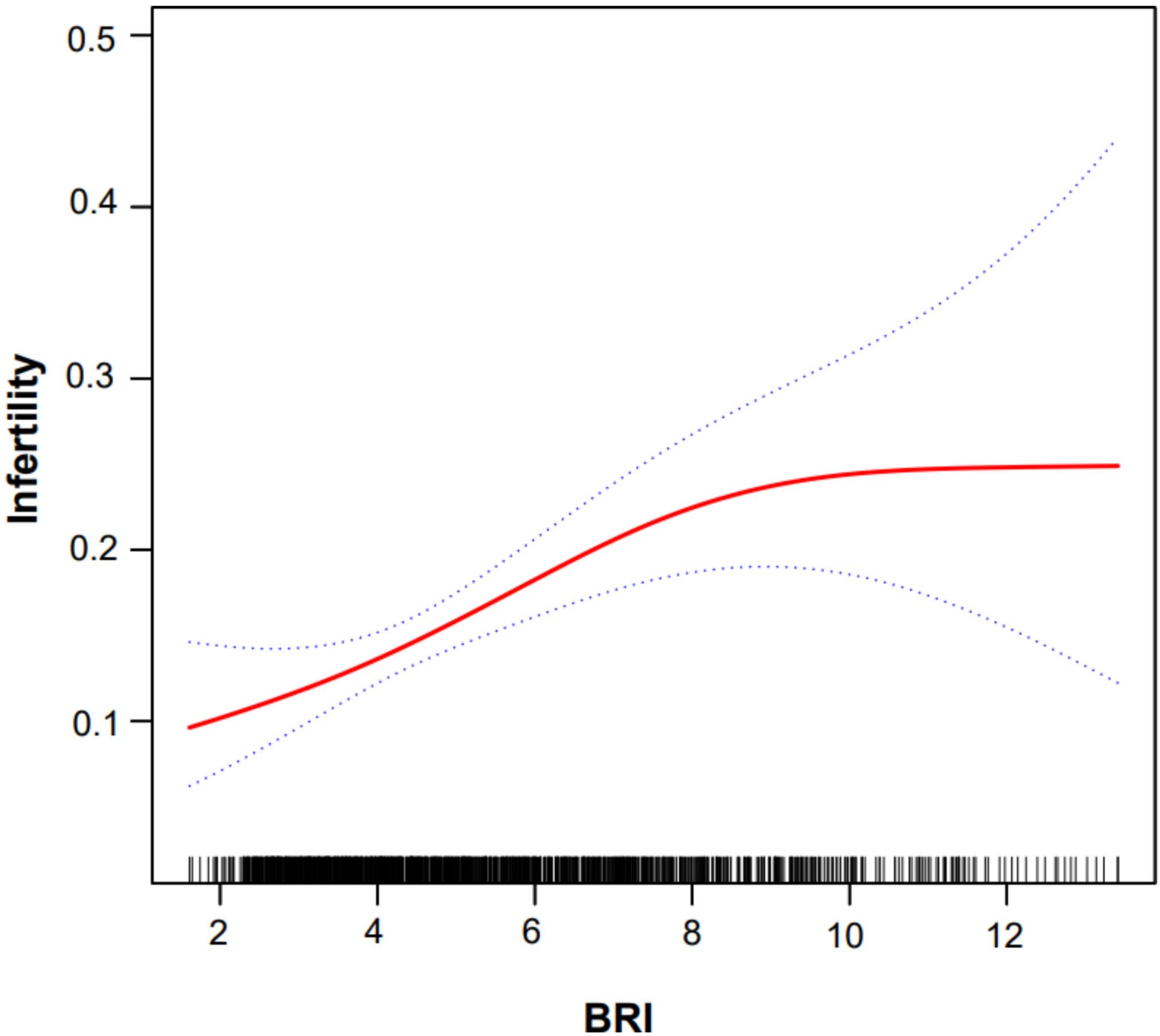

Fig. 2. Association between BRI and the prevalence of infertility.

Infertility	Adjusted OR (95% CI), *P* value
BRI	
Fitting by the standard linear model	1.13 (1.05, 1.21) 0.0009
Fitting by the two-piecewise linear model	
Inflection point	7.95
< 7.95	1.23 (1.10, 1.36) 0.0002
> 7.95	0.93 (0.76, 1.14) 0.4895
Log likelihood ratio	0.038

Table 3. Generalized additive modeling and smoothed curve fitting. Adjusted as Model 4.

	Infertility	
	OR (95%CI), *P* value	*P* for interaction
Stratified by age		0.0972
Younger than 35	1.20 (1.09, 1.33) 0.0004	
Older than 35	1.07 (0.97, 1.18) 0.1911	
Stratified by race		0.5015
Mexican American	1.18 (0.97, 1.43) 0.0966	
Other Hispanic	1.51 (1.06, 2.16) 0.0240	
Non-Hispanic White	1.13 (1.02, 1.25) 0.0150	
Non-Hispanic Black	1.06 (0.87, 1.29) 0.5477	
Other	1.09 (0.88, 1.34) 0.4452	
Stratified by alcohol consumption		0.2566
No Yes	1.08 (0.97, 1.20) 0.1724 1.17 (1.07, 1.27) 0.0007	
Stratified by smoking status		0.3683
No	1.15 (1.06, 1.25) 0.0010	
Yes	1.08 (0.96, 1.22) 0.1941	
Stratified by diabetes		0.4200
No	1.12 (1.04, 1.21) 0.0028	
Yes	1.23 (0.99, 1.52) 0.0615	
Stratified by hyperlipidemia		0.2738
No	1.11 (1.03, 1.20) 0.0074	
Yes	1.23 (1.03, 1.47) 0.0199	
Stratified by regular periods in past 12 months		0.9614
No	1.14 (0.87, 1.49) 0.3457	
Yes	1.13 (1.05, 1.22) 0.0011	
Stratified by hormone use		0.7736
No	1.13 (1.05, 1.22) 0.0009	
Yes	1.20 (0.83, 1.72) 0.3377	

Table 4. Subgroup analysis. Adjusted for all covariates except effect modifier.

Subgroup analysis

We conducted subgroup analyses to evaluate the robustness and consistency of the BRI-infertility relationship, as detailed in Table 4. These analyses considered potential modifiers such as age, race, alcohol consumption, smoking status, diabetes, hyperlipidemia, menstrual regularity in the past 12 months, hormone use. No significant interactions were observed (all p for interaction > 0.05), indicating that these factors did not significantly modify the observed relationship.

Diagnostic efficacy of obesity indices for infertility

The efficacy of various obesity indices in distinguishing individuals with infertility was assessed through ROC curves and AUC values (Fig. 3). In the subgroup of participants aged ≤ 35 years, the AUC values for BRI, BMI, WWI, and VAI were 0.6546 (95% CI: 0.5882,0.7210), 0.6412 (95% CI: 0.5749,0.7076), 0.6449 (95% CI: 0.5845,0.7052), and 0.5808 (95% CI: 0.5186,0.6430), respectively. Notably, BRI demonstrated the highest AUC among these indices (Table 5). Conversely, in participants older than 35 years, the diagnostic utility of these indices was limited, with AUC values for BRI, BMI, WWI, and VAI were 0.5347 (95% CI: 0.4782, 0.5912), 0.5542

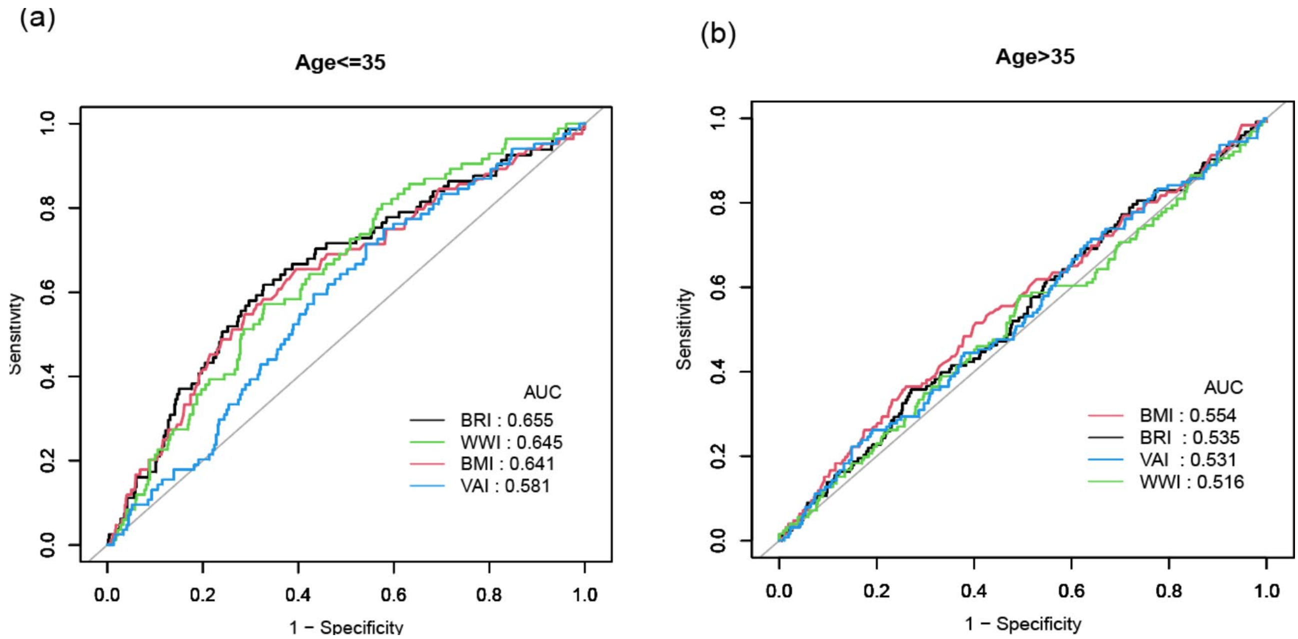

Fig. 3. ROC curves of different obesity indices for the prediction of infertility risk.

Obesity indices	ROC area (AUC)	Best threshold	Specificity	Sensitivity
BRI	0.6546(0.5882, 0.7210)	5.6535	0.6729	0.6173
BMI	0.6412(0.5749, 0.7076)	30.5500	0.7124	0.5476
WWI	0.6449(0.5845, 0.7052)	11.2695	0.6716	0.5714
VAI	0.5808(0.5186, 0.6430)	0.8103	0.4583	0.7143

Table 5. ROC curves of obesity indices for discriminating infertility (age ≤ 35).

Obesity indices	ROC area (AUC)	Best threshold	Specificity	Sensitivity
BRI	0.5347(0.4782, 0.5912)	6.9768	0.7293	0.3577
BMI	0.5542(0.4974, 0.6111)	30.2500	0.5962	0.5159
WWI	0.5157(0.4583, 0.5731)	11.0227	0.5070	0.5794
VAI	0.5309(0.4748, 0.5870)	0.8932	0.3601	0.7143

Table 6. ROC curves of obesity indices for discriminating infertility (age > 35).

(95% CI: 0.4974, 0.6111), 0.5157 (95% CI: 0.4583, 0.5731), and 0.5309 (95% CI: 0.4748, 0.5870), respectively (Table 6).

Discussion

This pioneering study explores the association between the BRI and infertility within a nationally representative sample of American women aged 20 to 45 who are married. We found a consistent positive nonlinear association between BRI and infertility, maintained across both unadjusted and adjusted models. Notably, we identified a critical inflection point: below this threshold, each additional unit increase in BRI was associated with 23% higher odds of infertility (OR = 1.23; 95% CI: 1.10–1.36; $p = 0.0002$). Subgroup analyses confirmed the robustness of this association across diverse demographic groups. While indices such as BRI, BMI, WWI, and VAI showed significant diagnostic value in younger women, their relevance diminished in the 36 to 45 age group.

The burgeoning prevalence of obesity is now a major public health concern, affecting approximately 20% of American women of reproductive age[1].Traditionally, BMI has been the standard for assessing overweight conditions in studies investigating obesity's impact on fertility. However, the diverse presentations of obesity—generalized versus central—suggest that BMI alone may not capture the nuances of body fat distribution and muscle composition effectively[26,27]. This realization has prompted the introduction of novel obesity indices over recent decades, designed specifically to measure central obesity[12–14,21,22,24,25,28–31] .The BRI, by providing a more accurate estimation of visceral fat, offers significant insights into the role of abdominal obesity in reproductive challenges[15]. The BRI is well-documented as a robust predictor of diabetes, including prediabetes, cardiometabolic disorders, and metabolic syndrome[32–34].In this investigation, we expanded the scope of BRI to assess its relevance as a potential determinant of infertility. Our results affirm the association between increased visceral fat, as measured by BRI, and a higher prevalence of infertility, with a notable 13% increase in infertility odds for each unit increment in BRI among women with marital status. It effectively bridges a critical gap in the current literature by linking specific body composition metrics with reproductive health outcomes.

Despite these promising associations, the underlying mechanisms through which higher BRI levels influence infertility remain unclear, and there exist several possible explanations. Excess fat, particularly in the abdominal region, can elevate estrogen levels in obese women, disrupting hormonal balance and causing irregularities in ovulation and menstrual cycles[35,36]. Additionally, abdominal obesity is often associated with conditions such as polycystic ovary syndrome (PCOS), which exacerbates ovulatory dysfunction and hormonal imbalances[37]. Moreover, the inflammatory cytokines released by visceral fat may negatively impact fertility by impairing the endometrial receptivity necessary for successful implantation[20,38].These findings collectively highlight the complex interconnections between abdominal obesity, reproductive health, and cellular mechanisms, emphasizing the need for further research to elucidate these intricate biological processes and their implications for fertility.

Magnetic resonance imaging (MRI) and computed tomography (CT) are universally recognized as the gold standards for assessing visceral fat. Nevertheless, the widespread adoption of these imaging modalities is curtailed by their significant costs and the complex nature of the procedures involved[39]. Consequently, exploring alternative obesity metrics for evaluating infertility presents a pragmatic approach. Our ROC analysis established that four obesity indices, including BRI, BMI, WWI, and VAI, demonstrate good diagnostic prowess in women under the age of 35, Notably, BRI exhibited the highest AUC among these indices. However, the efficacy of these indices in women aged 36 to 45 remains uncertain, underscoring an urgent need for targeted research to develop more effective diagnostic tools for this age group. This insight directs future investigations aimed at enhancing fertility evaluations and interventions.

Our study's conclusions are substantiated by data obtained from the NHANES, with a strategic focus on married women to enhance the accuracy of responses regarding infertility issues. By excluding divorced, separated, or unmarried individuals from our analysis, we minimized potential biases, thereby improving the reliability of our findings. However, we acknowledge that this approach resulted in a smaller sample size for each cycle. To address this limitation, we included data from three cycles of the NHANES, spanning from 2013 to 2018. This adjustment enhances the robustness of our findings. Furthermore, the incorporation of appropriate sample weights ensures not only the reliability but also the broader applicability of our results. We advocate for the adoption of these obesity metrics in clinical practice to facilitate timely interventions for women under 35 who are at risk of or currently experiencing infertility. However, the study's reliance on self-reported infertility via questionnaires could introduce bias due to potential recall inaccuracies. Furthermore, as the study leverages data exclusively from the United States, its generalizability to other populations might be limited. Additionally, the cross-sectional design of this study precludes definitive causal inferences between BRI and infertility, underscoring the need for future longitudinal research to substantiate and expand upon these findings.

Conclusions

Our analysis confirms a positive nonlinear association between BRI and infertility. To improve fertility outcomes, it is recommended that women prioritize maintaining a healthy weight and waist circumference. Considering the cost-effectiveness and accessibility of these obesity indices, we strongly recommend their integration into clinical protocols. However, it is vital to note that these conclusions are primarily relevant to the cohort of U.S. women studied. Therefore, further research is essential to validate whether these findings are applicable to female populations in other geographical areas.

Data availability

Publicly available datasets were analyzed in this study. Those data can be found here: www.cdc.gov/nchs/nhanes/.

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Author contributions
FY and XQY designed the research. FY, RDF, XQY, and PJL collected and analyzed the data. FY, XQY, and RDF drafted the manuscript. FY and XQY revised the manuscript. All authors contributed to the article and approved the submitted version.

Declarations

Competing interests
The authors declare no competing interests.

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