Open Access

Relationship of comprehensive dietary antioxidant index and hypothyroidism risk: evidence from the National Health and Nutrition Examination Surveys 2007–2012



Jie Chang¹, Ningning Wang¹, Yanxia Cheng² and Xiaoyan Chen^{1*}

Abstract

Background Hypothyroidism is a common thyroid disease affecting the health of the global population and oxidative stress and inflammation are involved in the pathophysiological process of hypothyroidism. Comprehensive dietary antioxidant index (CDAI), representing the overall dietary antioxidant capacity, has been proved to be associated with a variety of diseases. However, association between CDAI and hypothyroidism risk remains unclear. This study aims to evaluate the association of CDAI and hypothyroidism risk.

Methods Data of this study were extracted from the National Health and Nutrition Examination Surveys (NHANES) database 2007–2012. CDAI, represents the overall dietary nutrients capacity, was calculated by selenium, zinc, magnesium, vitamin A, C and E. Thyroid stimulating hormone (TSH) > 5.6 mIU/L was defined as hypothyroidism. The weighted multivariate logistic regression models and propensity score matching (PSM) analysis were utilized to evaluate the relationship between CDAI and hypothyroidism, with odds ratio (ORs) and 95% confidence intervals (CIs). Subgroup and sensitivity analysis were further evaluated the relationship between CDAI and hypothyroidism. Moreover, the association between the components of CDAI and hypothyroidism was also explored.

Results Totally, 7,959 subjects with information of complete dietary intake and thyroid function measurement were included. Of whom, 213 (2.68%) subjects had hypothyroidism. After adjusted all covariates, we observed high CDAI was related to low hypothyroidism risk (OR = 0.44, 95%CI: 0.27–0.71). This relationship was prominent in subjects with aged < 65 years old (OR = 0.32, 95%CI: 0.16–0.62), male (OR = 0.39, 95%CI: 0.15–0.99) and BMI \geq 25 kg/m² (OR = 0.38, 95%CI: 0.19–0.76). The association between high CDAI and low hypothyroidism risk remained significant when subjects using thyroid hormones were excluded (OR = 0.47, 95%CI: 0.27–0.81).

Conclusion High CDAI was related to low hypothyroidism risk among U.S. adults. Our finding showed that the intake of an antioxidant-rich dietary is a potential method to reduce the risk of hypothyroidism.

Keywords Comprehensive dietary antioxidant index, Hypothyroidism, Oxidative stress, NHANES database

*Correspondence: Xiaoyan Chen cxy15163052135@hotmail.com

¹Department of Endocrinology, Heze 3rd people's Hospital, Heze, Shandong Province 274000, China ²Department of Nursing, Heze 3rd people's Hospital, Heze, Shandong Province 274000, China

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creative.commons.org/licenses/by-nc-nd/4.0/.

Introduction

A healthy endocrine system is a condition for normal human development and reproduction. Thyroid is one of the important glands of the endocrine system, which has an essential effect on the homeostasis, growth and development, and normal reproduction [1]. Hypothyroidism is an endocrine condition featured by lower serum thyroxin levels, with the clinical spectrum varies from no signs and symptom to serious complications [2, 3]. Approximately, 4-10% of populations suffer from hypothyroidism [4]. Since hypothyroidism may lead to damage to the eight system of human body, early prevention and treatment of hypothyroidism can reduce this damage.

Inflammation is closely related to oxidative stress, and oxidative stress is also associated with hormonal disorders. Thyroid hormone is one of the vital hormones that affect the antioxidant balance, since both hyperthyroidism and hypothyroidism have been shown to be associated with oxidative stress in animals and humans [5, 6]. Dietary modification may be considered as effective way to reduce the oxidative stress level in the body [7]. The association between the several antioxidant nutrients intake, such as zinc, selenium, magnesium and vitamin A, and thyroid function has been proven by previous epidemiological studies [8-10]. These nutrients may play an important role in maintaining normal thyroid function by regulating thyrotropin-releasing hormone (TRH) and thyrotropin synthesis hormone (TSH), as well as enzymatic reactions necessary for thyroid hormone homeostasis.

Numerous researches have built the relationship between foods and overall dietary patterns, rather than just antioxidant individual nutrients, and chronic diseases. Then, the comprehensive dietary antioxidant index (CDAI) focused on six antioxidant nutrients including vitamins A, C, E, zinc, selenium and magnesium has come into being. Luu et al. [11] reported that CDAI was significantly negatively correlated with the oxidative stress level and inflammatory markers including IL-1 β and tumor necrosis factor- α (TNF- α). Moreover, high CDAI was also related to high bone mineral density, lower blood pressure and lower atherosclerotic cardiovascular disease risk [12–14]. Less is known, however, the association between CDAI and hypothyroidism.

Herein, we explored the association between CDAI and hypothyroidism risk based on National Health and Nutrition Examination Surveys (NHANES) database. From the perspective of improving diet, the aim of this study is to provide a theoretical basis for reducing the burden of thyroid diseases.

Methods

Study design and population

Data from this cross-sectional were extracted from the NHANES database 2007–2012. NHANES is a nationally representative survey assessing the health and nutritional status of the civilian population. In this survey, approximately 5,000 individuals were surveyed from across the country each year. NHANES contains demographic data, dietary data, examination data, laboratory data and limited access data. The requirement of ethical approval for this was waived by the Institutional Review Board of Heze 3rd people's Hospital, because the data was accessed from NHANES (a publicly available database). The need for written informed consent was waived by the Institutional Review Board of Heze 3rd people's Hospital due to retrospective nature of the study. All methods were performed in accordance with the relevant guidelines and regulations.

In the present study, the inclusion criteria were: (1) participants aged \geq 18 years old; (2) participants with thyroid function measurement; (3) participants with complete information of dietary intake. The exclusion criteria were: 1): participants with extreme energy intake (female: <500 kcal/day or >5,000 kcal/day; male: <500 kcal/day or >8,000 kcal/day); 2) participants diagnosed as hyperthyroidism; 3) pregnant and lactating women; (4) participants with thyroid cancer history; (5) participant missing important variables.

Measurement of hypothyroidism

All participants received a thorough thyroid function laboratory measurement. The thyroid function included measures for TSH and free thyroxine (FT4). The serum TSH levels between 0.34 and 5.6 mIU/L and FT4 levels between 0.6 and 1.6 ng/dL were defined as normal by The American Association of Clinical Endocrinologists according to Medical Guidelines for Clinical Practice [15]. Both FT4 and TSH level were in the normal range representing the normal thyroid function. TSH level > 5.6 mIU/L was defined as hypothyroidism. Hyperthyroidism was defined as TSH level < 0.34 mIU/L or patients who were receiving anti-thyroid medication currently. In present study, participants diagnosed as hyperthyroidism were excluded.

Assessment of CDAI

Participants' dietary intake information was collected by the NHANES through 24-h dietary recall interview. The first dietary recall was conducted face-to-face, and the second dietary recall proceeded 3–10 days later via the telephone. Two days' dietary recall data were used to calculate the average daily intake. The CDAI was calculated by using the method proposed by Wright et al. [16] and was calculated based on six dietary antioxidant micronutrients, including vitamins A, C, E, zinc, magnesium and selenium. To calculate CDAI, we subtracted the mean and divided the result by its standard deviation (SD) from the six dietary micronutrients as follows:

 $CDAI = \sum_{i=1}^{n=6} (Individual Intake - Mean)/SD$

Covariates

Covariates were adopted to reduce deviation, which included age, gender, race, education level, marital status, poverty-to income (PIR), lifestyle information such as smoking and drinking status, physical examination such as body mass index (BMI), and self-reported health status such as medical and drug history. Height and weight were used to calculate BMI. PIR was calculated by dividing the family income by the poverty threshold, and categorized into two levels: low income (≤ 1.85) and high income (>1.85). Smoking was categorized into never smoker (less than 100 cigarettes in lifetime), former smoker (more than 100 cigarettes in lifetime and quit smoking now), current smoker (more than 100 cigarettes in lifetime and was still smoking at the time of the survey). Never drinker was defined as subjects answered negatively to the question "Had at last 12 alcoholic drinks/lifetime?", otherwise were considered as drinkers. The medication history included anticoagulants, thyroid hormone medications, and anti-thyroid drugs. Thyroid problem was assessed by the question "Ever told you had thyroid problem?" Autoimmune thyroiditis (AIT) was defined as the presence of positive thyroid peroxidase antibody (TPOAb) or positive thyroglobulin antibody (TgAb) (positive TPOAb: \geq 9.0 IU/mL; positive TgAb \geq 4.0 IU/mL).

Statistical analysis

All data were analyzed via SAS 9.4 (SAS Institute Inc., Cary, NC, USA). For continuous variables, and the weighted t-test was used for comparison between groups. Categorical variables were described as the number and percentage [n (%)], and comparisons between groups used the weighted χ^2 test. The weighted univariable and multivariable logistics regression models were used to assess the relationship of CDAI level and hypothyroidism odds, with odds ratio (ORs) and confidence intervals (CIs). The model was a crude model. Model 2 adjusted age, gender, race, examination session, thyroid hormones use, energy intake, thyroid problem and autoimmune thyroiditis. Subgroup analysis were conducted to further assess this association based on different age, gender and BMI. A sensitivity analysis of CDAI and the risk of hypothyroidism was performed after excluding participants who used thyroid hormones drugs. A random forest method was further used to explore the contributions of each variable of CDAI to hypothyroidism, and evaluated with mean decrease gini. To avoid potential bias, and

Results

Characteristics of participants

The flow chart of screen process of the participants was exhibited in Fig. 1. A total of 18,619 participants were screened. Among them, 9,586 participants missing thyroid function assessment indicators, 448 missing complete antioxidant dietary intake information, 85 participants with extreme energy intake, 211 participants with hyperthyroidism, 81 were pregnant or lactating, 10 participants with thyroid cancer history and 239 participants missing important covariates of iodine intake were excluded. Finally, 7,959 participants were included, with a mean age of $45.84 (\pm 0.37)$ years old. Among them, 213 (2.68%) participants had hypothyroidism. The characteristics of the study HF patients were listed in Table 1. The proportion of participants with low CDAI levels were significantly higher among the hypothyroidism group than the normal thyroid function group (45.80% vs. 32.92%). Differences were found in age, gender, race, examination session, thyroid hormones use, CDAI levels, energy intake, thyroid problem and autoimmune thyroiditis history between the two groups (all P < 0.05).

Relationship between CDAI level and hypothyroidism

The relationship between CDAI level and hypothyroidism was explored, as exhibited in Table 2. In fully adjusted model 2, we observed that participants with high CDAI levels (\geq 1.43) had a 56% reduction in the odds of hypothyroidism (OR = 0.44, 95%CI: 0.27–0.71).

Relationship between CDAI level and hypothyroidism based on age, gender and BMI

The relationship between CDAI level and hypothyroidism was further explored based on different populations of age, gender and BMI (Fig. 2). After all covariates were adjusted, we found the relationship of CDAI level and hypothyroidism remains robust. Among participants with male (OR = 0.39, 95%CI: 0.15–0.99), aged < 65 years old (OR = 0.32, 95%CI: 0.16–0.62) and BMI \ge 25 kg/m² (OR = 0.38, 95%CI: 0.19–0.76), high CDAI was more significantly associated with low odds of hypothyroidism.

PSM analysis

PSM analysis was performed to evaluate the association between CDAI and hypothyroidism. We set the hypothyroidism group as the control group and matched the non-hypothyroidism group by PSM at a ratio of 1:2. The propensity score distribution diagram after matching and the table of study population characteristics are shown in Fig. 3 and Table S1, respectively. The baseline



Fig. 1 The flow chart of population screening

characteristics of subjects in hypothyroidism and nonhypothyroidism groups did not significantly differ. Logistics regression analysis shown that high CDAI was also associated with lower odds of hypothyroidism (Table 3) (OR = 0.55, 95%CI: 0.35-0.85).

Sensitivity analysis of the CDAI and hypothyroidism

We also conducted a sensitivity analysis in which participants who received any thyroid hormones were excluded (n = 443) because the application of medication can influence thyroid function. Results of the sensitivity analysis were consistent with those in the main analysis. CDAI, whether as a continuous variable or a categorical variable, was related to the odds of hypothyroidism. In fully adjusted model, participants with high CDAI had a 43% reduction in the odds of hypothyroidism (OR = 0.47, 95%CI: 0.27–0.81) (Table 4).

Association between components of CDAI with hypothyroidism

Then, the random forest method was utilized to explore the contribution of individual microelements components in CDAI to hypothyroidism (Fig. 4) (Table 5). Mean decrease gini is an indicator that reflects the impact of each variable on the heterogeneity of the observed values of each node on the classification tree, thereby comparing the importance of the contribution of each variable on the outcome. The large the mean decrease gini value, the greater the importance of the variable. Figure 3 suggested that zinc contributed the most to hypothyroidism in CDAI, followed by vitamin E, vitamin C, selenium, vitamin A and magnesium.

Discussion

The present study suggested that a high overall antioxidant nutrients intake level, indicated by CDAI, was associated with lower odds of hypothyroidism after adjusting for multiple covariates. As far as we know, this is the first study evaluating the association between CDAI and hypothyroidism risk based on U.S. adults.

Previous studies have extensively proved the association between antioxidant diets and thyroid diseases. A cross-section analysis of the ELSA-Brasil study suggested that compared with dietary selenium intake as the first quantile, the second quantile and third quantile have a 21% and 28% reduction of subclinical hypothyroidism risk, respectively [9]. The thyroid includes high levels of selenium and expresses a variety of selenoproteins involved in protecting against oxidative stress and thyroid hormones. Insufficient selenium leads to disturbances in synthesis of selenoproteins and thyroid hormones metabolism [17]. Another cross-sectional study of Lu et al. [18] observed that low zinc intake had a higher risk of newonset hypothyroidism and a significant interaction effect between dietary selenium level intake and dietary zinc level intake on new-onset hypothyroidism risk. Similar

Table 1 Characteristics of participants

Variables	Total (n = 7959)	Non-hypothyroidism (n=7746)	Hypothyroidism (n=213)	Statistics	Р
Age, years, Mean (S.E)	45.84 (0.37)	45.71 (0.38)	50.13 (1.63)	t=-2.63	0.012
Gender, n (%)				$\chi^2 = 9.057$	0.003
Female	3881 (50.38)	3755 (50.02)	126 (62.29)		
Male	4078 (49.62)	3991 (49.98)	87 (37.71)		
Race, n (%)				$\chi^2 = 32.896$	< 0.001
Non-Hispanic White	3668 (69.90)	3532 (69.49)	136 (83.57)		
Non-Hispanic Black	1577 (10.33)	1562 (10.55)	15 (2.94)		
Mexican American	1320 (8.30)	1286 (8.36)	34 (6.31)		
Other	1394 (11.46)	1366 (11.59)	28 (7.18)		
Education level, n (%)				$\chi^2 = 3.132$	0.209
Less Than High School	2277 (19.02)	2214 (19.06)	63 (17.81)		
High School or equivalent	1839 (23.31)	1795 (23.44)	44 (18.97)		
College or above	3843 (57.67)	3737 (57.51)	106 (63.22)		
Marital Status, n (%)				$\chi^2 = 1.354$	0.245
Married	4805 (63.92)	4670 (63.80)	135 (67.77)		
Unmarried	3154 (36.08)	3076 (36.20)	78 (32.23)		
PIR, n (%)				$\chi^2 = 1.632$	0.201
≤1.85	3642 (32.76)	3541 (32.88)	101 (28.76)		
>1.85	4317 (67.24)	4205 (67.12)	112 (71.24)		
Smoking, n (%)				$\chi^2 = 1.946$	0.378
Never smoke	4280 (54.08)	4165 (54.02)	115 (56.30)		
Former smoker	2026 (24.88)	1967 (24.81)	59 (27.16)		
Current smoker	1653 (21.04)	1614 (21.17)	39 (16.54)		
Drinking, n (%)				$\chi^2 = 0.270$	0.603
Non-drinkers	1110 (10.90)	1077 (10.94)	33 (9.80)		
Drinkers	6849 (89.10)	6669 (89.06)	180 (90.20)		
Six-month time period, n (%)				$\chi^2 = 0.519$	0.471
November 1 through April 30	3587 (38.96)	3499 (39.06)	88 (35.58)		
May 1 through October 31	4372 (61.04)	4247 (60.94)	125 (64.42)		
Examination session, n (%)				$\chi^2 = 11.633$	0.003
Morning	3913 (48.96)	3795 (48.87)	118 (52.25)		
Afternoon	2813 (33.43)	2763 (33.80)	50 (21.30)		
Evening	1233 (17.60)	1188 (17.34)	45 (26.45)		
Thyroid hormones use, n (%)				$\chi^2 = 52.522$	< 0.001
No	7516 (94.02)	7359 (94.53)	157 (76.94)		
Yes	443 (5.98)	387 (5.47)	56 (23.06)		
Thyroid problem, n (%)				$\chi^2 = 52.309$	< 0.001
No	7296 (90.79)	7163 (91.62)	133 (63.28)		
Yes	663 (9.21)	583 (8.38)	80 (36.72)	_	
Autoimmune thyroiditis, n (%)				$\chi^2 = 184.992$	< 0.001
No	6839 (85.07)	6740 (86.41)	99 (40.24)		
Yes	1120 (14.93)	1006 (13.59)	114 (59.76)	2	
BMI, kg/m², n (%)				$\chi^2 = 1.267$	0.531
<25	2692 (33.85)	2620 (33.96)	72 (30.40)		
25-29.9	2414 (32.72)	2357 (32.78)	57 (30.90)		
≥30	2853 (33.42)	2769 (33.26)	84 (38.70)		
Blood cadmium, nmol/L, Mean (S.E)	4.57 (0.12)	4.56 (0.12)	4.79 (0.32)	t=-0.72	0.473
CDAI, Mean (S.E)	0.42 (0.13)	0.44 (0.13)	-0.32 (0.35)	t=2.33	0.024
CDAI Level, n (%)				$\chi^2 = 10.067$	0.007
<-1.80	2987 (33.29)	2888 (32.92)	99 (45.80)		
-1.80-1.43	2672 (33.41)	2613 (33.60)	59 (26.99)		
≥1.43	2300 (33.30)	2245 (33.48)	55 (27.21)		
Urine lodine, ug/mg, Mean (S.E)	5.86 (3.32)	5.94 (3.41)	3.24 (0.49)	t=0.80	0.429

Table 1 (continued)

Variables	Total (n = 7959)	Non-hypothyroidism (n=7746)	Hypothyroidism (n = 213)	Statistics	Р
Energy, kcal, Mean (S.E)	2188.52 (17.54)	2194.20 (17.26)	1999.43 (85.40)	t=2.33	0.024
Protein energy ratio, %, Mean (S.E)	15.54 (0.09)	15.53 (0.09)	15.66 (0.42)	t=-0.33	0.746
Carbo energy ratio, %, Mean (S.E)	48.98 (0.30)	49.02 (0.29)	47.86 (1.12)	t=1.08	0.287
Fat energy ratio, %, Mean (S.E)	33.53 (0.18)	33.55 (0.18)	32.89 (0.82)	t=0.84	0.405
2					

t: t-test; χ^2 : chi-square test; S.E: standard error; PIR: poverty-to-income ratio; BMI: body mass index; CDAI: composite dietary antioxidant index

 Table 2
 Association of CDAI and hypothyroidism

Variables	Model 1		Model 2		
	OR (95%CI)	Р	OR (95%CI)	Р	
CDAI	0.95 (0.90–0.99)	0.046	0.92 (0.87–0.98)	0.009	
CDAI level					
<-1.80	Ref		Ref		
-1.80-1.43	0.58 (0.35–0.96)	0.033	0.51 (0.31–0.83)	0.008	
≥1.43	0.58 (0.39–0.87)	0.009	0.44 (0.27-0.71)	0.001	

OR: odds ratio; CI: confidence interval; Ref: reference; CDAI: composite dietary antioxidant index

Model 1: crude model

Model 2: adjusted age, gender, race, examination session, thyroid hormones use, energy, thyroid problem; and autoimmune thyroiditis

beneficial effects of antioxidant diet on thyroid function were also found in micronutrients such as vitamin A, E and C [10, 19]. However, not all studies have observed the beneficial effect between dietary nutrient intake and thyroid function. The data from two cross-sectional and three interventional studies were analyzed by Thomson et al. [20] and found there were no significant correlations between selenium intake and thyroid metabolism, even after selenium supplementation.

Studies examining relationship between single nutrients and thyroid function may be biased due to these studies ignored the complex interactions and correlations among various dietary antioxidants. Recently, profits from the rapid development of nutritional epidemiology, researchers have shifted their attention from a focus on individual antioxidant nutrients to a composite dietary pattern. The CDAI, calculated by selenium, zinc, magnesium, vitamin A, C and E, was brought into being as a compound index to evaluate the antioxidant levels of overall nutrients [7]. In present study, we observed high CDAI was related to low occurrence of hypothyroidism. Our finding adds to the evidence that beneficial association of CDAI and several diseases have already been observed. A study by Han et al. [12] included 14,069 subjects from NHANES database and suggested that high CDAI was related to total spine bone mineral density, as well as femoral neck and trochanter. Zhao et al. [7] evaluated the association of CDAI and mental health and found that there was a negative non-linear relationship between CDAI and depression. Before the inflection point of 0.16, each unit increase od CDAI was related to a 30% decrease in depression risk. Ma et al. [21] conducted a cross-sectional study and found that compared to the lowest CDAI quartile, the OR for heart failure risk was 0.68 for the highest CDAI quartile. Another crosssectional study focused on overall antioxidant dietary intake and cardiovascular health also reported consistent

Subgroup	OR (95%CI)	Р		Subgroup	OR (95%CI)	P
Age<65 years (n=6115)			Age≥65 years (n=1844)		1
CDAI	0.88 (0.82-0.95)	0.001		CDAI	1.00 (0.91-1.11)	0.985
CDAI level				CDAI level		1
<-1.80	Ref			<-1.80	Ref	
-1.80-1.43	0.47 (0.25-0.85)	0.014	-	-1.80-1.43	0.55 (0.22-1.36)	0.189
≥1.43	0.32 (0.16-0.62)	0.001		≥1.43	0.69 (0.26-1.87)	0.461
Male (n=4078)				Female (n=3881)		1
CDAI	0.94 (0.85-1.04)	0.248		CDAI	0.92 (0.84-0.99)	0.037
CDAI level				CDAI level		
<-1.80	Ref			<-1.80	Ref	
-1.80-1.43	0.44 (0.23-0.86)	0.017		-1.80-1.43	0.58 (0.31-1.09)	0.091
≥1.43	0.39 (0.15-0.99)	0.049	-	≥1.43	0.47 (0.23-0.95)	0.035
BMI<25/m ² (n=2414)				BMI≥25kg/m ² (n=5545)		
CDAI	0.92 (0.82-1.04)	0.174		CDAI	0.92 (0.85-0.99)	0.044
CDAI level				CDAI level		
<-1.80	Ref			<-1.80	Ref	
-1.80-1.43	0.57 (0.22-1.47)	0.236		• -1.80-1.43	0.49 (0.28-0.86)	0.014
≥1.43	0.56 (0.18-1.68)	0.291		≥1.43	0.38 (0.19-0.76)	0.008

Fig. 2 Association of CDAI and hypothyroidism risk based on age, gender and BMI. Note, comprehensive dietary antioxidant index; BMI, body mass index



Fig. 3 Distribution of PSM scores. Note, propensity score matching

 Table 3
 Association between CDAI and hypothyroidism after

 PSM
 PSM

Variable	OR (95%CI)	Р
CDAI	0.94 (0.90–0.99)	0.012
CDAI level		
<-1.80	Ref	
-1.80-1.43	0.67 (0.37-1.19)	0.162
≥1.43	0.55 (0.35–0.85)	0.009

OR: odds ratio; CI: confidence interval; Ref: reference; CDAI: composite dietary antioxidant index; PSM, propensity score matching

Model 1: crude model

Model 2: adjusted age, gender, race, examination session, thyroid hormones use, energy, thyroid problem; and autoimmune thyroiditis

Table 4 Sensitivity analysis of association between CDAI and hypothyroidism

Variables	OR (95%CI)	Р	
CDAI	0.93 (0.87–1.01)	0.075	
CDAI level			
<-1.80	Ref		
-1.80-1.43	0.55 (0.28–1.05)	0.070	
≥ 1.43	0.47 (0.27-0.81)	0.008	

 $\mathsf{OR:}$ odds ratio; $\mathsf{CI:}$ confidence interval; $\mathsf{Ref:}$ reference; $\mathsf{CDAI:}$ composite dietary antioxidant index

Model 1: crude model

Model 2: adjusted age, gender, race, examination session, thyroid hormones use, energy and autoimmune thyroiditis



Fig. 4 Contribution of individual components of CDAI to hypothyroidism. Note, comprehensive dietary antioxidant index

results that there was a negative non-linear correlation between CDAI and coronary heart disease in U.S. adults [22]. As one of the vital factors of cell injury, oxidative stress has an important role in the pathogenesis of heart failure, fracture, depression, coronary heart disease, as well as hypothyroidism [23]. Due to the intake of dietary nutritional plays an important role as antioxidative, the role of dietary total antioxidative capacity was increasing. Dietary intakes can regulate the plasma redox and protect from reactive oxygen species. Moreover, an animal study showed that thyroid hormones influence lipid

Table 5 Association between individual nutrients in CDAI and hypothyroidism

Variables	Model 1		Model 2		
	OR (95%CI)	Р	OR (95%CI)	Р	
magnesium	0.80 (0.64–0.99)	0.047	0.73 (0.53-1.00)	0.053	
zinc	0.96 (0.78–1.18)	0.706	0.96 (0.79–1.16)	0.656	
selenium	0.87 (0.74–1.02)	0.090	0.92 (0.72–1.18)	0.513	
Vitamin A	0.84 (0.62–1.13)	0.248	0.77 (0.56–1.06)	0.109	
Vitamin E	0.83 (0.65–1.07)	0.140	0.79 (0.60–1.03)	0.080	
Vitamin C	0.87 (0.68–1.11)	0.260	0.79 (0.59–1.07)	0.130	

OR: odds ratio; CI: confidence interval; Ref: reference

Model 1: crude model

Model 2 adjust: age, gender, race, examination session, thyroid hormones use, energy, thyroid problem and autoimmune thyroiditis

composition of rat tissues and consequently the oxidative stress susceptibility [24]. The overall antioxidative dietary nutrients intake may maintain normal thyroid function by regulating TRH, TSH and enzymatic reactions required to maintain thyroid hormone homeostasis [5].

In subgroup analysis, we observed the relationship between CDAI and hypothyroidism risk was more prominent in males and BMI \ge 25 kg/m². Gender differences in thyroid function have been discussed in previous studies [25, 26]. Costa et al. [26] evaluated changes in thyroid function during aging by an animal model. The results suggested that aging causes real changes in thyroid function and regulation in rats, affecting at least pituitary, thyroid, and liver function. Some of these changes are gender-related, suggesting that gonadal hormones may modulate thyroid function and regulation. Thyroid hormones influence energy expenditure by regulating cellular respiration and thermogenesis and by determining the resting metabolic rate. TSH may also affect thermogenesis, suppress appetite, and suppress fat storage through lipolysis and lipogenesis [27]. Our results suggested that a higher intake of dietary antioxidant nutrients may have beneficial effects on the maintenance of thyroid function in men and people with BMI \ge 25 kg/m².

Herein, based on NHANES database 2007-2012, the relationship of CDAI and hypothyroidism risk was evaluated. CDAI was proposed according to the proven antiinflammatory efficacy of dietary antioxidants, predicted upon its capacity to inhibit pro-inflammatory cytokines such as TNF- α and IL- β . Higher intake of antioxidant dietary supplements may have potential benefits for the maintenance of normal thyroid function in the general population, especially for subjects with aged < 65 years old, males and BMI \ge 25 kg/m². Compared with a previous study from the same NHANES population [28], our study has the following advantages: first, in our study, the total antioxidative intake included both dietary and supplement sources, which can more comprehensively represent the level of antioxidants consumed by people in their daily diet; second, several covariates affecting the hypothyroidism were considered comprehensively, such as the six-month time period when the examination was performed (November 1 through April 30 and May 1 through October 31) and examination session (morning, afternoon and evening); third, the endpoint of this study was the odds of hypothyroidism, which may be more epidemiologically meaningful than focusing only on thyroid function. However, we want to mention some limitations of our study. First, a causal relationship between CDAI and hypothyroidism risk cannot be confirmed due to the type of cross-sectional study. Second, because of the low prevalence of clinical hypothyroidism, our study did not explore the association of hypothyroidism subtypes and hypothyroidism risk. Third, due to significant differences in dietary habits among different races, the conclusions from the study mainly apply to the American adults. Fourth, although we considered as many confounding factors that may affect hypothyroidism as possible, some potential confounders that were not considered, such as physical activity, may have biased the results to a certain extent. The association of CDAI and hypothyroidism risk is needed to explore by large-scale prospective cohort study.

Conclusion

The present study suggested that high CDAI was related to the low hypothyroidism risk in U.S. adults. However, further large-scale prospective studies are still needed to reveal their relationship.

Abbreviations

TRH	Thyrotropin-releasing hormone
TSH	Thyrotropin synthesis hormone
CDAI	Comprehensive dietary antioxidant index
TNF-α	Tumor necrosis factor-α
NAHNES	National health and nutrition examination surveys
BMI	Body mass index
ORs	Odds ratio
Cls	Confidence intervals

Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s12902-024-01806-y.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

Xiaoyan Chen designed the study, Jie Chang wrote the manuscript, Ningning Wang and Yanxia Cheng collected, analyzed and interpreted the data, Xiaoyan Chen critically reviewed, edited the manuscript, all authors read and approved the manuscript.

Funding

Not applicable.

Data availability

The datasets generated during and/or analyzed during the current study are available in the NHANES database, https://wwwn.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate

The requirement of ethical approval for this was waived by the Institutional Review Board of Heze 3rd people's Hospital, because the data was accessed from NHANES (a publicly available database). The need for written informed consent was waived by the Institutional Review Board of Heze 3rd people's Hospital due to retrospective nature of the study. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 23 May 2024 / Accepted: 9 December 2024 Published online: 25 February 2025

References

- Zhou Q, Xue S, Zhang L, Chen G. Trace elements and the thyroid. Front Endocrinol (Lausanne). 2022;13:904889.
- Chaker L, Bianco AC, Jonklaas J, Peeters RP, Hypothyroidism. Lancet. 2017;390:1550–62.
- Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med. 2000;160:526–34.
- 4. Udovcic M, Pena RH, Patham B, Tabatabai L, Kansara A. Hypothyroidism and the Heart. Methodist Debakey Cardiovasc J. 2017;13:55–9.
- Mancini A, Di Segni C, Raimondo S, Olivieri G, Silvestrini A, Meucci E et al. Thyroid Hormones, Oxidative Stress, and Inflammation. Mediators Inflamm. 2016;2016: 6757154.
- 6. Resch U, Helsel G, Tatzber F, Sinzinger H. Antioxidant status in thyroid dysfunction. Clin Chem Lab Med. 2002;40:1132–4.
- Zhao L, Sun Y, Cao R, Wu X, Huang T, Peng W. Non-linear association between composite dietary antioxidant index and depression. Front Public Health. 2022;10:988727.
- Severo JS, Morais JBS, de Freitas TEC, Andrade ALP, Feitosa MM, Fontenelle LC, et al. The Role of Zinc in Thyroid Hormones Metabolism. Int J Vitam Nutr Res. 2019;89:80–8.
- Andrade GRG, Gorgulho B, Lotufo PA, Bensenor IM, Marchioni DM. Dietary Selenium Intake and Subclinical Hypothyroidism: A Cross-Sectional Analysis of the ELSA-Brasil Study. Nutrients. 2018;10.
- Rabbani E, Golgiri F, Janani L, Moradi N, Fallah S, Abiri B, et al. Randomized Study of the Effects of Zinc, Vitamin A, and Magnesium Co-supplementation on Thyroid Function, Oxidative Stress, and hs-CRP in Patients with Hypothyroidism. Biol Trace Elem Res. 2021;199:4074–83.
- 11. Luu HN, Wen W, Li H, Dai Q, Yang G, Cai Q, et al. Are dietary antioxidant intake indices correlated to oxidative stress and inflammatory marker levels? Anti-oxid Redox Signal. 2015;22:951–9.

- Han H, Chen S, Wang X, Jin J, Li X, Li Z. Association of the composite dietary antioxidant index with bone mineral density in the United States general population: data from NHANES 2005–2010. J Bone Min Metab. 2023;41:631–41.
- Wu M, Si J, Liu Y, Kang L, Xu B. Association between composite dietary antioxidant index and hypertension: insights from NHANES. Clin Exp Hypertens. 2023;45:2233712.
- Zhang J, Lu X, Wu R, Ni H, Xu L, Wu W, et al. Associations between composite dietary antioxidant index and estimated 10-year atherosclerotic cardiovascular disease risk among U.S. adults. Front Nutr. 2023;10:1214875.
- Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr Pract. 2012;18:988–1028.
- Wright ME, Mayne ST, Stolzenberg-Solomon RZ, Li Z, Pietinen P, Taylor PR, et al. Development of a comprehensive dietary antioxidant index and application to lung cancer risk in a cohort of male smokers. Am J Epidemiol. 2004;160:68–76.
- O'Kane SM, Mulhern MS, Pourshahidi LK, Strain JJ, Yeates AJ. Micronutrients, iodine status and concentrations of thyroid hormones: a systematic review. Nutr Rev. 2018;76:418–31.
- Lu L, Huang Z, Wang X, Chen J. Interaction Between Dietary Selenium and Zinc Intakes on Hypothyroidism. Biol Trace Elem Res. 2023;201:4667–76.
- Liu S, Lu C, He L, Shan Z, Teng W, Li Y et al. Vitamin E Intake and Prevalence Rates of Thyroid Dysfunction and Autoimmune Thyroiditis: A Cross-Sectional Analysis of NHANES Data. Thyroid. 2024.
- Thomson CD, McLachlan SK, Grant AM, Paterson E, Lillico AJ. The effect of selenium on thyroid status in a population with marginal selenium and iodine status. Br J Nutr. 2005;94:962–8.
- 21. Ma Y, Liu J, Sun J, Cui Y, Wu P, Wei F, et al. Composite dietary antioxidant index and the risk of heart failure: A cross-sectional study from NHANES. Clin Cardiol. 2023;46:1538–43.
- 22. Ma R, Zhou X, Zhang G, Wu H, Lu Y, Liu F, et al. Association between composite dietary antioxidant index and coronary heart disease among US adults: a cross-sectional analysis. BMC Public Health. 2023;23:2426.
- Bergamini C, Cicoira M, Rossi A, Vassanelli C. Oxidative stress and hyperuricaemia: pathophysiology, clinical relevance, and therapeutic implications in chronic heart failure. Eur J Heart Fail. 2009;11:444–52.
- 24. Venditti P, Di Meo S. Thyroid hormone-induced oxidative stress. Cell Mol Life Sci. 2006;63:414–34.
- Bauer M, Glenn T, Pilhatsch M, Pfennig A, Whybrow PC. Gender differences in thyroid system function: relevance to bipolar disorder and its treatment. Bipolar Disord. 2014;16:58–71.
- da Costa VM, Moreira DG, Rosenthal D. Thyroid function and aging: genderrelated differences. J Endocrinol. 2001;171:193–8.
- 27. Walczak K, Sieminska L. Obesity and Thyroid Axis. Int J Environ Res Public Health. 2021;18.
- Liu J, Lu X, Song J, et al. The association between the composite dietary antioxidant index and thyroid functionality among adults in the USA: NHANES 2007–2012. Heliyon. 2024;10(7):e29082. Published 2024 Apr 4.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.