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# The association between composite dietary antioxidant index and rheumatoid arthritis: evidence from NHANES 2001–2020

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## Abstract

**Background** This study aimed to investigate the relationship between the composite dietary antioxidant index (CDAI) and rheumatoid arthritis (RA) using data from the National Health and Nutrition Examination Survey (NHANES) spanning from 2001 to 2020.

**Methods** CDAI is based on the intake of vitamins A, C, E, manganese, selenium, and zinc from the diet. RA patients were identified through questionnaire responses. Weighted multivariate regression analysis was employed to examine the association between CDAI and RA. Additionally, restricted cubic splines were utilized to assess potential non-linear relationships. Subgroup analyses were used to explore whether the relationship between CDAI and RA remained consistent across subgroups (e.g., sex, age, smoking status, etc.). We also used interaction terms to assess whether these subgroup variables influence the relationship between CDAI and RA risk. Finally, we also performed sensitivity analyses to assess the robustness of the main findings after excluding patients with a history of diabetes.

**Results** The study included a total of 11,266 patients. After adjusting for all covariates, the multivariate logistic regression analysis showed that each unit increase in CDAI was associated with a 4% reduction in the odds of RA (odds ratio = 0.96, 95% confidence interval = 0.94–0.99). The incidence of RA was found to decrease as CDAI levels increased (P for trend < 0.05). In the restricted cubic spline analysis, a linear relationship between CDAI and RA was observed. Subgroup analyses and interactions demonstrated that the negative association between CDAI and RA was consistent across all subgroups and was influenced by smoking.

**Conclusion** This study indicates a negative correlation between CDAI and RA, suggesting that CDAI may serve as a valuable and convenient marker for reducing the risk of RA in US adults.

**Clinical trial number** Not applicable.

**Keywords** Composite dietary antioxidant index, Rheumatoid arthritis, NHANES, Cross-sectional study, Association

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## Introduction

Obesity has emerged as a significant global health issue, with strong associations with a variety of chronic diseases, including cardiovascular diseases, diabetes mellitus (DM), and certain types of cancer [1, 2]. In recent years, the connection between obesity and rheumatoid arthritis (RA) has garnered considerable research attention. RA is a chronic inflammatory autoimmune disorder characterized by symmetrical joint inflammation and deformity, leading to loss of function and a diminished quality of life [3]. It is estimated that the prevalence of RA worldwide reached 17.6 million cases in 2020, with projections predicting a rise to 31.7 million cases by 2050, posing a substantial challenge to public health systems [4]. The pathogenesis of RA is complex, involving a confluence of genetic, environmental, and lifestyle factors [5]. Current literature suggests that obesity is a risk factor for RA, potentially exacerbating the disease's pathological processes through increased inflammation and oxidative stress, which may contribute to or intensify the condition [6]. Furthermore, obesity may also impact the pharmacokinetics and pharmacodynamics of medications used to treat RA, affecting the efficacy of treatment [7].

Oxidative stress, a condition resulting from an imbalance between pro-oxidants and antioxidants within the cell, leads to an overproduction of reactive oxygen species (ROS), which plays a significant role in the pathogenesis of RA [8]. This stress not only exacerbates the inflammatory response in individuals with RA but also contributes to the destruction of articular cartilage, underscoring the need for strategies that modulate oxidative stress levels to prevent and treat RA. Dietary antioxidants, such as vitamins C and E, β-carotene, and selenium, have been shown to mitigate oxidative stress by neutralizing ROS and reducing the production of inflammatory mediators [9, 10]. The composite dietary antioxidant index (CDAI) serves as a comprehensive metric for assessing an individual's dietary intake of antioxidants and has been utilized in numerous epidemiological studies to evaluate the relationship between dietary antioxidant intake and the risk of chronic diseases [11, 12]. While some studies have indicated that a higher intake of antioxidants may reduce the risk of RA or improve the condition of those afflicted, the findings are not uniformly consistent [13]. Obesity itself is a state of chronic inflammation and oxidative stress, which could influence the efficacy of dietary antioxidants [14, 15]. Therefore, examining the association between CDAI and RA within the context of obesity could provide novel insights into the prevention and management of RA, particularly against the backdrop of the growing public health concern of obesity.

This study aims to investigate the association between CDAI and the risk of RA in obese individuals. We hypothesize that a higher CDAI may be associated with a reduced risk of RA in this population.

## Method

### Study design and participant selection

This study utilized a cross-sectional analysis approach, sourcing data from the National Health and Nutrition Examination Survey (NHANES) database. NHANES is an ongoing survey conducted by the Centers for Disease Control and Prevention (CDC) aimed at assessing the health and nutritional status of adults and children in the United States. The survey encompasses interviews, physical examinations, and laboratory tests to gather detailed information from participants.

We included data from NHANES spanning the years 2001 to 2020, focusing on individuals aged 20 years and older. After excluding participants who were not obese, had missing information on RA and CDAI, or lacked covariates, we ultimately enrolled 11,266 participants. The detailed process of participant inclusion and exclusion is depicted in Fig. 1.

### Definition of key variables

Participants were asked whether a doctor or other health professional had ever told them they had arthritis, with follow-up questions to specify the type of arthritis. RA was defined as participants who responded "Rheumatoid arthritis" to the question "Which type of arthritis was it?" Obesity was defined as having a body mass index (BMI) calculated from height and weight measurements exceeding 30 $kg/m^2$. The CDAI was calculated as follows: firstly, food intake was collected through a 24-hour dietary recall, which collected detailed information on all foods and beverages consumed by the participant over a 24-hour period. The first interview was conducted via face-to-face at the mobile testing centre and the second interview was conducted via telephone 3–10 days later. Next was the determination of antioxidant content, using the United States Department of Agriculture (USDA) food composition database to determine the antioxidant content of the foods consumed by the participants. Finally, the CDAI was calculated, with intake of the six main antioxidants (vitamins A, C, E, manganese, selenium and zinc) standardised by subtracting the mean and dividing by the standard deviation (SD), and then summed to obtain the CDAI index. The calculation of CDAI followed the recommendations by Wright et al. [16].

$$\mathrm{CDAI} = \sum_{i=1}^{n=6} \frac{\text{Individual Intake} - \text{Mean}}{\text{SD}}$$

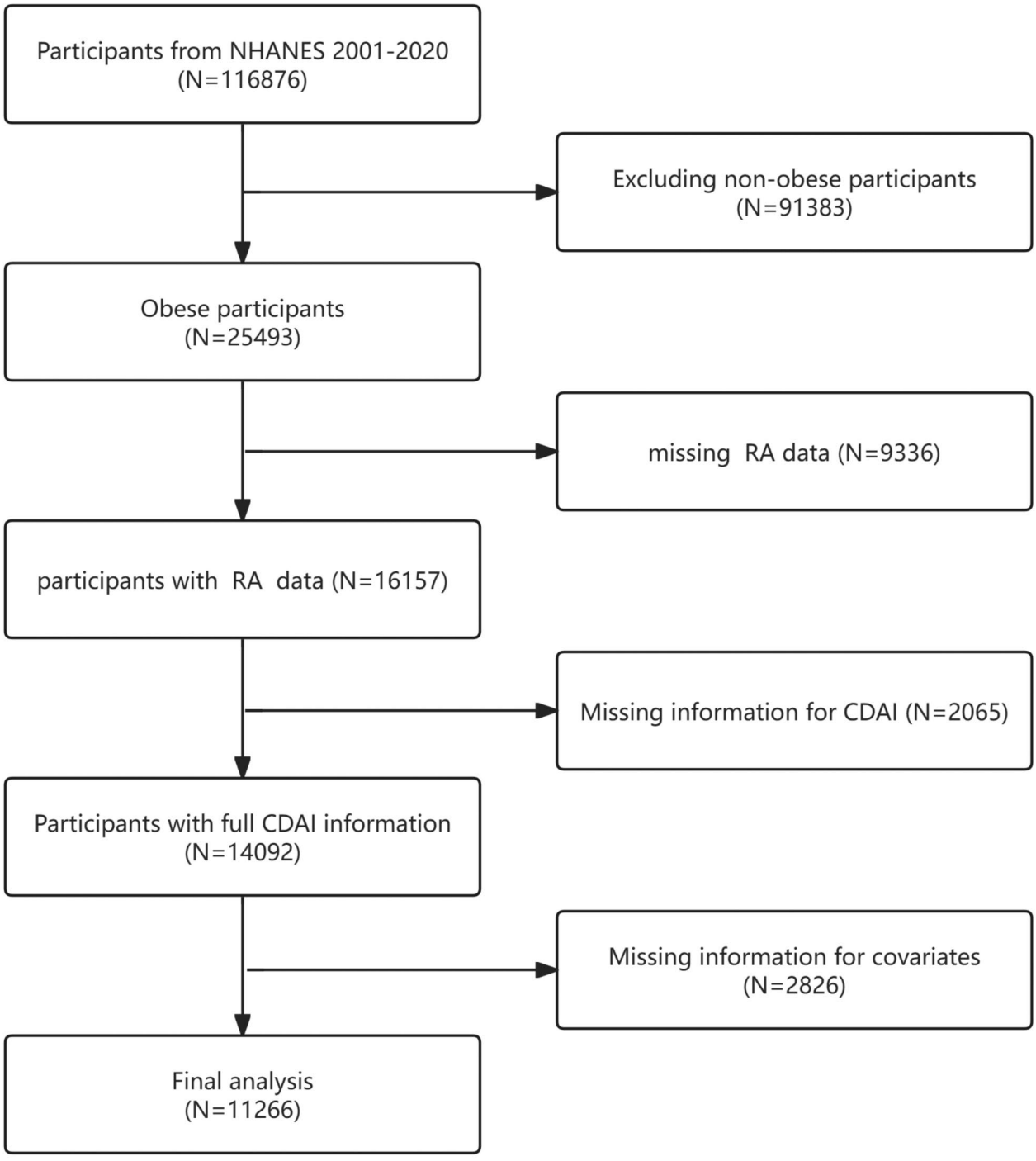


**Fig. 1** Flowchart of the participant selection from NHANES 2001–2020

In our study, we categorized the study population into quartiles based on the CDAI, which are designated as Q1, Q2, Q3, and Q4.

#### Assessment of covariates

For this study, we collected covariates associated with RA based on previous research [17–19]. The primary demographic information included age, sex, race, education level, poverty income ratio (PIR), and marriage. Race categories were divided into Mexican American, Non-Hispanic Black, Non-Hispanic White, Other Hispanic, and other race. Body measurements include BMI. Questionnaire data on smoking and drinking status were also collected. Participants who had smoked fewer than 100

cigarettes in their lifetime were classified as never smokers, those who had smoked more than 100 cigarettes but do not currently smoke were defined as former smokers, and the remaining individuals were categorized as now smokers. Alcohol intake over the past 12 months was divided into never, mild, and heavy drinking based on the number of drinking occasions in the past year. Hypertension was assessed using systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, as well as patients who were on antihypertensive medication during the survey period. DM was evaluated based on a physician's diagnosis of DM, HbA1c ≥ 6.5%, fasting blood glucose ≥ 7.0 mmol/L, random blood glucose ≥ 11.1 mmol/L, 2-hour oral glucose tolerance test blood glucose ≥ 11.1 mmol/L, or those currently undergoing treatment with diabetes medication and insulin.

### Statistical analysis

In our study, continuous variables are expressed as mean ± standard error, and categorical variables are presented as frequencies and percentages. Weighted two-tailed t-tests were used for continuous variables, and weighted chi-square tests were applied to categorical variables.

We used multivariate logistic regression models to assess the relationship between CDAI and the risk of RA when CDAI was used as a continuous variable and as a categorical variable grouped by quartiles. Three models were constructed with varying degrees of adjustment. Model I was unadjusted, Model II was adjusted for age, sex, and race, and Model III was further adjusted for PIR, education level, marriage, BMI, smoking, drinking, DM, and hypertension, which are potential confounding factors. Restricted cubic spline (RCS) analysis was employed to explore the nonlinear relationship between CDAI and the risk of RA when CDAI was used as a continuous variable. Subgroup analysis and interaction tests were conducted to evaluate the association between CDAI and RA risk among populations with different characteristics when CDAI was used as a continuous variable. In sensitivity analyses, patients with DM were excluded to assess the robustness of the association between CDAI and RA risk when CDAI was used as a continuous variable and as a categorical variable grouped by quartiles.

All analyses were performed using R software (version 4.3.1), and two-tailed *P*-values less than 0.05 were considered statistically significant. The study results were weighted according to the NHANES survey design to represent the total U.S. population.

## Results

### Participant baseline characteristics by CDAI quartiles

A total of 11,266 participants from the NHANES database were included in our study, grouped according to quartiles of CDAI (Q1<-2.195, -2.195 ≤ Q2<-0.263, -0.263 ≤ Q3 < 2.171, and Q4 ≥ 2.171) (Table 1). Sex, race, PIR, marriage, education level, smoking, drinking, and RA prevalence were significantly different across CDAI groups. In particular, within the Q4 population, there were higher proportions of males, non-Hispanic whites, higher PIR, married or living with partner, individuals with higher levels of education, never smokers, and light drinkers. In addition, the prevalence of RA decreased significantly with increasing CDAI quartiles from 9.64% in Q1 to 5.58% in Q4 ($P < 0.001$).

In addition, this study further explored the status of RA (Table 2). Compared to the non-RA population, RA patients were older, had a higher proportion of females, a higher proportion of non-Hispanic blacks, were more divorced, widowed, or separated, had a higher BMI, and had higher rates of DM and hypertension. Conversely, RA patients had a lower PIR, a lower proportion with higher education, and lower CDAI values.

### Associations between CDAI levels and risks of RA

In this study, we used multivariate logistic regression modeling to investigate the relationship between CDAI and RA (Table 3). When CDAI was considered as a continuous variable, in Model I (uncorrected), the odds ratio (OR) and 95% confidence interval (CI) of CDAI to RA was 0.94 (95% CI: 0.91–0.97).

In Model II (corrected for age, sex, and race), the OR of CDAI with RA increased slightly to 0.95 (95% CI: 0.92–0.98), which remained statistically significant ($P < 0.001$). Model III further corrected for PIR, education level, marriage, BMI, smoking, drinking, DM, and hypertension, at which point the OR of CDAI with RA was 0.96 (95% CI: 0.94–0.99)。.

In addition, when CDAI was grouped according to quartiles and considered as a categorical variable, the odds of RA was reduced by 27%, 15%, and 33% in Q2, Q3, and Q4, respectively, compared with the lowest quartile (Q1, the reference group) (*P* values of 0.013, 0.200, and 0.002, respectively). The trend test showed that the risk of RA was significantly reduced with increasing quartiles of CDAI (P for trend < 0.05).

### Dose-response relationship

In addition, When CDAI was considered as a continuous variable, our study explored the nonlinear association between CDAI and RA by RCS analysis (Fig. 2). The results showed that the association between CDAI and the risk of RA was linear rather than nonlinear (P non-linear > 0.05).

### Subgroup analysis

Finally, subgroup analyses revealed the association between CDAI and RA risk among different subgroups

**Table 1** Weighted baseline characteristics of our participants grouped by CDAI quartiles

| | Total (*n* = 11266) | CDAI quartiles | | | | *P* |
|---|---|---|---|---|---|---|
| | | Q1 (*n* = 2818) | Q2 (*n* = 2816) | Q3 (*n* = 2817) | Q4 (*n* = 2815) | |
| Age, years | 44.13(0.21) | 43.67(0.39) | 44.67(0.31) | 44.29(0.42) | 43.86(0.37) | 0.181 |
| Sex, *n* (%) | | | | | | < 0.001 |
| female | 5823(49.39) | 1605(55.90) | 1420(49.02) | 1403(47.27) | 1395(46.26) | |
| male | 5443(50.61) | 1213(44.10) | 1396(50.98) | 1414(52.73) | 1420(53.74) | |
| Race, *n* (%) | | | | | | < 0.001 |
| Mexican American | 2210(10.91) | 484(9.71) | 564(10.83) | 571(10.75) | 591(12.18) | |
| Non-Hispanic Black | 3063(14.42) | 924(18.82) | 762(14.26) | 656(11.97) | 721(13.20) | |
| Non-Hispanic White | 4377(64.48) | 1011(60.80) | 1117(65.56) | 1177(67.68) | 1072(63.44) | |
| Other Hispanic | 982(5.78) | 246(6.27) | 236(5.23) | 245(5.23) | 255(6.43) | |
| Other race | 634(4.42) | 153(4.40) | 137(4.12) | 168(4.37) | 176(4.75) | |
| PIR | 2.97(0.03) | 2.66(0.06) | 2.90(0.05) | 3.09(0.05) | 3.19(0.04) | < 0.001 |
| Marriage, *n* (%) | | | | | | < 0.001 |
| widowed/divorced/separated | 2217(16.55) | 610(18.26) | 564(17.22) | 544(17.48) | 499(13.50) | |
| married/living with partner | 6863(65.04) | 1576(60.73) | 1707(64.50) | 1762(65.10) | 1818(69.22) | |
| never married | 2186(18.41) | 632(21.02) | 545(18.28) | 511(17.42) | 498(17.27) | |
| Education level, *n* (%) | | | | | | < 0.001 |
| below high school | 1021(4.47) | 309(5.49) | 264(4.51) | 240(4.19) | 208(3.85) | |
| high school | 4272(35.64) | 1226(43.41) | 1109(37.48) | 971(31.43) | 966(31.42) | |
| above high school | 5973(59.89) | 1283(51.10) | 1443(58.01) | 1606(64.38) | 1641(64.74) | |
| BMI, kg/m$^2$ | 35.72(0.07) | 35.74(0.16) | 35.59(0.15) | 35.60(0.14) | 35.95(0.14) | 0.271 |
| Smoking, *n* (%) | | | | | | < 0.001 |
| never | 6496(56.77) | 1534(50.97) | 1599(56.16) | 1658(59.18) | 1705(59.95) | |
| former | 2616(24.42) | 587(21.82) | 698(24.74) | 651(23.87) | 680(26.92) | |
| now | 2154(18.81) | 697(27.22) | 519(19.10) | 508(16.96) | 430(13.13) | |
| Drinking, *n* (%) | | | | | | < 0.001 |
| no | 3224(24.75) | 927(28.73) | 814(24.86) | 754(22.71) | 729(23.26) | |
| mild | 5443(51.11) | 1251(44.82) | 1395(52.68) | 1403(53.02) | 1394(53.19) | |
| heavy | 2599(24.13) | 640(26.45) | 607(22.45) | 660(24.27) | 692(23.55) | |
| DM, *n* (%) | | | | | | 0.550 |
| no | 8710(81.60) | 2154(81.36) | 2139(80.55) | 2191(82.03) | 2226(82.36) | |
| yes | 2556(18.40) | 664(18.64) | 677(19.45) | 626(17.97) | 589(17.64) | |
| Hypertension, *n* (%) | | | | | | 0.131 |
| no | 6087(57.66) | 1458(56.27) | 1514(58.56) | 1577(59.45) | 1538(56.22) | |
| yes | 5179(42.34) | 1360(43.73) | 1302(41.44) | 1240(40.55) | 1277(43.78) | |
| RA, *n* (%) | | | | | | < 0.001 |
| no | 10,202(92.82) | 2491(90.36) | 2559(93.19) | 2562(92.98) | 2590(94.42) | |
| yes | 1064(7.18) | 327(9.64) | 257(6.81) | 255(7.02) | 225(5.58) | |

CDAI, composite dietary antioxidant index; PIR, poverty income ratio; BMI, body mass index; DM, diabetes mellitus; RA, rheumatoid arthritis. CDAI quartiles: Q1<-2.195, -2.195 ≤ Q2 <-0.263, -0.263 ≤ Q3 < 2.171, and Q4 ≥ 2.171. All continuous variables are expressed as mean (SD) and categorical variables are expressed as *n* (%)

by forest plot analysis (Fig. 3). The association between CDAI and the risk of RA development remained negative in populations with different characteristics when CDAI was considered as a continuous variable. For example, in people under 50 years of age, each 1-unit increase in CDAI was associated with a 7% reduction in the odds of RA (OR: 0.93, 95% CI: 0.88–0.98). In addition, the odds of RA was reduced by 8% for each unit increase in CDAI in those who smoked (OR: 0.92, 95% CI: 0.86–0.97), and by 5% for each unit increase in CDAI in those who had never smoked (OR: 0.95, 95% CI: 0.92–0.99), whereas the association between CDAI and RA was not statistically significant in those who had quit smoking. The interaction test showed that the association between CDAI and RA in different states of smoking was statistically different (P interaction < 0.05), suggesting that CDAI is more protective against RA in smokers and never smokers.

### Sensitivity analysis

The negative association of the CDAI with the risk of RA remained significant in sensitivity analyses that excluded patients with DM (Table 4). When CDAI was considered

**Table 2** Weighted characteristics of RA status

| | Total (*n* = 11266) | non-RA (*n* = 10202) | RA (*n* = 1064) | *P* |
|---|---|---|---|---|
| Age, years | 44.13(0.21) | 43.26(0.22) | 55.30(0.46) | < 0.001 |
| Sex, *n* (%) | | | | < 0.001 |
| female | 5823(49.39) | 5168(48.59) | 655(59.75) | |
| male | 5443(50.61) | 5034(51.41) | 409(40.25) | |
| Race, *n* (%) | | | | < 0.001 |
| Mexican American | 2210(10.91) | 2054(11.17) | 156(7.49) | |
| Non-Hispanic Black | 3063(14.42) | 2694(13.99) | 369(19.91) | |
| Non-Hispanic White | 4377(64.48) | 3963(64.50) | 414(64.19) | |
| Other Hispanic | 982(5.78) | 902(5.90) | 80(4.22) | |
| Other race | 634(4.42) | 589(4.43) | 45(4.19) | |
| PIR | 2.97(0.03) | 3.00(0.03) | 2.52(0.06) | < 0.001 |
| Marriage, *n* (%) | | | | < 0.001 |
| widowed/divorced/separated | 2217(16.55) | 1830(15.48) | 387(30.30) | |
| married/living with partner | 6863(65.04) | 6302(65.37) | 561(60.84) | |
| never married | 2186(18.41) | 2070(19.15) | 116(8.86) | |
| Education level, *n* (%) | | | | < 0.001 |
| below high school | 1021(4.47) | 879(4.24) | 142(7.48) | |
| high school | 4272(35.64) | 3835(35.33) | 437(39.64) | |
| above high school | 5973(59.89) | 5488(60.43) | 485(52.89) | |
| BMI, kg/m$^2$ | 35.72(0.07) | 35.64(0.07) | 36.75(0.30) | < 0.001 |
| CDAI | 0.48(0.05) | 0.53(0.05) | -0.17(0.14) | < 0.001 |
| Smoking, *n* (%) | | | | < 0.001 |
| never | 2616(24.42) | 2254(23.62) | 362(34.80) | |
| former | 6496(56.77) | 6009(57.77) | 487(43.94) | |
| now | 2154(18.81) | 1939(18.62) | 215(21.26) | |
| Drinking, *n* (%) | | | | < 0.001 |
| no | 3224(24.75) | 2801(23.87) | 423(36.15) | |
| mild | 5443(51.11) | 4982(51.45) | 461(46.77) | |
| heavy | 2599(24.13) | 2419(24.68) | 180(17.08) | |
| DM, *n* (%) | | | | < 0.001 |
| no | 8710(81.60) | 8052(82.66) | 658(67.86) | |
| yes | 2556(18.40) | 2150(17.34) | 406(32.14) | |
| Hypertension, *n* (%) | | | | < 0.001 |
| no | 6087(57.66) | 5776(59.57) | 311(32.99) | |
| yes | 5179(42.34) | 4426(40.43) | 753(67.01) | |

CDAI, composite dietary antioxidant index; PIR, poverty income ratio; BMI, body mass index; DM, diabetes mellitus; RA, rheumatoid arthritis. All continuous variables are expressed as mean (SD) and categorical variables are expressed as *n* (%)

as a continuous variable, the OR for RA were shown to be 0.94 ($P$=0.001), 0.95 ($P$=0.006), and 0.96 ($P$=0.019) with increasing CDAI in model III. And when the CDAI was grouped according to quartiles and considered as a categorical variable, the OR (95% CI) was 0.64 (0.48–0.86), 0.59 (0.44–0.80), and 0.56 (0.42–0.75) for Q2, Q3, and Q4, respectively, compared with Q1(the reference group), all showing a significant reduction in RA risk. The trend test confirmed the significance of RA risk reduction with increasing CDAI ($p$<0.001).

## Discussion

This study explored the association between CDAI and RA within an obese population. By analyzing data from the NHANES database, we found that the OR for RA significantly decreased with increasing CDAI. This inverse relationship remained robust after adjusting for potential confounding factors such as age, sex, race, PIR, education level, marriage, BMI, smoking, drinking, DM, and hypertension. Specifically, participants in CDAI Q4 had a 33% lower odds of developing RA compared to the Q1 population. Sensitivity analyses, excluding patients with DM, further confirmed the robustness of the negative association between CDAI and RA.

Obesity is a known risk factor for RA. Studies by Bing et al., drawing from two large prospective cohorts involving over 200,000 women, found that the risk of RA increased by 27% in overweight or obese women, with this risk being related to the duration and age of obesity [6]. Additionally, Sang et al. recently corroborated the association between BMI and RA risk using Mendelian randomization methods [20]. Obesity may lead to a state of chronic low-grade inflammation, increasing circulating inflammatory cytokines such as IL-6 receptor inhibitor (IL-6) and tumor necrosis factor-α (TNF-α), which play a pivotal role in the pathogenesis of RA [21–23]. Kazuhiro et al. reported an increase in osteoclast bone absorption induced by TNF and IL-6, with the number positively correlating with the total score of the modified Sharp score for RA [24]. Another study by Kim showed that both TNF inhibitors and IL-6 inhibitors have good

**Table 3** Multivariate logistic regression analysis between CDAI and RA

| | Model I | | Model II | | Model III | |
|---|---|---|---|---|---|---|
| | OR (95%CI) | P | OR (95%CI) | *P* | OR (95%CI) | *P* |
| CDAI | 0.94(0.91,0.97) | < 0.0001 | 0.95(0.92,0.98) | < 0.001 | 0.96(0.94,0.99) | 0.010 |
| CDAI quartiles | | | | | | |
| Q1 | ref | | ref | | ref | |
| Q2 | 0.68(0.54,0.86) | 0.001 | 0.68(0.53,0.87) | 0.002 | 0.73(0.57,0.94) | 0.013 |
| Q3 | 0.71(0.56,0.89) | 0.004 | 0.74(0.57,0.94) | 0.015 | 0.85(0.66,1.09) | 0.200 |
| Q4 | 0.55(0.43,0.70) | < 0.0001 | 0.60(0.47,0.77) | < 0.001 | 0.67(0.53,0.86) | 0.002 |
| P for trend | | < 0.0001 | | < 0.001 | | 0.008 |

Model I: no adjusted. Model II: adjusted for age, sex, and race. Model III: adjusted for age, sex, race, PIR, education, marriage, BMI, smoking, drinking, DM, and hypertension. CDAI: continuous variable, CDAI quartiles: categorical variable

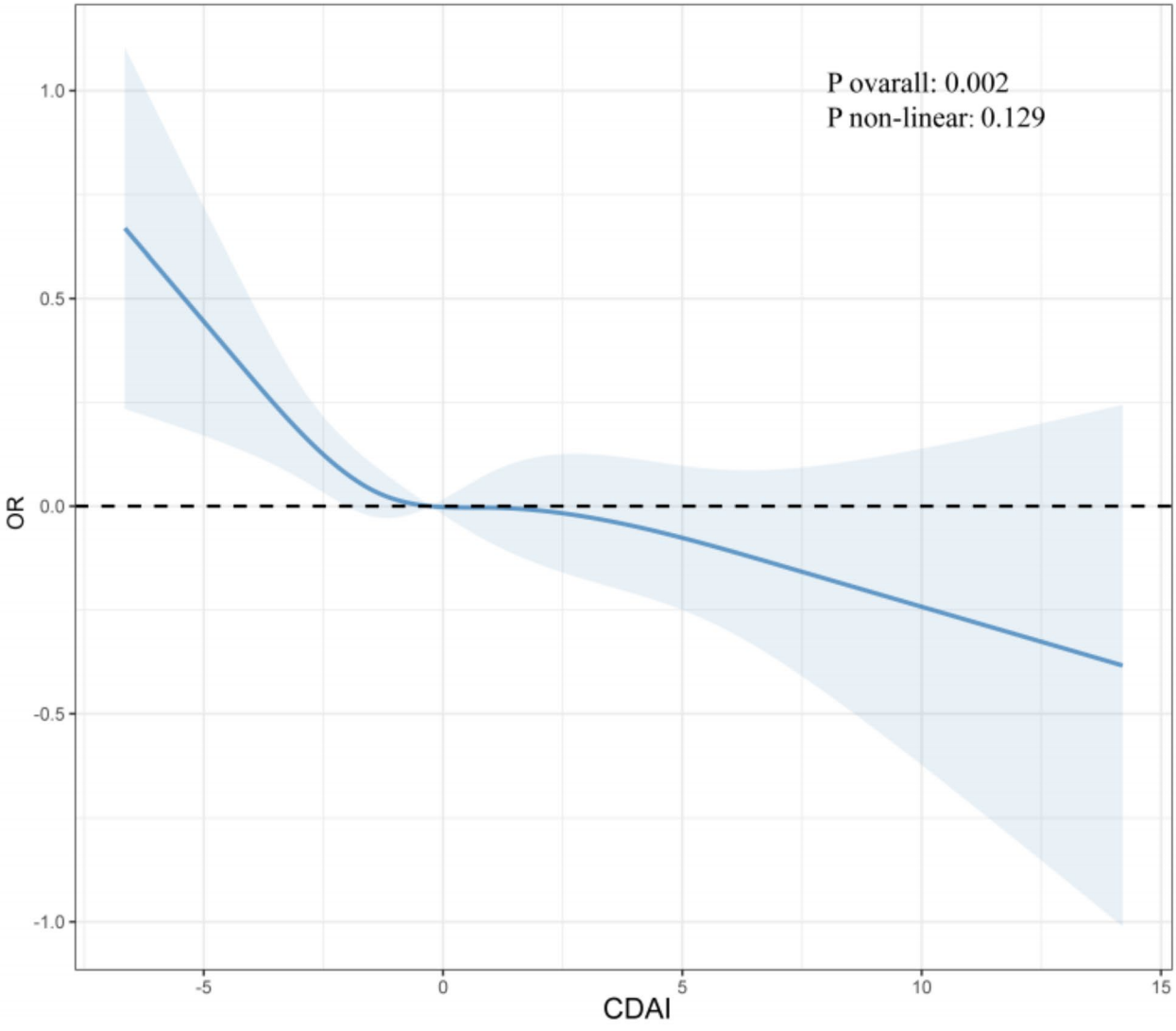


**Fig. 2** Dose-response relationship between CDAI and RA

1-year response rates in RA [23]. Furthermore, obesity may increase the risk of RA by affecting lipid metabolism and hormonal balance [25].

Oxidative stress plays a significant role in the pathogenesis of RA, promoting inflammatory responses and participating in the destruction of articular cartilage [26, 27]. Dietary antioxidants contribute to reducing oxidative stress by neutralizing free radicals, inhibiting the production of inflammatory mediators, and decreasing oxidative damage [28, 29]. A cross-sectional study by Xiao et al. among RA patients in the United States found that higher dietary selenium intake was associated with a decreased risk of RA, with the highest quartile of dietary selenium intake reducing the risk of RA by 53% [30]. Additionally, a review by Hai et al., which included nine studies with 39,845 participants, found that vitamin E supplements could help alleviate joint discomfort, swelling, and stiffness in RA patients, potentially by restoring intestinal barrier function and improving gastrointestinal capacity [31]. However, findings on the relationship between dietary antioxidants and RA have been inconsistent. Xun et al. evaluated the association between blood antioxidant levels from dietary sources, including vitamin E, β-carotene, lycopene, vitamin C, and retinol, with RA and found that circulating metabolites of retinol, rather than other antioxidants, were protective against RA and seropositive RA [13]. Our study, by considering the overall antioxidant effect of the diet, supports the hypothesis that dietary antioxidants may reduce the risk of RA, especially in obese populations.

Dietary antioxidants may reduce the risk of RA through several mechanisms. First, antioxidants can neutralize ROS, reduce oxidative stress, and thus decrease the inflammatory response. Second, antioxidants may

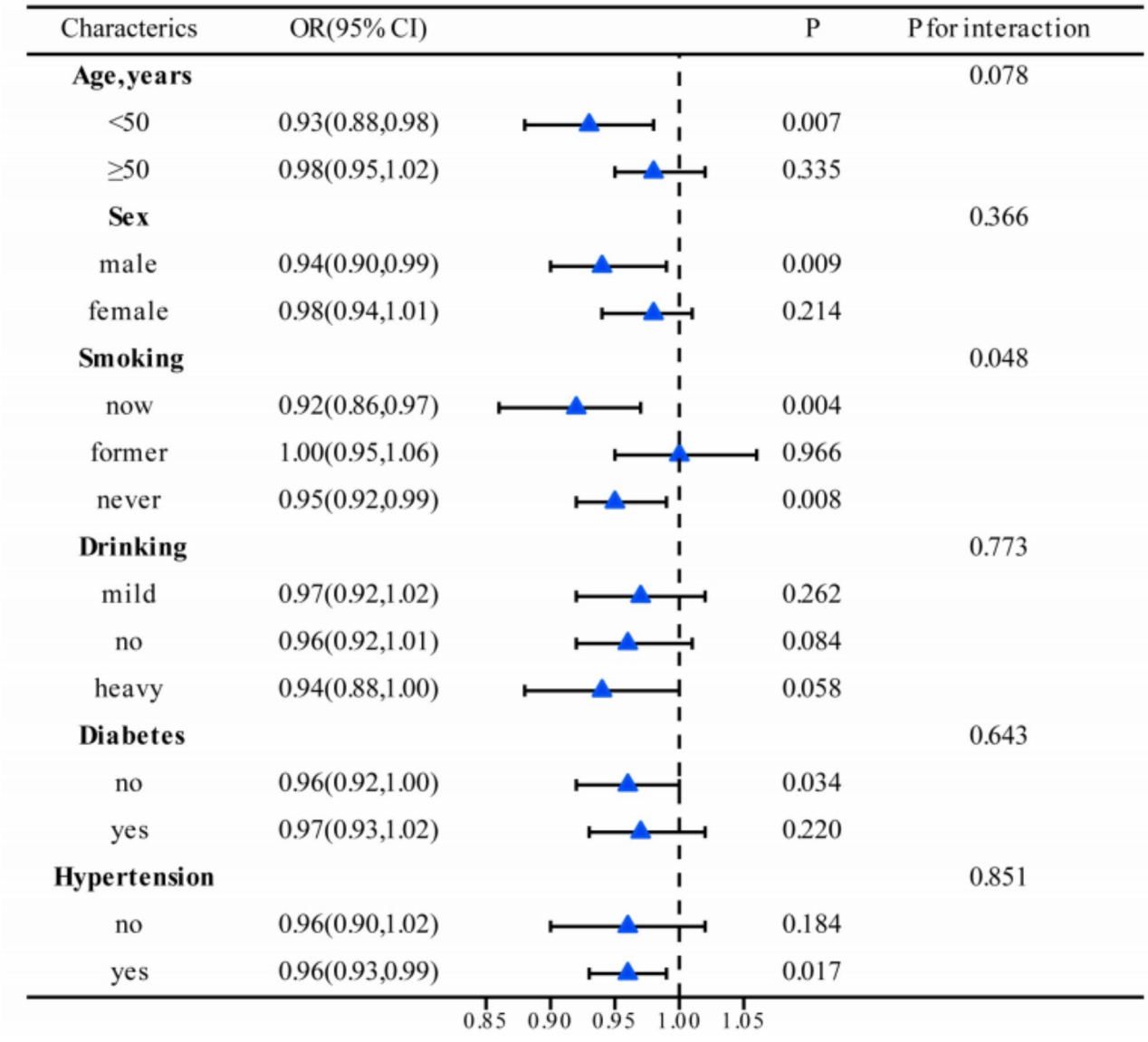


**Fig. 3** Subgroup analysis for the association between CDAI and RA

**Table 4** Sensitivity analysis after exclusion of DM patients

| | Model I | | Model II | | Model III | |
|---|---|---|---|---|---|---|
| | OR (95%CI) | P | OR (95%CI) | P | OR (95%CI) | P |
| CDAI | 0.94(0.91,0.98) | 0.001 | 0.95(0.91,0.98) | 0.006 | 0.96(0.92,0.99) | 0.019 |
| CDAI quartiles | | | | | | |
| Q1 | ref | | ref | | ref | |
| Q2 | 0.64(0.48,0.86) | 0.003 | 0.62(0.45,0.84) | 0.002 | 0.67(0.49,0.92) | 0.013 |
| Q3 | 0.59(0.44,0.80) | < 0.001 | 0.59(0.43,0.81) | 0.001 | 0.65(0.47,0.91) | 0.011 |
| Q4 | 0.56(0.42,0.75) | < 0.001 | 0.58(0.43,0.78) | < 0.001 | 0.63(0.47,0.86) | 0.004 |
| P for trend | | < 0.001 | | < 0.001 | | 0.004 |

Model I: no adjusted. Model II: adjusted for age, sex, and race. Model III: adjusted for age, sex, race, PIR, education, marriage, BMI, smoking, drinking, and hypertension. CDAI: continuous variable, CDAI quartiles: categorical variable

modulate cellular signaling pathways, such as inhibiting the activation of nuclear factor kappa-B (NF-KB), reducing the production of inflammatory cytokines, and thereby affecting the pathogenesis of RA. Additionally, some antioxidants, like vitamin E, may reduce the risk of RA by enhancing gastrointestinal capacity.

Our findings suggest that a higher CDAI is associated with a lower risk of RA. This suggests that increased intake of antioxidant-rich foods may help reduce the risk of developing RA in individuals at risk for RA. Specifically, encouraging the intake of foods rich in vitamins A, C, E, manganese, selenium, and zinc may have a positive effect on RA prevention. In addition, for patients already diagnosed with RA, our findings suggest that increasing antioxidant intake through diet or supplements may help improve their symptoms and quality of life. However, the use of supplements should be guided by a healthcare professional to ensure safety and appropriateness.

While our study found a negative association between CDAI and RA using data representative of the entire U.S. population and adjusting for potential confounding factors, there are still some limitations to the research. First, the cross-sectional design of the study does not allow for the determination of causality or the temporal sequence. Secondly, the assessment of dietary intake relies on self-reported data from participants, which may be subject to reporting bias. The diagnosis of RA depends on self-reported information, which may lead to misdiagnosis. Third, although the six classes of antioxidants included in the CDAI are the most common in the diet, it is true that some other antioxidants may be overlooked due to the diversity of dietary habits. It may not fully capture all individual dietary variations. Fourth, although we adjusted for multiple potential confounding factors, there may still be unmeasured confounding factors such as genetic factors and environmental exposure. Finally, due to database limitations, race and ethnicity were combined into a single "race" category, and we suggest that in future studies, consideration should be given to treating race and ethnicity as separate variables in order to more accurately analyse and interpret the results of the study.

## Conclusion

In summary, this study provides evidence that a higher intake of dietary antioxidants, as indicated by CDAI, is associated with a reduced risk of RA in obese individuals. This finding supports the possibility of dietary intervention to prevent RA and suggests the potential role of dietary antioxidants in the management of RA.

### Abbreviations

| | |
|---|---|
| CDAI | Composite dietary antioxidant index |
| RA | Rheumatoid arthritis |
| DM | Diabetes mellitus |
| ROS | Reactive oxygen specie |
| CDC | Centers for Disease Control and Prevention |
| NHANES | National Health and Nutrition Examination Survey |
| BMI | Body mass index |
| PIR | Poverty income ratio |
| SBP | Systolic blood pressure |
| DBP | Diastolic blood pressure |
| RCS | Restricted cubic spline |
| OR | Odd ratio |
| CI | Confidence interval |
| IL-6 | Interleukin-6 |
| TNF | Tumor necrosis factor |
| NF-KB | Nuclear factor kappa-B |

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### Author contributions

G.B. M. and S.L. Z. performed the data analysis and wrote the manuscript. Y.Y. L, C.C. Z and W.N. X contributed to data collection and the literature search.Y.L. W oversighted and managed responsibility for the research activity. All authors contributed to the design of the study protocol and reviewed the manuscript. The author(s) read and approved the final manuscript.

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### Data availability

Full study data are readily available upon email request.Publicly available datasets were analyzed in this study. This data can be found here: The NHANES dataset at https://www.cdc.gov/nchs/nhanes/index.htm.

## Declarations

### Ethics approval and consent to participate

The NCHS Ethics Review Board (ERB) approval waived the requirement for informed consent from all patients.

### Competing interests

The authors declare no competing interests.

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