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Impact of dietary antioxidants on female infertility risk: evidence from NHANES

Yifeng Shao[1,2], Lisha Ma[1,2], Jianqing Zhou[1,2], Kang Wu[1,2]✉ & Xuedong Tang[1,2]✉

The composite dietary antioxidant index (CDAI) serves as a valuable instrument for evaluating the intake of dietary antioxidants. This research aims to clarify the connection between CDAI and the risk of female infertility by analyzing data from the National Health and Nutrition Examination Survey from 2013 to 2018. Participants underwent two 24-h dietary recall interviews to calculate CDAI. Female infertility was determined through two questionnaires. Logistic regression model, restricted cubic spline and subgroup analysis were employed to examine the association between CDAI and female infertility. The study encompassed 2162 participants. Participants with female infertility had lower CDAI levels compared to those without. Following adjustment for confounding variables, a negative association between CDAI levels and female infertility was observed (Q4 vs. Q1, OR [95% CI] 0.392 [0.193, 0.795], *P* = 0.016). RCS demonstrated a statistically significant linear negative relationship between CDAI and female infertility. Subgroup analysis showed no significant interaction. This study illustrates a negative link between the CDAI and female infertility, indicating that higher consumption of dietary antioxidants may be associated with a reduced risk of female infertility. Additional rigorously designed prospective studies are necessary to validate these results.

Keywords Composite dietary antioxidant index, Female infertility, NHANES, Cross-sectional study

Infertility, characterized by the failure to achieve a clinical pregnancy following 12 months or longer of consistent unprotected sexual intercourse, represents a major public health issue worldwide[1]. It affected millions of women worldwide, presenting substantial challenges in the field of reproductive health. Epidemiological studies suggested that approximately 8–12% of couples of reproductive age encounter difficulties achieving pregnancy[2], with significant proportion of these cases can be attributed to factors specific to females[3]. The relationship between female infertility and oxidative stress (OS), marked by a disproportion between the generation of reactive oxygen species (ROS) and the body's antioxidant defense systems, has garnered considerable attention[4]. OS is known to impact key reproductive processes adversely, including oocyte quality, folliculogenesis, and endometrial receptivity, thus influencing a woman's fertility potential[5,6].

The importance of antioxidant defenses in female reproductive health is highlighted by the impact of OS, with the composite dietary antioxidant index (CDAI) serving as a crucial metric[7,8]. The CDAI quantifies the cumulative antioxidant capacity derived from an individual's diet, encapsulating the consumption of a variety of antioxidants, including vitamins A, C, and E, zinc, selenium, and carotene[9]. A higher CDAI score suggests a dietary pattern abundant in compounds capable of neutralizing ROS, potentially mitigating oxidative damage within reproductive tissues[10]. By assessing the CDAI, researchers and clinicians can gain insights into how dietary antioxidants may influence OS levels and female fertility outcomes. Delving deeper into the specifics of the CDAI, it is important to appreciate the methodological nuances that contribute to its robustness as an index. The calculation of the CDAI is determined by the consumption levels of essential dietary antioxidants, adjusted for total energy intake to account for variations in dietary patterns and caloric needs among individuals[11]. This adjustment ensures that the CDAI provides a relative measure of antioxidant consumption that is comparable across different populations and dietary contexts[12]. Furthermore, the index considers the cumulative impact of antioxidants, recognizing that the protective effects against OS likely result from a complex interplay among various compounds rather than a single nutrient acting in isolation[13].

The utilization of data from the National Health and Nutrition Examination Survey (NHANES) enables a comprehensive examination of the correlation between dietary patterns and reproductive health within a

[1]Department of Obstetrics and GynecologyJiaxing Women and Children's Hospital, Wenzhou Medical University, Jiaxing 314000, China. [2]Department of Obstetrics and Gynecology, Jiaxing University Affiliated Women and Children Hospital, Jiaxing 314000, China. ✉email: leichan123@wmu.edu.cn; tangxuedong@wmu.edu.cn

heterogeneous sample population[14]. NHANES database offers robust, representative data that elucidate the nutritional habits and health outcomes, enabling the exploration of how dietary antioxidant consumption correlates with female fertility parameters. It provides a unique vantage point from which to examine the interplay between dietary antioxidant and female reproductive health. This research seeks to offer tangible insights that could guide dietary recommendations for women facing fertility challenges.

Results

Baseline characteristics

The baseline characteristics of the 2162 participants were presented in Table 1. The prevalence of female infertility within the cohort was identified at 13.46%. Statistical analysis revealed significant differences between the infertility and non-infertility groups across various variables, including age, marital status, poverty income ratio (PIR), diabetes mellitus (DM), hypertension, hyperlipidemia, pelvic inflammatory disease (PID), female hormones taken, body mass index (BMI), CDAI, vitamin C, Se, carotenoid. Compared to the non-infertility group, the CDAI, vitamin C, Se and carotenoid were markedly elevated in the infertility group. Furthermore, the infertility group demonstrated a higher combined prevalence of comorbid conditions, such as hypertension, DM, hyperlipidemia.

Relationship between CDAI and infertility

Table 2 displays the findings of a multivariate logistic regression analysis that examined the relationship between the CDAI and the incidence of female infertility. In the crude model, there was no statistically significant association found between CDAI levels and female infertility (OR [95% CI] 0.948 [0.897, 1.002], $P = 0.057$). After controlling for pertinent covariates, a statistically significant negative relationship was observed in both Model 1 (OR [95% CI] 0.939 [0.889, 0.993], $P = 0.028$) and Model 2 (OR [95% CI] 0.942 [0.890, 0.997], $P = 0.040$). When CDAI was categorized into quartiles, this negative association persisted (P for trend < 0.05 in all models). In model 2, there was a significant decrease in female infertility in the fourth quartile compared to the first quartile (OR [95% CI] 0.392 [0.193, 0.795], $P = 0.016$). Similar results were also observed with vitamin C and selenium (Supplementary Table S1).

Restricted cubic spline

The study utilized the restricted cubic spline (RCS) method to examine the relationship between the CDAI and female infertility. The results indicated a linear negative correlation between CDAI and the incidence of female infertility (Fig. 1). We identified a U-shaped relationship between vitamin A intake and the risk of female infertility (P for nonlinear = 1.82E−4, inflection point: 710.033). Additionally, an L-shaped association between carotenoid intake and female infertility was also observed in this study (P for nonlinear = 0.011, inflection point: 17,041.49). Linear associations were detected among vitamin C, vitamin E, zinc, and selenium (Fig. 2).

Subgroup analyses

Subgroup analyses demonstrated a consistent relationship between the CDAI and female infertility across different groups, including age, ethnicity, marital status, education, PIR, menarche age, regular periods, PID, female hormones and birth control pills taken, DM, hypertension and hyperlipidemia, as well as among lifestyle factors, such as BMI, smoking status, drinking status, work activity and recreational activity (all P for interactions > 0.05). Notably, this correlation was more distinct in groups with menarche ages of 11–13 years, heavy drinking, and those lacking recreational activities, yet no statistical significance was found in the interactions (Fig. 3).

Discussion

We investigated the association between the CDAI and female infertility in this study. Utilizing data from the NHANES and adjusting for multiple covariates, the results revealed a negative correlation between CDAI and female infertility, suggesting a potential protective role of CDAI against the onset of infertility in women. Subgroup analyses revealed that the association between CDAI and female infertility was consistent across different groups. While no statistically significant interactions were found, the relationship was notably stronger in individuals with an earlier menarche age, heavy drinkers, and those without recreational activity.

Although the precise mechanisms through which dietary antioxidants influence the risk of female infertility remain unclear, it is apparent that OS plays a significant role in this relationship[15]. OS results from a dysregulation in the generation and clearance of ROS in cellular environments. The intrinsic antioxidant defense mechanisms play a vital role in counteracting OS in the female reproductive system, thereby preserving the integrity of normal reproductive functions and female fertility[16–18]. OS is implicated in a range of reproductive disorders, including ovulatory dysfunction, endometriosis, polycystic ovary syndrome (PCOS), and even early pregnancy loss[19]. PCOS is a common endocrine disorder and a leading cause of infertility, characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries[20]. OS has been shown to negatively impact oocyte quality in women with PCOS. The excess ROS can damage the oocyte's cellular structures, including DNA, lipids, and proteins, leading to reduced oocyte viability and developmental competence[21]. OS also impairs endometrial receptivity in women with PCOS. The endometrium, which must undergo complex remodeling to allow for embryo implantation, is particularly sensitive to oxidative damage. High levels of ROS can disrupt the expression of key genes and signaling pathways involved in endometrial receptivity, leading to an unfavorable environment for embryo implantation[22]. The endogenous antioxidant system, comprised of enzymatic antioxidants like superoxide dismutase (SOD), catalase, and glutathione peroxidases (GPxs), is essential in mitigating ROS and safeguarding reproductive tissues against oxidative harm. The delicate equilibrium between ROS generation and the antioxidant defense mechanism underscores the significance of dietary antioxidants in maintaining

Variables	Total (n = 2162)	Infertility		*P* value
		No (n = 1871)	Yes (n = 291)	
Age (years), n (%)				< 0.001
20–29	824 (41.431)	752 (43.708)	72 (27.680)	
30–39	849 (40.022)	710 (39.211)	139 (44.921)	
40–44	489 (18.547)	409 (17.082)	80 (27.399)	
Ethnicity, n (%)				0.687
Mexican American	359 (12.309)	312 (12.387)	47 (11.843)	
Non-Hispanic White	753 (56.628)	641 (55.946)	112 (60.747)	
Non-Hispanic Black	471 (13.064)	403 (13.169)	68 (12.431)	
Other Hispanic	214 (6.774)	194 (6.955)	20 (5.683)	
Other Race	365 (11.225)	321 (11.544)	44 (9.296)	
Marital status, n (%)				0.001
Divorced/separated/widowed	234 (10.006)	201 (9.665)	33 (12.061)	
Married/living with partner	1231 (57.839)	1027 (55.752)	204 (70.444)	
Never married	697 (32.155)	643 (34.583)	54 (17.495)	
Education, n (%)				0.897
Less than high school	297 (9.627)	259 (9.542)	38 (10.144)	
High school	404 (18.189)	347 (18.368)	57 (17.107)	
College or above	1461 (72.184)	1265 (72.090)	196 (72.749)	
PIR, n (%)				0.016
≤ 1.3	773 (28.732)	679 (29.947)	94 (21.391)	
1.3–3.5	809 (36.845)	697 (35.158)	112 (47.037)	
> 3.5	580 (34.423)	495 (34.895)	85 (31.571)	
DM, n (%)				0.044
No	1994 (93.621)	1734 (94.142)	260 (90.477)	
Yes	168 (6.379)	137 (5.858)	31 (9.523)	
Hypertension, n (%)				0.007
No	1802 (86.916)	1581 (88.200)	221 (79.156)	
Yes	360 (13.084)	290 (11.800)	70 (20.844)	
Hyperlipidemia, n (%)				0.003
No	1016 (48.467)	905 (50.563)	111 (35.809)	
Yes	1146 (51.533)	966 (49.437)	180 (64.191)	
Menarche age (years), n (%)				0.208
≤ 10	233 (9.192)	190 (8.616)	43 (12.674)	
11–13	1425 (67.769)	1244 (67.959)	181 (66.623)	
≥ 14	504 (23.038)	437 (23.425)	67 (20.703)	
Regular periods, n (%)				0.706
No	224 (10.483)	194 (10.317)	30 (11.482)	
Yes	1938 (89.517)	1677 (89.683)	261 (88.518)	
PID, n (%)				0.002
No	2059 (95.682)	1794 (96.592)	265 (90.191)	
Yes	103 (4.318)	77 (3.408)	26 (9.809)	
Birth control pills taken, n (%)				0.234
No	695 (26.086)	624 (26.758)	71 (22.027)	
Yes	1467 (73.914)	1247 (73.242)	220 (77.973)	
Female hormones taken, n (%)				0.006
No	2081 (95.380)	1812 (96.509)	269 (88.561)	
Yes	81 (4.620)	59 (3.491)	22 (11.439)	
BMI, n (%)				0.005
< 18.5	31 (1.479)	26 (1.432)	5 (1.762)	
18.5–24.9	681 (33.647)	607 (35.105)	74 (24.845)	
25.0–29.9	512 (23.955)	464 (24.985)	48 (17.736)	
≥ 30.0	938 (40.919)	774 (38.478)	164 (55.657)	
Smoking status, n (%)				0.146
Never	1553 (69.292)	1361 (70.232)	192 (63.611)	
Former	231 (12.757)	196 (12.624)	35 (13.560)	
Continued				

Variables	Total (n = 2162)	Infertility		*P* value
		No (n = 1871)	Yes (n = 291)	
Now	378 (17.951)	314 (17.143)	64 (22.829)	
Drinking status, n (%)				0.129
Never	352 (13.542)	312 (14.196)	40 (9.587)	
Former	116 (5.017)	96 (4.805)	20 (6.293)	
Mild	605 (27.222)	523 (27.631)	82 (24.754)	
Moderate	565 (28.211)	497 (28.599)	68 (25.867)	
Heavy	524 (26.009)	443 (24.769)	81 (33.498)	
Work activity, n (%)				0.994
No	1212 (51.725)	1048 (51.753)	164 (51.551)	
Moderate	555 (29.442)	487 (29.378)	68 (29.828)	
Vigorous	395 (18.833)	336 (18.868)	59 (18.621)	
Recreational activity, n (%)				0.807
No	928 (35.943)	798 (35.573)	130 (38.176)	
Moderate	532 (25.647)	448 (25.911)	84 (24.051)	
Vigorous	702 (38.410)	625 (38.516)	77 (37.773)	
CDAI	0.849 (0.154)	0.970 (0.162)	0.120 (0.361)	0.029
Vitamin A (mcg/day)	575.376 (12.275)	577.283 (12.134)	563.861 (46.027)	0.779
Vitamin C (mg/day)	71.047 (2.082)	73.554 (2.321)	55.906 (3.372)	< 0.0001
Vitamin E (mg/day)	8.614 (0.203)	8.700 (0.224)	8.089 (0.391)	0.168
Zinc (mg/day)	9.608 (0.138)	9.636 (0.140)	9.435 (0.381)	0.607
Selenium (mcg/day)	102.875 (1.444)	104.025 (1.516)	95.925 (3.359)	0.029
Carotenoid (mcg/day)	8837.575 (277.150)	9031.773 (296.621)	7664.770 (631.223)	0.049

Table 1. Baseline characteristics of the study population. *PIR* poverty income ratio, *DM* diabetes mellitus, *PID* pelvic inflammatory disease, *BMI* body mass index, *CDAI* composite dietary antioxidant index.

Variables	Crude model		Model 1		Model 2	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
CDAI (continuous)	0.948 (0.897, 1.002)	0.057	0.939 (0.889, 0.993)	0.028	0.942 (0.890, 0.997)	0.040
CDAI (quartile)						
Q1 [−8.553, −2.156]	Reference		Reference		Reference	
Q2 (−2.156, 0.076]	0.650 (0.345, 1.223)	0.176	0.655 (0.349, 1.230)	0.180	0.710 (0.349, 1.446)	0.299
Q3 (0.076, 2.749]	0.703 (0.412, 1.201)	0.191	0.671 (0.402, 1.122)	0.124	0.801 (0.454, 1.414)	0.395
Q4 (2.749, 42.973]	0.434 (0.246, 0.764)	0.005	0.398 (0.220, 0.717)	0.003	0.392 (0.193, 0.795)	0.016
P for trend		0.005		0.002		0.008

Table 2. The associations between CDAI and female infertility. Crude model: no covariate was adjusted; Model 1: adjusted for age, ethnicity, marital status, PIR, education; Model 2: adjusted for age, ethnicity, marital status, PIR, education, DM, hypertension, hyperlipidemia, menarche age, regular period. *PID* birth control pills taken, female hormones taken, *BMI* smoking status, drinking status, work activity, recreational activity, *OR* odds ratio, *CI* confidence interval, *CDAI* composite dietary antioxidant index, *PIR* poverty income ratio, *DM* diabetes mellitus, *PID* pelvic inflammatory disease, *BMI* body mass index.

reproductive health[23–25]. While the body possesses a robust system to manage OS, exogenous factors, including dietary intake of antioxidants, can significantly influence the efficiency of this system[26]. Adequate intake of dietary antioxidants may bolster the body's natural defenses, reduce oxidative damage, and thereby potentially lower the risk of conditions leading to female infertility[27]. The importance of vitamin A is highlighted by its involvement in the activation of the retinoic acid receptor and retinoid X receptor transcription factors, its interaction with retinoic acid response element sites in DNA, and its promotion of gene expression related to developmental processes[28,29]. Vitamin C serves as a crucial antioxidant in the body's antioxidant defense system by utilizing the ascorbate peroxidase-glutathione reductase antioxidant pathway to effectively neutralize superoxide and hydroxyl radicals, ultimately converting into ascorbate radicals[6,19,30]. Vitamin E scavenges peroxyl radicals present in cell membranes, halting the lipid peroxidation reaction cascade. This mechanism is essential in protecting cells from oxidative damage, particularly in the lipid-laden milieu of cell membranes where peroxyl radicals have the potential to propagate lipid peroxidation, resulting in cellular dysfunction or demise[31,32]. Through neutralizing

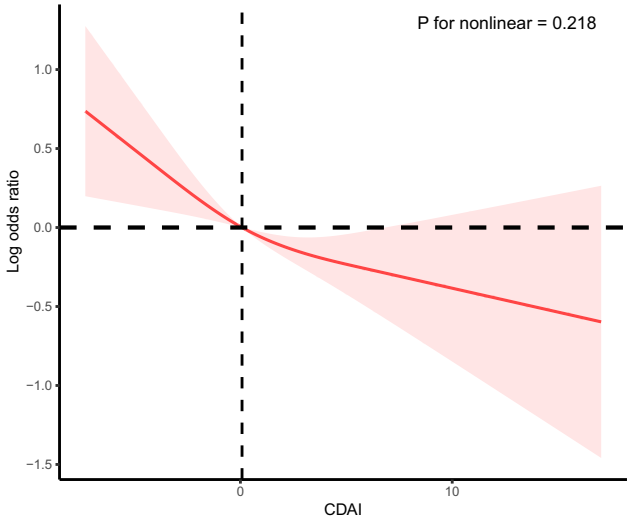

Fig. 1. Restricted cubic spline model between CDAI and female infertility. The solid line represented the OR, while the shaded area showed the 95% CI. A negative slope indicated that higher CDAI was associated with a reduced risk of infertility. *CDAI* composite dietary antioxidant index, *OR* odds ratio, *CI* confidence interval.

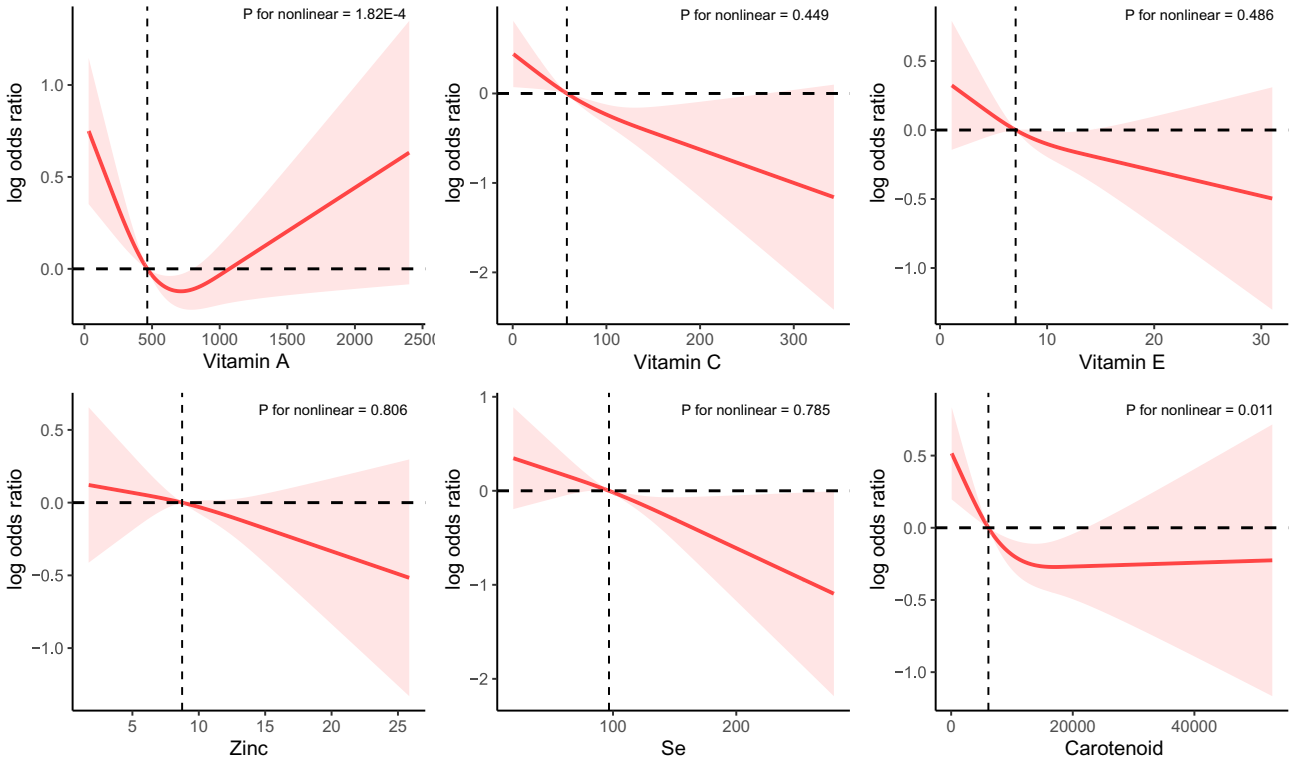

Fig. 2. Restricted cubic spline model between CDAI components and female infertility. The solid line represented the OR, while the shaded area showed the 95% CI. Negative slopes indicate that higher levels of a component were associated with a reduced risk of infertility, while positive slopes suggested an increased risk. Negative slopes indicate that higher component levels were associated with a reduced risk of infertility, while positive slopes suggested an increased risk. The slope changes across different intake levels highlighted potential non-linear relationships. *CDAI* composite dietary antioxidant index, *OR* odds ratio, *CI* confidence interval.

these radicals, vitamin E upholds the structural integrity of cell membranes, thereby safeguarding cellular function and viability[7,33,34]. The role of zinc and selenium in the body's defense against OS is critical due to their involvement in key antioxidant enzymes. Zinc is a crucial component of SOD, which catalyzes the conversion of superoxide radicals into less harmful molecules, thereby protecting cells from oxidative damage. Selenium is a

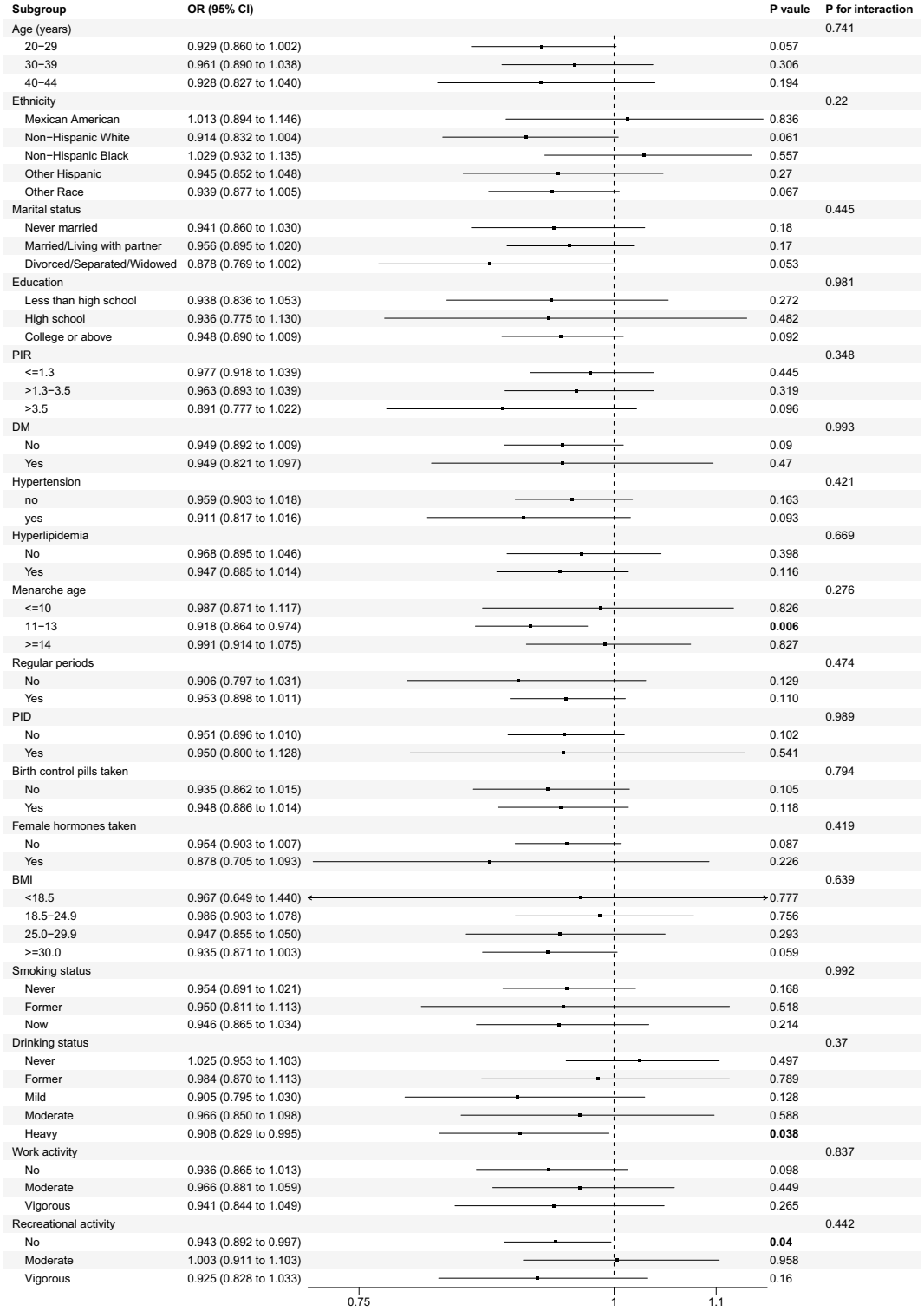

Fig. 3. Subgroup analysis of risk factors for the relationship between CDAI and female infertility. Each subgroup was represented with its corresponding OR and 95% CI. The analysis highlighted where the relationship between CDAI and infertility was stronger or weaker across different population segments. Negative ORs in the subgroups indicated a protective effect of higher CDAI against infertility, whereas positive ORs suggested an increased risk. *CDAI* composite dietary antioxidant index, *PIR* poverty income ratio, *DM* diabetes mellitus, *PID* pelvic inflammatory disease, *BMI* body mass index, *OR* odds ratio, *CI* confidence interval.

vital part of GPxs, enzymes that reduce hydrogen peroxide and lipid hydroperoxides, preventing the formation of free radicals that can damage cellular structures[35–39].

This study has some advantages. Firstly, the integration of data from NHANES serves to bolster the generalizability and practical relevance of our research outcomes. NHANES is widely recognized for its methodological thoroughness and its capability to deliver a sample that precisely represents the U.S. population, encompassing a diverse range of demographic, lifestyle, and health-related variables. This comprehensive dataset enables a thorough analysis of the relationships between CDAI and female infertility, while accounting for potential confounding factors. The inclusion of a diverse population sample allows for the exploration of these relationships across various subgroups. Secondly, the CDAI provides a comprehensive assessment that considers the combined impact of dietary antioxidants, departing from conventional methodologies that typically evaluate individual antioxidants in isolation. This integrated approach is crucial for capturing the synergistic interactions among different antioxidants found in the diet, potentially offering a more accurate representation of actual dietary habits and their influence on health outcomes.

This study is subject to certain limitations. Firstly, the primary limitation arises from the cross-sectional design of the NHANES dataset, which hinders our capacity to establish causal relationships between CDAI and female infertility. Secondly, the reliance on self-reported dietary data in this study introduces the possibility of recall bias and inaccuracies in estimating antioxidant intake. Despite the employment of validated dietary assessment tools, the inherent nature of self-reported data may result in underestimation or overestimation of actual intake, consequently impacting the accuracy of the CDAI calculation and its correlation with infertility outcomes. Thirdly, the study's external validity may be impacted by the demographic and health characteristics of the NHANES participants. Despite NHANES' goal of representing the U.S. population, certain factors related to diet, lifestyle, or healthcare availability may be inadequately recorded or significantly differ from other demographic cohorts. Additionally, although the study's efforts to account for various potential confounders, there remains the possibility of unmeasured variables that could impact the association between dietary antioxidant intake and female infertility. Genetic predispositions and environmental exposures may also have a substantial influence on fertility outcomes, yet were not included in the analysis. Fourthly, a limitation of our study is the broad definition of infertility used in the NHANES database, which relies on self-reported data and does not differentiate between specific causes of infertility, such as PCOS. Although our findings offer insights into the general association between CDAI and female infertility, they do not specifically address the effects of CDAI on women with PCOS. Finally, the CDAI predominantly emphasizes the consumption of antioxidants, potentially overlooking other dietary factors, both nutritional and non-nutritional that may impact female fertility, including dietary fats, sources of protein, and the overall nutritional adequacy of the diet.

This research presents innovative insights into nutritional interventions for addressing female infertility, particularly emphasizing the use of the CDAI as a metric for assessing the overall antioxidant capacity of the diet. The results highlight the role of increased dietary antioxidant intake in reducing the risk of female infertility. Furthermore, these results support the need for additional research on the correlation between dietary antioxidants and women's reproductive health, particularly in light of the potential for dietary modifications to serve as cost-effective preventive measures. This research underscores the significance of dietary antioxidants in preserving women's reproductive health and provides a solid basis for future research and public health interventions. More research is needed to understand how CDAI affects female infertility and how this can be used to develop targeted prevention and treatment strategies.

Methods

Study population

To ascertain the correlation between dietary antioxidants and female infertility, our investigation utilized the NHANES database. This data comprises a cross-sectional survey intended to evaluate the health and nutrition of individuals in United States[40]. The study was performed in accordance with the Declaration of Helsinki and was approved by the research ethics review board of the National Centre for Health Statistics. All participants in the study provided written informed consent. For the purpose of our study, we extracted data spanning from 2013 to 2018, encompassing a total of 29,400 participants. From this initial population, male participants were excluded from the analysis (n = 14,452). Additional exclusions were implemented according to age, specifically individuals under the age of 20 or over the age of 44 years (n = 11,241). Subsequent exclusions were based on missing data in several categories critical for our analysis: 373 participants had incomplete demographic information; 481 participants had missing data regarding infertility status; 472 participants had incomplete data for the CDAI calculation; and additional exclusions were made for missing data in key health variables: menarche age (n = 11), PID history (n = 15), female hormone or birth control pills usage (n = 4), as well as medical history including DM, hypertension, and hyperlipidemia (n = 121). Lifestyle factors were also considered, with exclusions for missing data in smoking and alcohol use (n = 73) and BMI (n = 11). The flow chart was presented in Fig. 4.

The measurement of CDAI

Dietary information and its components were meticulously gathered by well-trained NHANES personnel. Every participant completed two 24-h dietary recall interviews. Trained data collectors conducted a face-to-face dietary recall for 24 h, followed by a telephone recall 3–10 days later. To reduce bias, the average antioxidant intake over the 2 days was used in the final analysis for a more accurate measure of dietary antioxidant consumption. To calculate the CDAI, we included six dietary antioxidants: vitamin A, C, E, carotenoid, zinc, and selenium. Subsequently, the intake levels for each antioxidant were standardized and summed to the final score. The calculation formula was described in a previous study[41].

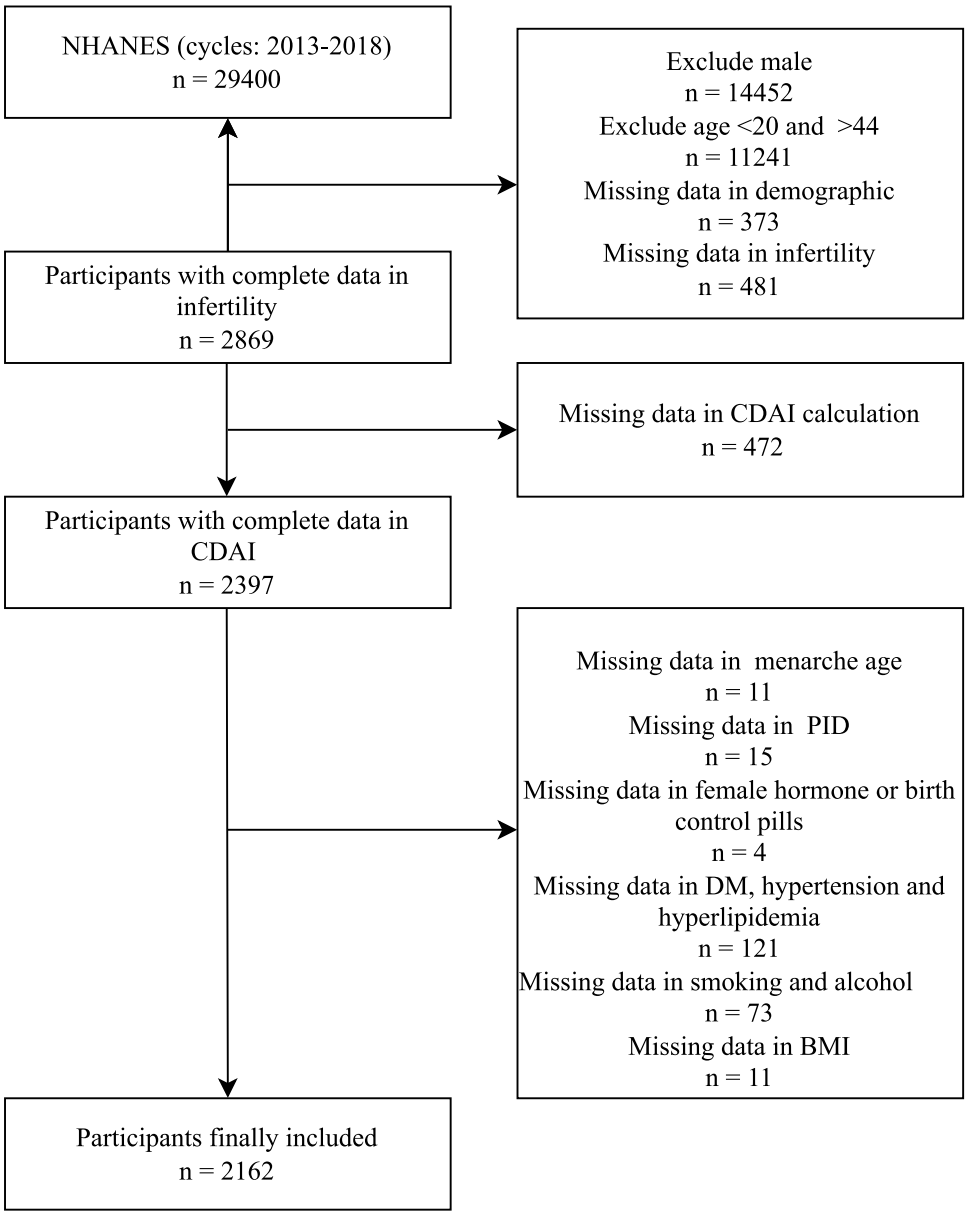

Fig. 4. Flowchart of participant selection. *NHANES* National Health and Nutrition Examination Survey, *CDAI* composite dietary antioxidant index, *DM* diabetes mellitus, *PID* pelvic inflammatory disease, *BMI* body mass index.

The definition of female infertility

The assessment of female infertility was conducted through responses to two specific questions in questionnaire: RHQ074 and RHQ076. A positive response to either of these questions qualified a participant as having a history of female infertility[42].

Covariates

A range of potential confounders were considered in our analyses to isolate the impact of CDAI on female infertility. These included age, ethnicity, marital status, education, PIR, DM, hypertension, hyperlipidemia, menarche age, regular period, PID, the use of birth control pills and female hormones, BMI, smoking and drinking status, physical activity, work and recreational activity. Data on these covariates were extracted from the demographics, dietary, examination and questionnaire data, ensuring a comprehensive adjustment for factors that might influence the study outcomes.

Statistical analyses

Sample weights were appropriately applied in accordance with the recommended selection criteria to adjust for the intricate survey design of NHANES. For baseline characteristics, Weighted means with standard errors (SE)

were utilized for the presentation of continuous variables, while weighted counts (percentages) were employed for the representation of categorical variables. Differences in categorical variables were assessed using the chi-square test, while the Student's t-test was utilized for continuous variables. We explored the association between the CDAI and female infertility using weighted logistic regression models. The participants were stratified into quartiles according to their CDAI levels, with the lowest quartile being designated as the reference group. A trend test was conducted to examine the linear trend across quartiles of CDAI risk estimates. Moreover, RCS was implemented to evaluate potential nonlinear associations between CDAI and female infertility. Sensitivity analyses were conducted through logistic regression within subgroups. Interactions between CDAI and each covariate were also assessed. Statistical analyses were conducted using R software (version 4.3.1), with statistical significance defined as a *P* value less than 0.05.

Data availability

The dataset used in this research is available for public access on the NHANES website at [https://wwwn.cdc.gov/Nchs/Nhanes/].

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Conceptualization, K.W. and X.T.; Methodology, Y.S.; Software, Y.S.; Validation, Y.S., L.M. and J.Z.; Formal analysis, Y.S., L.M. and J.Z.; Investigation, Y.S., L.M. and J.Z.; Resources, Y.S., L.M. and J.Z.; Data curation, Y.S., L.M. and J.Z.; Writing—original draft preparation, Y.S.; Writing—review and editing, Y.S. and X.T.; Visualization, L.M. and J.Z.; Supervision, K.W. and X.T.; Funding acquisition, K.W. and X.T.

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Correspondence and requests for materials should be addressed to K.W. or X.T.