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Association between composite dietary antioxidant index and cataract in American adults aged ≥50 years

A cross-sectional study from NHANES 2003–2008

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Abstract

Oxidative stress is one of the crucial pathogeneses of cataract. The composite dietary antioxidant index (CDAI) represents the antioxidant capacity of one's diet. The aim of this study was to explore the association between the CDAI and cataract. The data were obtained from the National Health and Nutrition Examination Survey 2003 to 2008. A weighted multiple logistic regression, generalized weighted models, and smoothed fitted curves were performed to investigate the association between the CDAI and cataract. A total of 5814 participants aged ≥50 years with complete data were included in the study. According to the fully adjusted model, the odds ratio (95% confidence interval) for the association between the CDAI and cataract was 0.95 (0.93, 0.98). After dividing continuous CDAI into tertiles, consistent negative associations between CDAI and cataract were observed in the highest tertile compared to the lowest tertile (odds ratio = 0.77; 95% confidence interval, 0.62–0.95). The CDAI components (zinc, magnesium, vitamin A, and vitamin E) were also negatively associated with cataract odds in the fully adjusted model. Subgroup analysis showed inconsistent associations among subgroups, but no statistically significant interaction effects were found. This cross-sectional study revealed that a higher CDAI was associated with lower odds of cataract. These findings may contribute to cataract prevention through antioxidant dietary patterns.

Abbreviations: AUC = area under the curve, CDAI = composite dietary antioxidant index, CI = confidence interval, CRP = C-reactive protein, DII = dietary inflammatory index, NHANES = National Health and Nutrition Examination Survey, OR = odds ratio.

Keywords: cataract, composite dietary antioxidant index, cross-sectional study, NHANES

1. Introduction

Cataract refers to the opacification of the lens. It is the priority reason for blindness and the main cause of vision impairment globally.[1] Cataract can be classified into age-related cataract, childhood cataract, secondary cataract and other types.[2] Despite technological and surgical advances, the financial burden of cataract surgery is the main challenge in developing countries. Hence, cataract prevention is highly important for alleviating the burden of cataract.

Excessive reactive oxygen species are the main cause of acquired cataract. Consequently, the antioxidants intake from the diet is a promising strategy for neutralizing reactive oxygen species and preventing or slowing cataract progression. Natural antioxidant therapy for cataract has been widely reported, including vitamin C, vitamin E, beta-carotene, and lutein.[3,4]

The composite dietary antioxidant index (CDAI) is a dietary index used to assess the antioxidant capacity of dietary components proposed by Wright et al, utilizing the score of zinc, magnesium, selenium, and vitamins A, C, and E.[5] The CDAI has been proven to be associated with aging, depression, coronary heart disease, and other diseases.[6–8] However, the association between the CDAI and cataract remains unclear.

In this article, we used the National Health and Nutrition Examination Survey (NHANES) database to reveal the relationship between the CDAI and cataract, to provide dietary guidance

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The datasets generated during and/or analyzed during the current study are publicly available.

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for reducing the incidence of cataract. We hypothesized that a higher CDAI is associated with lower cataract odds.

2. Materials and methods

2.1. Study population

The NHANES database uses a complex, stratified, multistage probability sampling design to represent the target population. Ethical approval was obtained through the Research Ethics Review Board of the National Center for Health Statistics (Protocol #98-12 and Protocol #2005-06). Written informed consent was obtained from the participants, and the dataset used in the analysis was fully deidentified. The 2003 to 2004, 2005 to 2006, and 2007 to 2008 NHANES cycles were utilized. Subjects without cataract data (n = 17,205) or dietary data (n = 2622) or with daily energy >5000 kcal (n = 185) or <500 kcal (n = 263) were then excluded. Additionally, subjects under 50 years old (n = 4167) and without complete information on other covariates were also excluded (n = 363). Ultimately, 5814 participants were analyzed in the investigation (Fig. 1).

2.2. Cataract assessment

In reference to other epidemiological research, self-reported cataract surgery is considered a clinically meaningful cataract.[9,10] Participants aged 20 years and older were asked if they had undergone ophthalmic surgery for cataracts, with answers of "yes" or "no." If the answer was "yes," they were diagnosed with a cataract.

2.3. Dietary assessment

The dietary information was collected through 2 separate 24-hour dietary recall interviews. The first interview was completed in person at a mobile examination center, while the second interview was completed via telephone after 3 to 10 days. Participants were asked about the details of dietary intake in the 24 hours, and the amount of various nutrients ingested was calculated by the NHANES staff. The average daily intake was calculated from 2 days of dietary recall information. Six dietary antioxidant elements, including zinc, magnesium, selenium, and vitamins A, C, and E, were included in our study to calculate the CDAI using the approach developed by Wright et al.[5] Standardized dietary antioxidant intake was calculated by subtracting the mean level of the intake and dividing by the standard deviation. Then, the CDAI was calculated by adding the individual standardized intake. The dietary inflammatory index (DII) was calculated by the R package "dietaryindexNDP."[11,12]

2.4. Covariates

Covariates included age, gender, race, education level, marital status, body mass index, poverty–income ratio, smoking status,

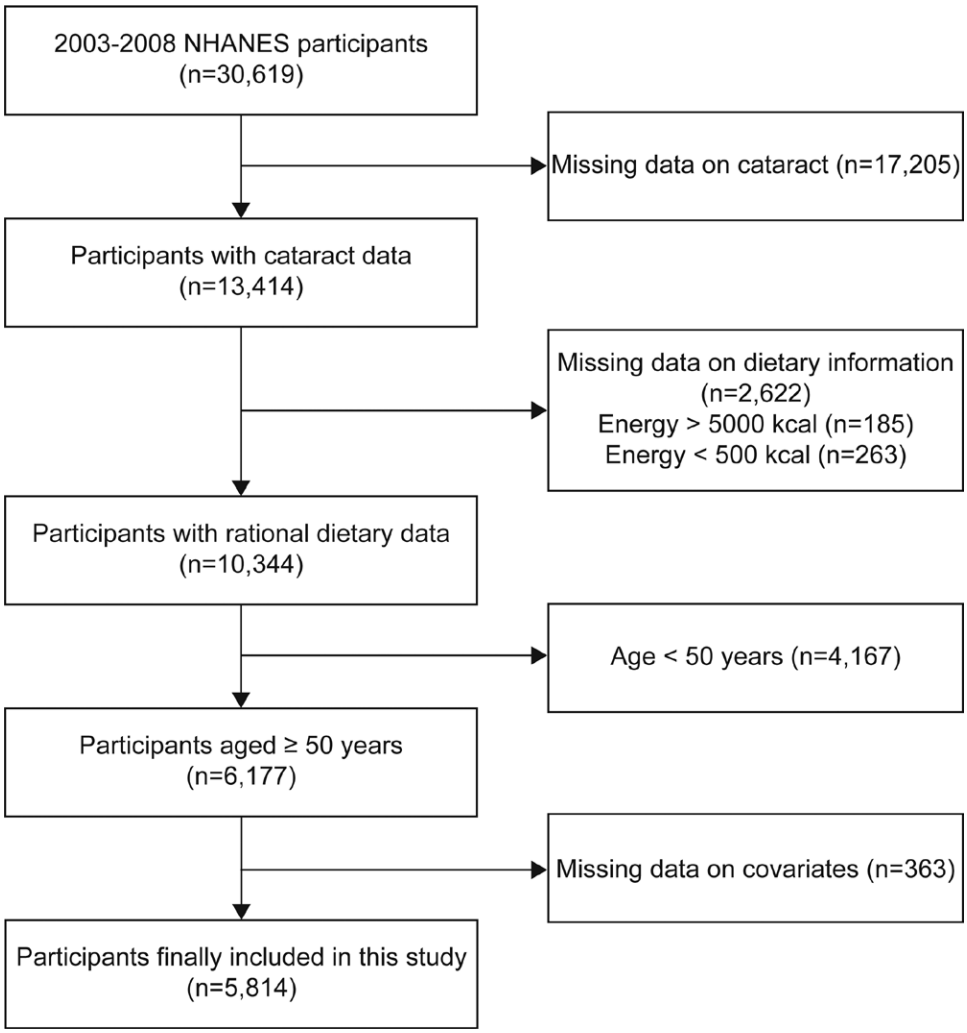

Figure 1. Flowchart of participant selection.

Table 1

Characteristics of the study population stratified by tertiles of the CDAI (n = 5814).

	CDAI tertiles			
	T1 n = 1938	T2 n = 1938	T3 n = 1938	*P* value
Age, yr	64.66 ± 10.22	63.86 ± 10.05	62.09 ± 9.60	<.0001
Poverty income ratio	2.75 ± 1.52	3.18 ± 1.51	3.57 ± 1.48	<.0001
BMI, kg/m^2	29.10 ± 6.37	28.94 ± 5.96	28.68 ± 6.18	.1006
CRP, mg/dL	0.53 ± 0.88	0.46 ± 0.78	0.37 ± 0.78	<.0001
Gender, %				<.0001
Male	29.83	44.23	59.54	
Female	70.17	55.77	40.46	
Race, %				<.0001
Non-Hispanic White	75.21	81.41	85.40	
Non-Hispanic Black	12.97	7.80	5.63	
Mexican American	4.88	4.19	2.76	
Other races	6.95	6.60	6.21	
Education level, %				<.0001
Less than high school	29.80	17.48	12.67	
High school	31.71	28.67	24.10	
More than high school	38.48	53.82	63.19	
Marital status, %				<.0001
Married/living with partner	60.03	67.37	72.23	
Widowed/divorced/ separated	35.03	28.95	23.51	
Never married	4.88	3.68	4.15	
Smoking status, %				.9123
No	45.82	46.44	46.44	
Yes	54.18	53.56	53.56	
Alcohol use, %				<.0001
No	41.89	33.71	24.93	
Yes	58.11	66.29	75.07	
Diabetes mellitus, %				<.0001
No	78.88	78.62	84.14	
Yes	21.12	21.38	15.86	
Hypertension, %				<.0001
No	40.49	43.80	47.87	
Yes	59.51	56.20	52.13	
Cardiovascular disease, %				.0017
No	85.21	85.49	88.63	
Yes	14.79	14.51	11.37	
Hyperlipidemia, %				.3766
No	23.62	24.81	25.57	
Yes	76.38	75.19	74.43	
Cataract, %				<.0001
No	80.78	82.73	88.64	
Yes	19.22	17.27	11.36	
CDAI	-3.05 ± 0.99	-0.47 ± 0.72	3.74 ± 2.85	<.0001

Mean ± standard deviation for continuous variables: *P* values were calculated by weighted logistic regression.

% for categorical variables: *P* values were calculated by the weighted chi-square test.

BMI = body mass index, CDAI = composite dietary antioxidant index, CRP = C-reactive protein.

alcohol use, diabetes mellitus, hypertension, cardiovascular disease, and hyperlipidemia. According to participants' responses to the question, "Have you smoked at least 100 cigarettes in your entire life?" We classified smoking status as "yes" or "no." According to the participants' responses to the question, " Had at least 12 alcohol drinks/1 year?" We classified alcohol use as "yes" or "no." Individuals who had glycohemoglobin ≥6.5% or who answered "Doctor told you have diabetes" positively were identified as having diabetes.[13] Individuals who had a systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or who answered "Told had high blood pressure—2+ times" were identified as having hypertension.[14]

Table 2

Association between the CDAI and cataract.

	Crude	Model 1	Model 2
CDAI	0.93 (0.91, 0.95) <.0001	0.95 (0.93, 0.98) .0004	0.96 (0.93, 0.98) .0021
CDAI tertiles			
T1	Ref	Ref	Ref
T2	0.98 (0.84, 1.14), .8147	1.06 (0.89, 1.27), .5288	1.12 (0.92, 1.36), .2638
T3	0.64 (0.54, 0.75), <.0001	0.75 (0.62, 0.92), .0045	0.78 (0.63, 0.96), .0209

Model 1: Adjusted for age, gender, and race. Model 2: Adjusted for age, gender, race, education level, marital status, poverty–income ratio, BMI, CRP, smoking status, alcohol use, diabetes mellitus, hypertension, cardiovascular disease, and hyperlipidemia.

BMI = body mass index, CDAI = composite dietary antioxidant index, CRP = C-reactive protein.

Individuals who had a positive answer to "Ever told you had coronary heart disease," "Ever told you had congestive heart failure," or "Ever told you had a heart attack" were identified as having cardiovascular diseases.[15] Individuals who had total cholesterol ≥200 mg/dL or had a positive answer to "Doctor told you—high cholesterol level" were identified as having hyperlipidemia.

2.5. Statistical analysis

All statistical analyses were conducted using R (https://www.r-project.org) and EmpowerStats (https://www.empowerstats.com), with the level of statistical significance set at $P < .05$. Categorical variables were described as proportions, whereas continuous variables were described as the means with standard deviations. Participants were divided into tertiles according to the CDAI. The association between the CDAI and the components, and cataract was examined using multiple logistic regression analyses. A weighted generalized additive model and smooth curve fitting were applied to investigate nonlinearity. In subgroups stratified by gender (men/women), age (≤60/>60, ≤70/>70 years), race (non-Hispanic White/non-Hispanic Black/Mexican American/other races), smoking status (no/yes), alcohol use (no/yes), diabetes mellitus status (no/yes), hypertension status (no/yes), cardiovascular disease status (no/yes), and hyperlipidemia status (no/yes), the relationships between the CDAI and cataract were examined. Model 1 was adjusted for demographic data (gender, age, and race), and model 2 was fully adjusted for age, gender, race, education level, marital status, poverty income ratio, body mass index, C-reactive protein (CRP), smoking status, alcohol use, diabetes mellitus, hypertension, cardiovascular disease, and hyperlipidemia. Additionally, the area under the receiver operating characteristic curve (AUC) was evaluated to compare the discriminatory power of CDAI, DII, and CRP for cataract.

3. Results

3.1. Characteristics of the study population

Table 1 demonstrates the participant characteristics according to CDAI tertiles (tertile 1: –3.05 ± 0.99; tertile 2: –0.47 ± 0.72; tertile 3: 3.74 ± 2.85). The mean (standard deviation) age of the 5814 adults was 66.28 (10.08) years, and 50.29% were females. The prevalence of cataract in this study population was 19.5%, which was observed to decrease with increasing CDAI tertiles (tertile 1: 19.22%; tertile 2: 17.27%; tertile 3: 11.36%; $P < .0001$). Initial evaluations revealed that compared to those in the reference group (T1), participants in the top CDAI group (T3) were more likely to be younger, male,

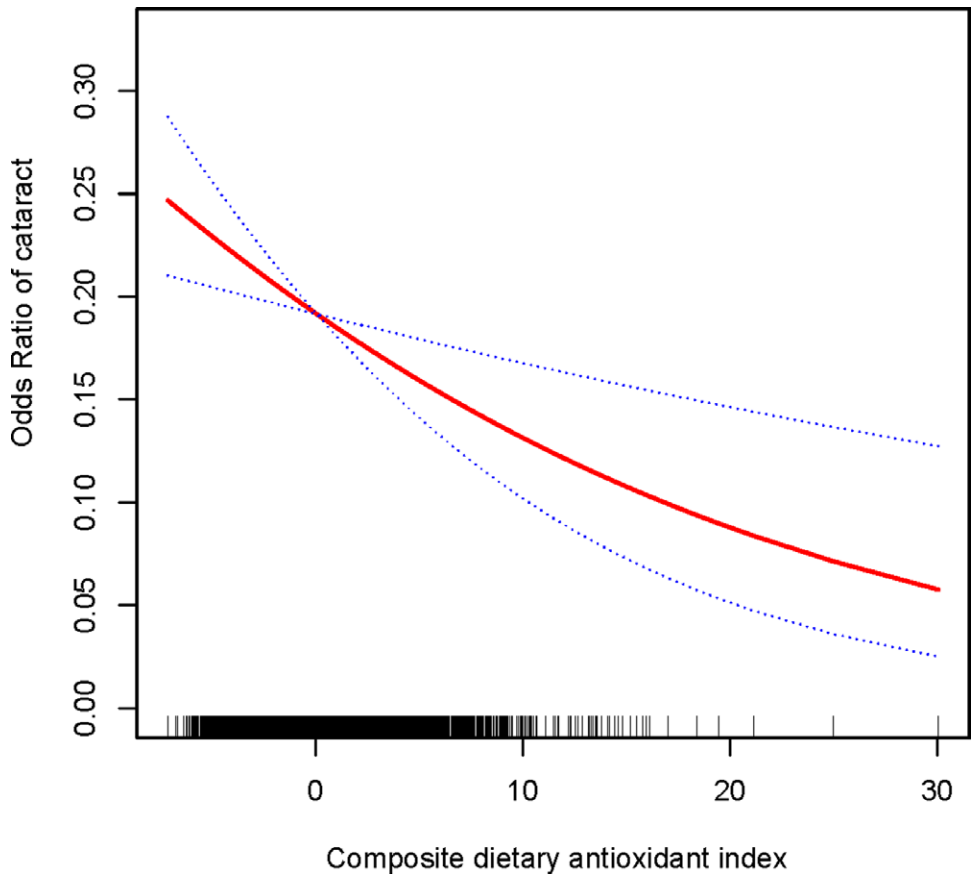

Figure 2. The association between the CDAI and cataract in the fully adjusted model (model 2). CDAI = composite dietary antioxidant index.

Table 3

Association between CDAI components and cataract.

CDAI component score	Crude	Model 1	Model 2
Zinc	0.72 (0.63, 0.81) <.0001	0.87 (0.76, 0.98) .0262	0.85 (0.74, 0.97) .0167
Magnesium	0.73 (0.67, 0.80) <.0001	0.84 (0.76, 0.93) .0009	0.86 (0.77, 0.96) .0089
Selenium	0.65 (0.59, 0.72) <.0001	0.87 (0.78, 0.97) .0129	0.90 (0.80, 1.01) .0787
Vitamin A	1.03 (0.95, 1.11) .4374	0.89 (0.79, 1.00) .0585	0.87 (0.76, 0.99) .00311
Vitamin C	0.98 (0.91, 1.06) .6603	0.92 (0.84, 1.02) .1089	0.94 (0.85, 1.04) .2429
Vitamin E	0.80 (0.72, 0.88) <.0001	0.86 (0.78, 0.96) .0076	0.89 (0.79, 0.99) .0404

Model 1: Adjusted for age, gender, and race. Model 2: Adjusted for age, gender, race, education level, marital status, poverty–income ratio, BMI, CRP, smoking status, alcohol use, diabetes mellitus, hypertension, cardiovascular disease, and hyperlipidemia.

BMI = body mass index, CDAI = composite dietary antioxidant index, CRP = C-reactive protein.

and White people. They were also more likely to possess higher family income and educational achievement, be married or living with a partner, and drinker. However, they were more likely to have lower diabetes mellitus, hypertension, and cardiovascular disease rates.

3.2. Association between the CDAI and cataract

The results of multiple logistic regression modeling are displayed in Table 2. A robust negative correlation was found between the CDAI and the probability of cataract ($P < .05$). In model 2, every unit increase in the CDAI was associated with a 4% decrease in the odds of developing cataract (odds ratio (OR) = 0.96; 95% confidence interval (CI), 0.93–0.98). Consistent results were obtained when we categorized the CDAI from a continuous variable to tertiles. Participants in the T3 subgroup had significantly lower odds of cataract in model 2 (OR = 0.78; 95% CI, 0.63–0.96). In addition, the negative nonlinear relationship between the CDAI and cataract was further verified by the generalized model and smoothed curve fitting (Fig. 2).

3.3. Association between CDAI components and cataract

Table 3 shows the results of multiple logistic regression modeling between each component of the CDAI and cataract incidence. In the crude model, zinc (OR = 0.72; 95% CI, 0.63–0.81), magnesium (OR = 0.73; 95% CI, 0.67–0.80), selenium (OR = 0.65; 95% CI, 0.59–0.72), and vitamin E (OR = 0.80; 95% CI, 0.72–0.88) were significantly negatively associated with cataract odds. In model 2, zinc (OR = 0.85; 95% CI, 0.74–0.97), magnesium (OR = 0.86; 95% CI, 0.77–0.96), vitamin A (OR = 0.87; 95% CI, 0.76–0.99) and vitamin E (OR = 0.89; 95% CI, 0.79–0.99) maintained a negative association with cataract odds.

Table 4

Subgroup analyses of the associations between the CDAI and cataract.

	OR (95% CI), *P* value	*P* for interaction
Stratified by gender		.9924
Men	0.96 (0.92, 0.99) .0242	
Women	0.96 (0.92, 1.00) .0402	
Stratified by age		.2719
≤60 yr	0.89 (0.80, 0.99) .0367	
>60, ≤70 yr	0.95 (0.90, 1.00) .0496	
>70 yr	0.96 (0.93, 0.99) .0105	
Stratified by race		.2865
Non-Hispanic White	0.95 (0.92, 0.99) .0066	
Non-Hispanic Black	1.02 (0.93, 1.10) .7091	
Mexican American	0.97 (0.88, 1.06) .4671	
Other races	0.82 (0.72, 0.94) .0037	
Stratified by smoking status		.3880
No	0.97 (0.93, 1.01) .1560	
Yes	0.95 (0.91, 0.98) .0046	
Stratified by alcohol use		.2796
No	0.98 (0.93, 1.03) .3621	
Yes	0.95 (0.91, 0.98) .0018	
Stratified by diabetes mellitus		.1013
No	0.97 (0.94, 1.00) .0578	
Yes	0.92 (0.87, 0.97) .0037	
Stratified by hypertension		.1412
No	0.93 (0.88, 0.98) .0035	
Yes	0.97 (0.94, 1.00) .0789	
Stratified by cardiovascular disease		.8406
No	0.95 (0.92, 0.99) .0052	
Yes	0.96 (0.91, 1.02) .1681	
Stratified by hyperlipidemia		.1701
No	0.92 (0.87, 0.98) .0056	
Yes	0.97 (0.93, 1.00) .0408	

Adjusted for age, gender, race, education level, marital status, poverty–income ratio, BMI, CRP, smoking status, alcohol use, diabetes mellitus, hypertension, cardiovascular disease, and hyperlipidemia.

BMI = body mass index, CDAI = composite dietary antioxidant index, CRP = C-reactive protein.

3.4. Subgroup analysis

To identify potential population-specific parameters, subgroup analyses of the associations between the CDAI and cataract, stratified by gender, age, race, smoking status, alcohol use, diabetes mellitus status, hypertension status, cardiovascular disease status, and hyperlipidemia status were conducted (Table 4). Inconsistent associations between the CDAI and cataract were found. The correlation between the CDAI and cataract was not statistically significant in the subgroups of women, participants aged 60 to 70 years, non-Hispanic Black people, Mexican American people, nonsmokers, nonalcohol consumers, participants with no diabetes mellitus, or participants with cardiovascular diseases ($P > .05$). Furthermore, no statistically significant interaction was observed between any of the stratified parameters.

3.5. CDAI as a predictor for cataract

We compared the predictive ability of CDAI, DII, and CRP for cataract likelihood by calculating the AUC (Fig. 3). In the analysis, CDAI demonstrated an advantage over the other 2 indicators with an AUC of 0.5567 (95% CI 0.5385–0.5749).

4. Discussion

In the present study, we used the NHANES from 2003 to 2008 to investigate the correlation between the CDAI and cataract among U.S. adults. A total of 5814 individuals were included. We found a negative association between the CDAI and cataract after adjusting for all potential covariates, indicating that the CDAI might be a protective index for the incidence of cataract. In addition, the association analysis between each component of the CDAI and cataract revealed a negative relationship between dietary zinc, magnesium, vitamin A and vitamin E intake, and cataract. In subgroup analysis, no stratification variables showed a statistically significant interaction. Overall, our findings suggested that the CDAI may serve as a potential indicator of the likelihood of cataract.

Since oxidative stress is a significant contributor to cataract development, natural antioxidants are always considered candidates for the antioxidative therapy of cataract, including fruits and vegetables, vitamins (vitamin C and vitamin E), essential minerals (zinc, magnesium, and selenium), carotenoids, lutein, flavonoids, and other antioxidants.[16] Many cohort studies have reported an association between antioxidant intake and cataract risk.[17] The Blue Mountains Eye Study investigated the relationships between antioxidant nutrient intake and the 10-year incidence of age-related cataract and reported that higher intakes of combined antioxidants (vitamin C, vitamin E, beta-carotene, and zinc) was protective for the development of nuclear cataract.[18] The Beaver Dam Eye Study also reported a small protective effect of vitamin A, vitamin D, zinc, and multivitamins on cortical cataracts.[19] A cross-sectional study reported a significant negative association between selenium intake and cataract.[20] However, results from intervention trials were inconsistent with the risk for age-related cataract prevalence.[21] The Age-Related Eye Disease Study revealed that nutrient supplementation had no obvious effect on the 7-year risk of age-related cataract.[22] However, the Linxian trial found that vitamin/mineral supplementation may decrease the 5- to 6-year risk of nuclear cataract.[23] With regard to cataract progression, the Roche European American Cataract Trial reported that nutrient supplementation slightly decreased the progression of age-related cataract.[24] In addition to nutrient supplementation, several antioxidant indices have been applied to evaluate synergistic effects on cataract risk. The Swedish Mammography Cohort Study investigated the association between the total antioxidant capacity of the diet and the 7-year incidence of age-related cataract. The results showed that dietary total antioxidant capacity was inversely associated with the risk of age-related cataract.[25] Healthy Eating Index-2015 was also used to assess age-related cataract odds, and a higher score was associated with lower odds of age-related cataract.[10] In addition, it was reported that an antioxidant dietary pattern and an omega-3 dietary pattern were associated with a significantly lower risk of age-related cataract.[26]

Considering the protective effect of an antioxidant diet or pattern in many cohort studies, the less encouraging effect of antioxidant supplementation on reducing the incidence of age-related cataract is puzzling. There are several possible reasons for this discrepancy.[17] First, the duration of the intervention studies was relatively short, usually <10 years. The development of lens opacity is a slow and continuous process, so it may take a long time for the protective effect of antioxidant intake to manifest. Second, since excessive intake of vitamins may produce adverse effects, the supplementation of antioxidant vitamins should be weighed carefully.[3] This may imply that the dietary intake of vitamins or other nutrient ingredients is more advantageous than the use of dietary supplements.[27] In addition, supplementation with a single antioxidant or several antioxidants may not play a synergistic role since there are much wider ranges of antioxidants in the diet, and the human body is a complex system.[25]

It has been proved that the total antioxidant capacity was significantly higher in healthy people than in cataract patients, and the serum total oxidant capacity was significantly lower in healthy people than in cataract patients.[28] One comparative study indicated the crucial role of hypomagnesemia in the

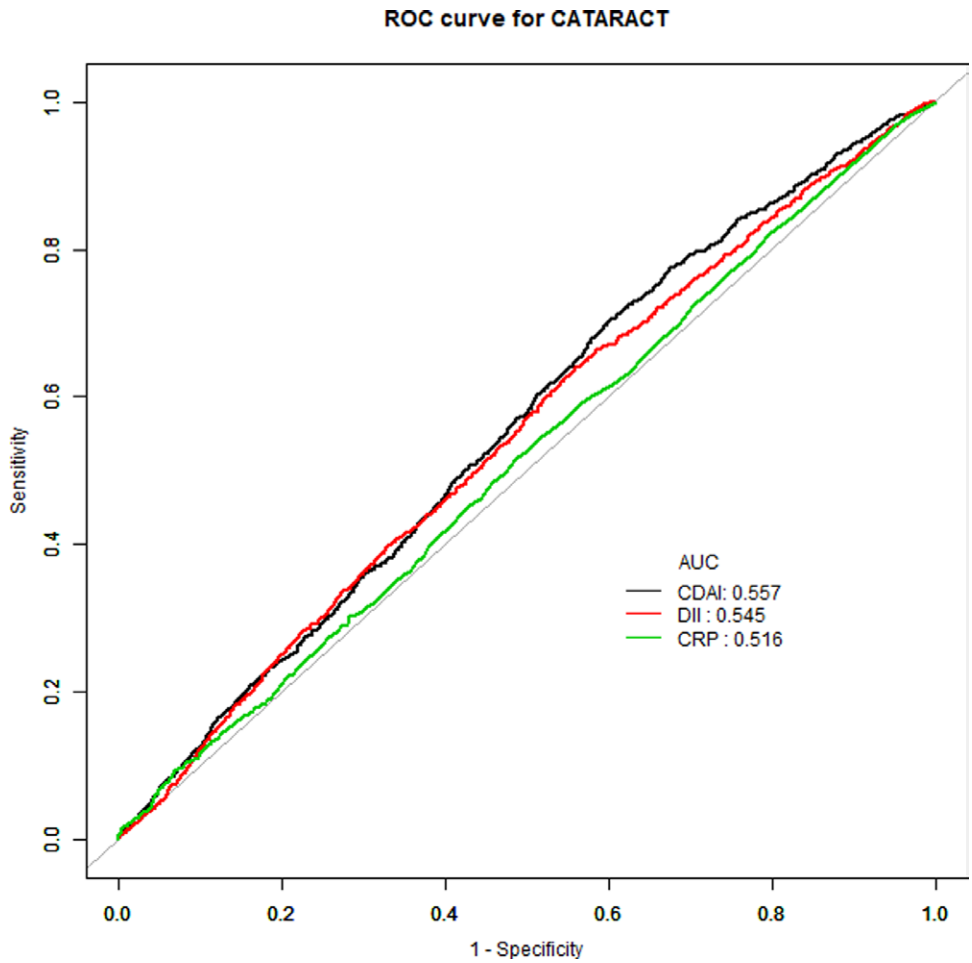

Figure 3. Receiver operating characteristic (ROC) curve analysis for cataract.

oxidative stress of cataract formation.[29] Therapies targeting oxidative stress have become promising choice for cataract. Zinc supplementation has been shown to protect a cataract rat model from metabolic abnormalities and oxidative stress.[30] Additionally, selenium supplementation could decelerate the development of naphthalene cataract by alleviating oxidative stress in the lens.[31] Astaxanthin, a carotenoid, reportedly alleviated human lens epithelial cell damage by inhibiting ferroptosis and ameliorating oxidative stress.[32] Other natural antioxidants, including hesperetin, esculetin, idebenone, and carnosine, also had a protective effect on human lens epithelial cells or the cataract animal model.[33–35]

The current study has several limitations. First, cataract surgery was used as a surrogate for cataract in the present study. Since the lens examination is not available in the NHANES, some previous epidemiological studies considered self-reported cataract surgery to be a clinically meaningful cataract.[9] However, this approach is a rough estimate of cataract occurrence based on the status of cataract surgery and may introduce misclassification bias, because not every cataract patient would undergo cataract surgery and some cases may remain undiagnosed. The decision to undergo cataract surgery may also be influenced by factors such as disease stage, financial conditions, and general health. Second, although the study included participants aged more than 50 years, information regarding the specific type of cataract (e.g., nuclear, cortical or posterior subcapsular) was not available in this database. This limits our ability to explore potential differences in associations between CDAI and specific cataract subtypes, which may have distinct pathophysiological mechanisms and responses to dietary antioxidants. Future studies with more detailed ophthalmologic data are needed to investigate these subtype-specific associations. Third, due to the cross-sectional design of this study, causal relationships between CDAI and cataract cannot be established. The observed associations should be interpreted with caution, as they may be influenced by reverse causality or unmeasured confounding factors. Fourth, as the NHANES is a nationally representative survey of the U.S. population, the findings of this study may not be fully generalizable to populations in other countries, especially in developing regions where dietary patterns, nutritional status, healthcare systems, and the prevalence of cataracts may differ substantially. Caution is therefore warranted when extrapolating these results beyond the U.S. population. Fifth, in this study, we focused on dietary intake of antioxidants; however, the use of antioxidant supplements (except for supplemental intake of vitamin E) were either unavailable or incomplete in NHANES, which may have led to underestimation of total antioxidant exposure. Finally, although multiple covariates were adjusted for in the analysis, the possibility of residual confounding cannot be ruled out. Unmeasured or unknown factors—such as genetic susceptibility, environmental exposures, or other lifestyle characteristics—may have influenced the observed association between CDAI and cataract. Nonetheless, this is still a large-scale nationally representative population-based survey, and this is the first study reporting the association between the CDAI and cataract. To establish a causal relationship between CDAI and cataract, future studies employing longitudinal or prospective cohort designs are warranted. These studies should include objective clinical evaluations of cataract presence and

subtype, as well as detailed data on antioxidant intake from both dietary and supplemental sources.

5. Conclusion

This cross-sectional study reveals a negative correlation between the CDAI and cataract, suggesting that a higher CDAI may be related to the incidence of cataract. Given these findings, antioxidant dietary patterns, rather than single antioxidant supplements, are recommended for cataract prevention. However, large-scale and multicenter prospective clinical trials are needed to examine the synergistic effects of daily diet on cataract development risk.

Author contributions

Funding acquisition: Xiaobo Xia.
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Software: Quyan Zhang.
Supervision: Xiaobo Xia.
Visualization: Quyan Zhang.
Writing – original draft: Quyan Zhang.
Writing – review & editing: Xiaobo Xia.

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