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Association between the age-adjusted visceral adiposity index (AVAI) and female infertility status: a cross-sectional analysis of the NHANES 2013–2018

Mingqin Kuang[1,2], Ying Yu[2] and Shanyang He[3*]

Abstract

Background Obesity stands as an essential factor contributing to infertility in women. Early identification of obese individuals leads to favorable results for female infertility. The objective of this research is to assess the association between the age-adjusted visceral adiposity index (AVAI) and female infertility.

Methods This study was conducted using NHANES data from 2013 to 2018, in which 1,231 women aged 20–45 were selected. Infertility was defined by survey questions. AVAI was calculated using anthropometric and serum data. Covariates included demographics and lifestyle factors. Statistical analysis with R, adjusting for covariates, and assessing nonlinearity and cutoff effects.

Results The study of 1,231 women from the NHANES database revealed that 11.94% were diagnosed with infertility. Individuals with higher AVAI scores showed increased age, WC, BMI, and reduced HDL levels, with a positive correlation between AVAI and female infertility (OR = 1.42, 95%CI: 1.26–1.60). AVAI quartiles showed a pronounced relationship with female infertility risk, with the highest quartile showing the greatest risk(OR = 9.35,95% CI: 2.96–29.55). Nonlinear and threshold effects in the relationship between AVAI and female infertility were identified, with an inflection point at -9.70. Subgroup analyses indicated significant interactions between AVAI and educational status and BMI, particularly in women with a BMI below 25 kg/m^2, where a high AVAI level was closely related to increased infertility risk(OR = 1.92, 95%CI: 1.44–2.58).

Conclusion The study identifies a strong association between elevated AVAI scores and female infertility risk, especially in women with a BMI under 25 kg/m^2. This suggests that AVAI could be a valuable predictor in female fertility assessments.

Keywords Female infertility, Age-adjusted visceral adiposity index, NHANES, Obesity, BMI

*Correspondence:
Shanyang He
heshanyang@gdph.org.cn
[1]Guangdong Cardiovascular Institute, Guangzhou, Guangdong 510080, People's Republic of China
[2]Gynecology and Oncology Department of Ganzhou Cancer Hospital, Ganzhou, Jiangxi 341000, People's Republic of China
[3]Department of Gynecology, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences, Southern Medical University, Guangzhou, Guangdong 510080, People's Republic of China

Introduction

Infertility is a reproductive health issue that affects many women worldwide [1–3]. Typically, it is diagnosed when a couple has regular sexual intercourse without any contraceptive measures for more than 12 months and fails to conceive [4, 5]. In the United States, approximately one in five married women aged 15 to 49 years suffer from infertility [6, 7]. Women with infertility generally do not experience physical discomfort, but the psychological burden it imposes, along with the potentially lengthy process of assisted reproductive technology treatments, can be very taxing [8, 9]. To some extent, female infertility is also one of the causes of family disharmony and rising divorce rates, adding to the social and economic burden [10, 11]. Therefore, female infertility is not just a reproductive health issue; it is also related to social and financial stability and the sustainable development of humanity. A variety of variables, such as age, ethnicity, body mass index (BMI), immune system anomalies, hormonal disorders, abnormalities of the reproductive system, and poor lifestyle choices, are associated with infertility status [12]. One of the main variables associated with female infertility is obesity status [13–17]. Research has shown that waist circumference (WC) and BMI are not as reliable indicators of obesity as visceral fat distribution (VFD) is in terms of the relationship between obesity and female infertility status [18, 19]. Nevertheless, investigating VFD frequently necessitates expensive imaging techniques, which might not be financially viable. In response, indices based on more easily available and reasonably priced data have been developed to assess VFD and help identify risk variables linked to female infertility [20–22].

The visceral adiposity index (VAI) serves as an indicator for gauging the presence of visceral fat, and is derived from measurements of WC, triglycerides (TG), BMI, and HDL-cholesterol (HDL) levels [23–25]. This metric is extensively applied in the assessment of conditions such as infertility, obesity, diabetes, and the risk of death from heart-related conditions [26–29]. Given the significant influence that age has on the incidence of several diseases, the VAI was improved by adding age-related adjustments, producing the age-adjusted visceral adiposity index (AVAI). This improved index stands out for its usefulness for accurately predicting the risk of cardiovascular and all-cause mortality [30].

Infertility, which is similarly influenced by age, might share a distinctive link with the AVAI. However, the relationship between the AVAI and female infertility remains uncharted in existing studies. As such, in this study, we examined National Health and Nutrition Examination Survey (NHANES) data from 2013 to 2018 to determine whether the AVAI and the prevalence of female infertility are related in some way.

Materials and methods

Study population and design

The NHANES serves as a pivotal cross-sectional study in the field of epidemiology, illuminating the health and nutritional profiles of the U.S. population. Each participant provided their informed consent in writing at the beginning of the program. Considering that the study had already received permission from the National Center for Health Statistics Ethics Review Board (https://www.cdc.gov/nchs/nhanes/irba98.htm) [31], no further external ethical approval needed to be obtained, and the study was carried out in accordance with ethical standards. This study included 29,419 participants from the NHANES (2013−1018). Among them, 3,874 female participants aged between 20 and 45 years were selected. The research also excluded individuals who lacked necessary data for VAI calculation (n=2,351), or infertility information (n=8), those who were pregnant at the time of the survey (n=19), and those who lacked data on other covariates (n=265). In the end, the analysis included 1,231 participants (Fig. 1). Moreover, the study population was weighted to improve the accuracy and representativeness of the results.

Measurement of infertility

Incorporating the relevant clinical guidelines, individuals in the NHANES reproductive health survey were defined as patients with infertility on the basis of questions RHQ074 and RHQ076. The content of.

item RHQ074 is “Have you been trying to conceive for over a year without success?” The content of item RHQ076 is “Have you sought medical attention because you were unable to conceive?” The group labeled as “infertile” was composed of participants who answered “yes” to both questions. In contrast, the group labeled as “non-infertile” was composed of participants who answered “no” to both questions. In this study, we included only participants who provided clear “yes” or “no” answers to the questions about trying to conceive and seeking medical attention for infertility. Participants who refused to respond or responded with “refused,” “do not know,” or any other non-binary responses, were not included in our study population. This strict inclusion criterion was applied to ensure the accuracy and reliability of our findings.

Definition of the VAI and AVAI

The data required for calculating the VAI and AVAI were collected from the examination and laboratory data sections of the NHANES. Anthropometric measurements included WC, height (HT), weight (WT), and BMI. The serum biochemical parameters included HDL and TG levels. The formula for BMI involves dividing weight (kg)

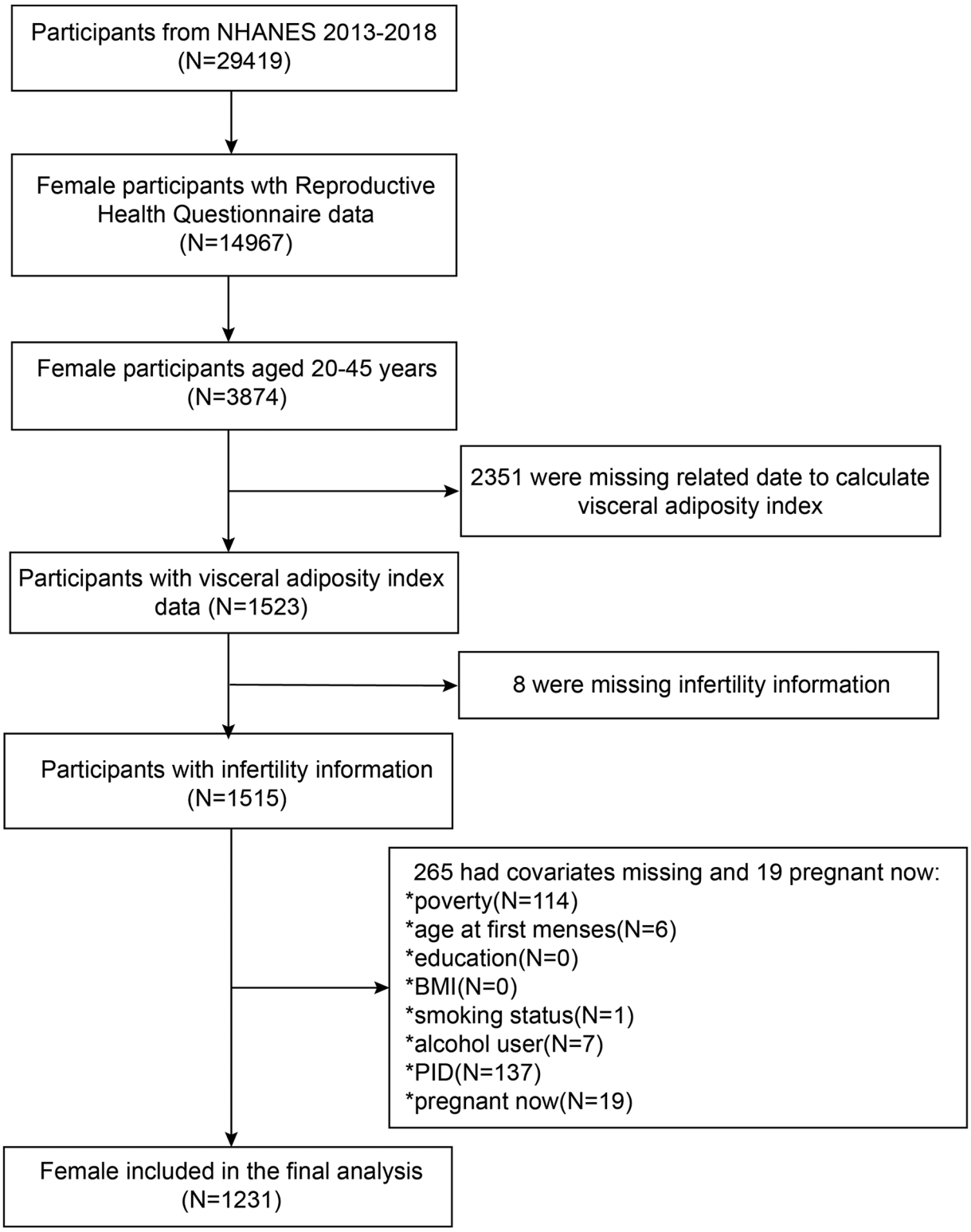

Fig. 1 Flowchart of participants selection

by the square of height (meters). The formula for determining the VAI is as follows:

$$\mathrm{VAI} = (1.31/\mathrm{HDL}) \times (\mathrm{TG}/1.03) \times (\mathrm{WC}/(36.58 + 1.89 \times \mathrm{BMI})).$$

In terms of clinical significance, age is significantly correlated with female infertility status. A new index known as the AVAI has been developed, that considers factors such as BMI, WC, age, HDL, and TG levels. The formula for calculating the AVAI is as shown below:

$$\mathrm{AVAI} = -16.186 - 1.369 \times \mathrm{HDL} + 0.038 \times \mathrm{WC} + 0.144 \times \mathrm{age} - 0.013 \times \mathrm{BMI} - 0.151 \times \mathrm{TG}.$$

HDL and TG are measured in millimoles per liter (mmol/L) in both formulas.

The rationale for including these indicators is as follows. For HDL, the inverse relationship with the AVAI is represented by a negative coefficient (-1.369). HDL is known as "good" cholesterol, and higher levels are generally associated with a lower risk of cardiovascular diseases and metabolic disorders, which can contribute to infertility. For WC, the positive coefficient (0.038) indicates that greater WC, a measure of central obesity, is associated with an increased risk of infertility. Central obesity is a significant predictor of metabolic syndrome and related hormonal imbalances that can affect fertility. For age, the positive coefficient (0.144) reflects the well-established fact that female fertility decreases with age. Age is a critical factor in female infertility, with the risk increasing significantly after the age of 35. For BMI, the negative coefficient (-0.013) suggests that a lower BMI is associated with a higher AVAI, which in turn may be linked to a greater risk of infertility. For TG levels, the negative coefficient (-0.151) indicates that higher levels of triglycerides, a marker of lipid metabolism, are inversely associated with the AVAI. Elevated TG levels can be indicative of metabolic dysfunction, which may impact fertility.

Covariates

On the basis of previous related research, this study considered age at menarche, BMI, education level, the poverty-income ratio (PIR), smoking status, race, alcohol consumption status, age, and pelvic inflammatory disease (PID) status as covariates. Age, race, education level, and the PIR were obtained through demographic information. Pregnant women aged 35 and above were categorized as having advanced maternal age, and infertility is closely related to a woman's age; therefore, age was divided into three groups (less than 35 years old, 35–40 years old, and 40 years old or older). Education level was categorized into "Over high school," " Under high school," and " High school." The PIR was categorized into three levels: under 1.5 for low, between 1.5 and 3.5 for moderate, and 3.5 or higher for high. The use of tobacco and alcohol was evaluated through questionnaires related to smoking and alcohol consumption status. A participant was categorized as a smoker if they had smoked in excess of 100 cigarettes throughout their life. Alcohol users were classified into three states: never (self-reported less than 12 drinks in a lifetime), heavy (more than four drinks daily), and mild. BMI was derived from anthropometric measurements collected during the examination. And BMI was categorized into three groups: normal or underweight (<25 kg/m^2), overweight (25–30 kg/m^2), and obese (≥ 30.0 kg/m^2). Age at menarche was classified into two groups on the basis of clinical relevance: either <15 years or ≥ 15 years. PID status was assessed through the RHQ078 question in the reproductive health survey, with an affirmative "yes" response indicating a PID patient. Consistent with the previously mentioned inclusion criteria for infertility, participants who did not provide direct responses to the questionnaire were not included in the scope of this study's reference population; in other words, these individuals were excluded to avoid potential confounding.

Statistical analysis

The weights used in this investigation are sourced from the NHANES and are available for viewing on the NHANES website (https://www.cdc.gov/nchs/nhanes/tutorials/Weighting.aspx). With the nonnormal distribution in mind, categorical variables are shown as counts and percentages, and continuous variables are presented as medians and quartiles (quantile 1, quantile 3). AVAI quartiles were analyzed in relation to female infertility status. For the comparison of infertile versus non-infertile groups, continuous variables were assessed via the Kruskal–Wallis test, whereas categorical variables were evaluated via the chi-square test. The initial analysis (Model 1) did not involve adjustment for any covariates. Model 2 was adjusted for age and race. Subsequently, Model 3 was additionally adjusted for alcohol consumption status, education level, the PIR, smoking status, BMI, age at menarche, and PID status. Furthermore, we utilized a sleek curve conversion to analyze the nonlinear correlation between the AVAI and fertility status following adjustments for an identical group of factors. Next, we devised a dual-section linear regression design to examine fluctuations in the correlation at a particular cutoff. The cutoff was pinpointed as the spot with the greatest probability among all conceivable values. A log-likelihood ratio examination was subsequently deployed to evaluate the distinction between the two parts of the linear regression structures.

Statistical analyses were conducted via R (version 4.3.0, accessible at https://www.r-project.org) and

EmpowerStats (X&Y Solutions Inc., Boston, MA; available at www.empowerstats.com). A *p*-value lesss than 0.05 was considered to indicate statistical significance.

Results

The baseline characteristics of the study participants

This study enrolled 1,231 women aged 20 to 45 years from the NHANES 2013–2018 database. In this cohort, 147 individuals were diagnosed with infertility, accounting for 11.94% of the sample, and the majority of participants identified as non-Hispanic whites, comprising 35.17% of the total. The demographic and initial traits of the subjects are outlined in Table 1 and were organized based on AVAI quartiles. Individuals with elevated AVAI typically exhibited advanced age, increased WC, diminished incomes, heightened levels of education, and elevated BMI ($p<0.01$). Concurrently, individuals within this group were likely to exhibit reduced HDL levels and elevated TG levels in their blood biochemistry ($P<0.001$). Furthermore, lifestyle habits among this

Table 1 Characteristics of the women participants categorized by AVAI scores

AVAI	Q1 (-14.97–11.58)	Q2 (-11.58–10.37)	Q3 (-10.37–9.25)	Q4 (-9.25–6.73)	*P*-value
WC, cm	79.40 (73.47–86.55)	90.20 (81.95-103.15)	96.45 (86.72–109.00)	109.90 (100.27-124.05)	< 0.001
HDL, mmol/L	1.68 (1.47–1.97)	1.47 (1.23–1.73)	1.34 (1.19–1.58)	1.19 (1.03–1.40)	< 0.001
TG, mmol/L	0.66 (0.47–0.96)	0.76 (0.54–1.17)	0.86 (0.61–1.31)	1.07 (0.74–1.61)	< 0.001
VAI	3.26 (2.21–4.97)	4.28 (2.97–7.59)	5.76 (3.57–9.34)	7.74 (4.87–13.37)	< 0.001
Age, years, n(%)					< 0.001
< 35	301 (97.73%)	242 (78.83%)	125 (40.58%)	36 (11.69%)	
35–40	3 (0.97%)	46 (14.98%)	105 (34.09%)	77 (25.00%)	
≥ 40	4 (1.30%)	19 (6.19%)	78 (25.32%)	195 (63.31%)	
Race, n (%)					0.070
Mexican	38 (12.34%)	44 (14.33%)	65 (21.10%)	57 (18.51%)	
Hispanic	37 (12.01%)	31 (10.10%)	25 (8.12%)	28 (9.09%)	
White	115 (37.34%)	106 (34.53%)	99 (32.14%)	113 (36.69%)	
Black	54 (17.53%)	68 (22.15%)	61 (19.81%)	68 (22.08%)	
Other Race	64 (20.78%)	58 (18.89%)	58 (18.83%)	42 (13.64%)	
Education, n (%)					0.005
Under high school	27 (8.77%)	43 (14.01%)	54 (17.53%)	60 (19.48%)	
High school	55 (17.86%)	59 (19.22%)	62 (20.13%)	60 (19.48%)	
Over high school	226 (73.38%)	205 (66.78%)	192 (62.34%)	188 (61.04%)	
PIR, n (%)					0.026
< 1.5	122 (39.61%)	130 (42.35%)	134 (43.51%)	136 (44.16%)	
1.5–3.5	89 (28.90%)	104 (33.88%)	92 (29.87%)	113 (36.69%)	
≥ 3.5	97 (31.49%)	73 (23.78%)	82 (26.62%)	59 (19.16%)	
BMI, kg/m2, n (%)					< 0.001
< 25	218 (70.78%)	115 (37.46%)	73 (23.70%)	16 (5.19%)	
25–30	63 (20.45%)	82 (26.71%)	93 (30.19%)	58 (18.83%)	
≥ 30	27 (8.77%)	110 (35.83%)	142 (46.10%)	234 (75.97%)	
Smoking status, n (%)					< 0.001
No	237 (76.95%)	214 (69.71%)	215 (69.81%)	188 (61.04%)	
Yes	71 (23.05%)	93 (30.29%)	93 (30.19%)	120 (38.96%)	
Alcohol user, n (%)					0.510
Never	68 (22.08%)	80 (26.06%)	78 (25.32%)	73 (23.70%)	
Mild	219 (71.10%)	200 (65.15%)	214 (69.48%)	210 (68.18%)	
Heavy	21 (6.82%)	27 (8.79%)	16 (5.19%)	25 (8.12%)	
Age of menarche, years, n (%)					0.169
< 15	259 (84.09%)	265 (86.32%)	273 (88.64%)	276 (89.61%)	
≥ 15	49 (15.91%)	42 (13.68%)	35 (11.36%)	32 (10.39%)	
PID, n (%)					0.006
No	301 (97.73%)	297 (96.74%)	291 (94.48%)	284 (92.21%)	
Yes	7 (2.27%)	10 (3.26%)	17 (5.52%)	24 (7.79%)	

Data were expressed as n (%) and median (interquartile range)

AVAI age-adjusted visceral adiposity index, WC waist circumference, HDL high-density lipoprotein, TG triglycerides, VAI visceral adiposity index, PIR poverty income ratio, BMI body mass index, PID pelvic inflammatory disease

Table 2 Weighted univariate logistic analyses between variables and infertility (odds ratios, 95% confidence intervals)

Variables	Univariate analysis (crude model)	
	95% CI	*P*-value
WC	1.02 (1.01, 1.03)	< 0.0001
BMI	1.04 (1.02, 1.06)	< 0.0001
VAI	1.00 (1.00, 1.01)	0.2818
AVAI	1.42 (1.26, 1.60)	< 0.0001

group might include tobacco use or a history of PID ($P<0.01$). No notable variances were observed in the AVAI based on age at menarche, alcohol consumption status, or ethnicity.

Correlations of infertility status with WC, BMI, the VAI and the AVAI

As shown in Table 2, WC (OR = 1.02, 95% CI: 1.01–1.03) and BMI (OR = 1.04, 95% CI: 1.02–1.06) were positively linked to female infertility status in the univariate analysis, whereas there was no significant correlation between the VAI and female infertility status (OR = 1.00, 95% CI: 1.00–1.01). Therefore, we considered the significant impact of age on female infertility status, and we used the AVAI to assess the relationship between visceral fat and female infertility status. We found that the AVAI was positively and strongly associated with female infertility status (OR = 1.42, 95% CI: 1.26–1.60).

The relationship between infertility and AVAI quartiles

As shown in Table 3, a greater AVAI quartile was associated with an elevated risk of female infertility status. In the unadjusted model, the AVAI quartile was positively correlated with the incidence of female infertility (Model 1). This association remained significant after partial adjustments were implemented via Model 2. Upon comprehensive adjustment for all conceivable confounding variables, the HRs for infertility status associated with the second (Q2), third (Q3), and fourth (Q4) quartiles, relative to the reference category (Q1), were estimated to be 3.64 (95% CI: 1.65–8.04), 7.02 (95% CI: 2.81–17.54), and 9.35 (95% CI: 2.96–29.55), respectively (Model 3, *P* for trend < 0.01). Additionally, after rigorously controlling for potential confounding variables, there was a 44% increase in the likelihood of female infertility status for each one-unit increment in the AVAI, as indicated by the OR.

By performing smoothing curve fitting and threshold effect analysis, we identified a potential nonlinear relationship between the AVAI and the risk of female infertility status. A pronounced nonlinear association between the two variables (Fig. 2). The threshold effect analysis revealed an inflection point for the AVAI at -9.70. As detailed in Table 4, the two-piece linear regression model revealed that a one-unit increase in the AVAI when the AVAI was at or below −9.70 corresponded to a nearly twofold increase in the odds of female infertility status (OR = 1.9, 95% CI = 1.5–2.4; $P<0.001$). In contrast, for AVAI values exceeding −9.70, the corresponding increase in the odds of female infertility was not markedly different (OR = 1.0, 95% CI = 0.7–1.3; $P=0.845$). Focusing on the delineation of the link between the AVAI and female infertility status, the segmented logistic regression model demonstrated superior performance over the standard linear logistic regression model($P<0.01$).

Subgroup analyses

As depicted in Table 5, we conducted a series of subgroup analyses and tests for interaction to evaluate the reliability of the association between the AVAI and female infertility and to uncover any potential disparities among different demographic groups. Among the majority of these subgroups, the AVAI was a substantial risk factor for female infertility. Notably, the AVAI had pronounced interaction with educational status and BMI, with *P*-values of 0.025 and 0.020, respectively, for the interactions. Specifically, within the group of individuals with a BMI below 25, there was a marked and significantly discernible positive correlation between the AVAI and female infertility status (OR = 1.92, 95% CI: 1.44–2.58, $P<0.0001$). These findings suggest that individuals, even those with a BMI within the normal or underweight

Table 3 Multivariate Cox regression analysis of AVAI with infertility

	AVAI	AVAI quartiles				*P* for trend
		Q1	Q2	Q3	Q4	
		(-14.97–11.58)	(-11.58–10.37)	(-10.37–9.25)	(-9.25–6.73)	
	OR (95%CI) *P*-value	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	
infertility		10 (3.25%)	31 (10.10%)	48 (15.58%)	58 (18.83%)	
Model 1	1.42 (1.26, 1.60) < 0.0001	Reference	3.35 (1.61, 6.95)	5.50 (2.73, 11.09)	6.91 (3.46, 13.81)	< 0.01
Model 2	1.51 (1.25, 1.83) < 0.0001	Reference	3.79 (1.79, 8.04)	7.23 (3.27, 16.01)	10.16 (4.20, 24.58)	< 0.01
Model 3	1.44 (1.03, 2.02) 0.0328	Reference	3.64 (1.65, 8.04)	7.02 (2.81, 17.54)	9.35 (2.96, 29.55)	< 0.01

Values are presented as weighted odds ratios (ORs), 95% confidence interval (95%CI), and *P* value

Model 1 adjusted for none

Model 2 adjusted for age and race

Model 3 adjusted for age, race, education level, PIR, alcohol user, smoking status, BMI, age at menarche and PID

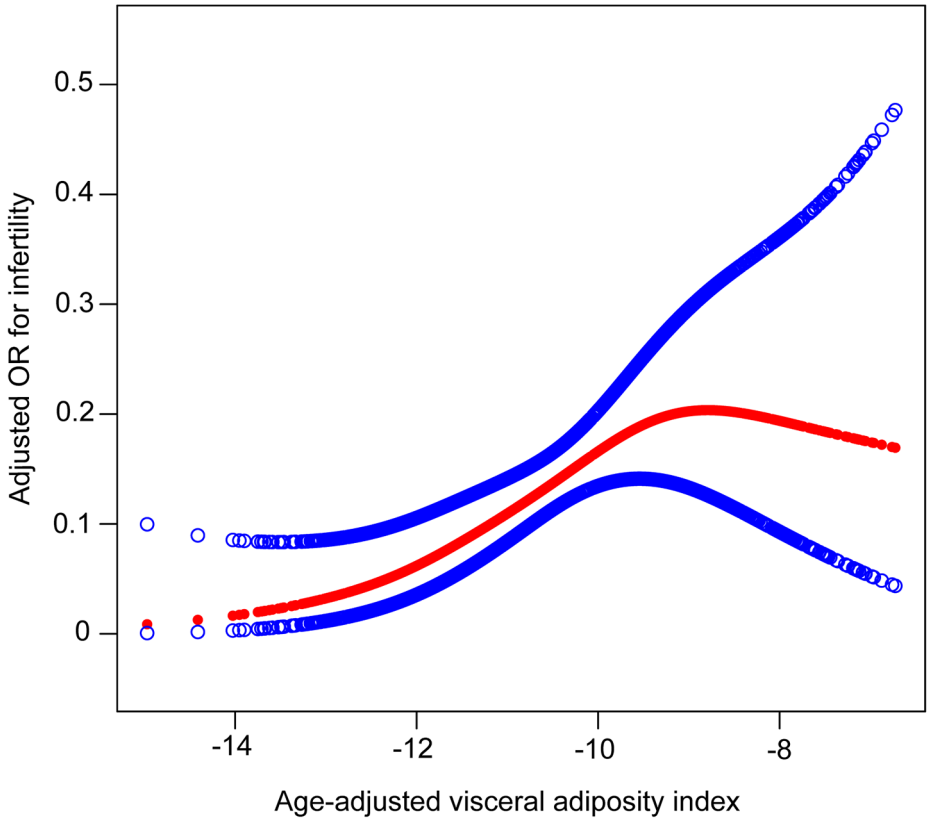

Fig. 2 Relationship between AVAI and the risk of female infertility status

Table 4 Threshold and saturation effect analysis of AVAI on infertility

Outcomes	Infertility	
	OR (95%CIs)	*P* value
Model a		
(Fitting model by standard linear regression)	1.4 (1.3, 1.6)	< 0.001
Model b		
(Fitting models by two-piecewise linear regression)		
Infection point	-9.70	
< Infection point	1.9 (1.5, 2.4)	< 0.001
> Infection point	1.0 (0.7, 1.3)	0.845
P for log-likelihood ratio test	0.004	

The two-piecewise regression models were adjusted for age, race, education level, PIR, alcohol user, smoking status, BMI, age at menarche and PID

OR odds ratios, 95% CI 95% confidence interval

Table 5 Stratified analysis of the correlation between AVAI and infertility in adults in the NHANES 2013–2018

Subgroup	AVAI	
	OR (95%CI) P-value	*P* for interaction
Age of menarche, years		0.578
< 15	1.43 (1.26, 1.63) < 0.0001	
≥ 15	1.28 (0.89, 1.85) 0.1808	
Education,		0.025
Under high school	1.67 (1.15, 2.42) 0.0072	
High school	1.03 (0.79, 1.34) 0.8429	
Over high school	1.53 (1.32, 1.78) < 0.0001	
BMI, kg/m2,		0.020
< 25	1.92 (1.44, 2.58) < 0.0001	
25–30	1.30 (0.88, 1.93) 0.1915	
≥ 30	1.19 (0.99, 1.43) 0.0687	
Smoking status		0.066
No	1.54 (1.32, 1.80) < 0.0001	
Yes	1.21 (0.99, 1.48) 0.0580	
Alcohol user		0.398
Never	1.58 (1.20, 2.06) 0.0009	
Mild	1.42 (1.22, 1.65) < 0.0001	
Heavy	1.17 (0.84, 1.63) 0.3454	
PID		0.290
No	1.43 (1.26, 1.63) < 0.0001	
Yes	1.10 (0.69, 1.75) 0.6935	

range, may face a heightened risk of female infertility status if they have a high AVAI.

Discussion

Infertility plagues a considerable number of women, profoundly affecting the survival and growth of our species. By examining NHANES data from 2013 to 2018, our research revealed a nonlinear link between the AVAI and

female infertility status, revealing an inflection point at -9.70. This suggested a pronounced positive correlation between the AVAI and the likelihood of female infertility within a specific range.

Obesity, characterized by an overabundance of body fat, not only leads to hormonal imbalances in women but also diminishes insulin sensitivity and disrupts the synthesis and secretion of sex hormones [32–34]. Studies have highlighted the multifaceted and profound impact of obesity on female infertility [35–37]. This process results in a cascade of physiological disruptions, including hormonal imbalances, impeded ovulation, degradation of egg quality, embryonic developmental issues, shifts in the uterine environment, and a state of chronic inflammation [38–41]. Fluctuations in adipose-related factors such as leptin, especially those prevalent in individuals with obesity, can directly influence both embryonic progression and the endometrial capacity to accept an embryo [42–45]. Consequently, this can, to a certain extent, result in female infertility. Moreover, age is an equally significant factor that profoundly affects a woman's probability of successful conception [46–48]. D. B. Dunson et al. investigated the effects of aging on the fertility of couples in good health. Their forward-looking study included demographic data for 782 couples from seven European sites, with women participants aged between 18 and 40. By meticulously documenting daily intercourse, the team evaluated the likelihood of conception among various age brackets. The data revealed a correlation between increasing age and decreasing fertility potential in women, with a more significant decline after age 35. The conclusions of this study emphasize that while older couples may face a decline in their ability to conceive, this does not equate to absolute female infertility. This suggests that for couples who have not been able to conceive within a year, the prospect of natural conception remains substantial if they persist in their attempts over the next year. These findings are instrumental in comprehending how age influences the risk of female infertility and are invaluable for guiding clinical advice and therapeutic choices [49]. A retrospective analysis involving 278 adult men was conducted, and the BMI and VAI for each participant were calculated. The research outcomes indicated a noteworthy inverse relationship between BMI and serum testosterone concentrations, along with the testosterone-to-estradiol ratio (T/E2), with statistical significance ($p<0.05$). These findings suggest that as BMI increases these hormone levels decrease. Nevertheless, the statistical analysis did not yield a significant link between BMI and the quality of semen ($p<0.05$). In contrast, a pronounced inverse correlation was identified between the VAI and various semen metrics, as well as between total serum testosterone levels and the T/E2, all with p-values less than 0.05. This correlation implies that an increase in visceral fat could negatively affect male reproductive potential [50]. Hence, the VAI may be utilized as a credible gauge to determine the likelihood of diminished fertility in males, highlighting that an increase in visceral obesity may pose a threat to men's reproductive health. Furthermore, when considering conditions heavily influenced by age, the AVAI has emerged with enhanced capabilities for assessment, providing a more nuanced evaluation. By incorporating age into its calculation, the AVAI provides a more nuanced assessment of the impact of visceral fat on health than does the traditional VAI, which does not account for age-related changes in fat distribution and function. Its superior usefulness for predicting all-cause and cardiovascular mortality makes the AVAI a valuable tool for risk stratification, especially among older adults. The ease of calculating the AVAI via common clinical measurements also enhances its practicality and accessibility in clinical settings and public health initiatives [30].

Through subgroup analysis and tests for interaction, this study revealed that for individuals with a BMI indicating a normal weight or leanness, a higher AVAI could significantly increase the risk of female infertility. This implies that there should be a greater focus on visceral fat distribution rather than just the magnitude of the BMI index. A cross-sectional survey, the Framingham Heart Study, revealed that the earlier the age of menarche was, the greater the BMI, WC, and visceral adipose tissue ($P<0.0001$) [51]. Another study reported that increased expression of adipocyte factors is associated with BMI. In women, leptin in abdominal fat increases with increasing in BMI, whereas adiponectin expression decreases. The leptin-to-adiponectin ratio is significantly correlated with BMI. This has a substantial impact on women's reproductive health [52]. In our research, we used the AVAI, which has distinct advantages. First, several simple indicators, including age, BMI, WC, TG, and HDL, can be used to assess visceral fat distribution conveniently. Second, this method is more cost-effective than imaging techniques such as CT and MR. Therefore, the AVAI is a more economical and reliable indicator for assessing the correlation between visceral fat distribution and female infertility status, with particular significance for clinical guidance.

Advantages and limitations of the study

Under rigorous inclusion criteria, this study selected data from the high-quality NHANES database, ensuring a certain level of persuasiveness in the results. Concurrently, we adjusted for a range of covariates to further ensure the reliability of the study's findings. However, several shortcomings must be acknowledged. The cross-sectional structure of the study means that it can suggest only potential associations, not causality, between

the AVAI and female infertility status. Additionally, while the study controlled for multiple covariates, other confounding factors may affect the relationship between the AVAI and female infertility status. In the present study, we could not rule-out the influence of all potential confounding effects.

Conclusion

In summary, these findings suggest a positive connection between the AVAI and the potential for female infertility status, underscoring the importance of considering visceral fat distribution when assessing the risk to fertility health and offering new perspectives and directions for further research. More large-scale prospective studies are needed to substantiate the findings of this study.

Author contributions

Mingqin Kuang: Writing – original draft. Mingqin Kuang and Ying Yu: Writing – review & editing. Supervision: Shanyang He. All authors will be informed about each step of manuscript processing including submission, revision, revision reminder, etc. via emails from our system or assigned Assistant Editor.

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Data availability

Research Ethicscan be accessed from the following website: https://www.cdc.gov/nchs/nhanes/irba98.htm. And NHANES data can be accessed from the following website: https://www.cdc.gov/nchs/nhanes/tutorials/Weighting.aspx.

Declarations

Competing interests

The authors declare no competing interests.

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