Original Article

Association between dietary carotenoid intakes and the risk of asthma in children and adolescents: evidence from the National Health and Nutrition Examination Survey 2007–2016

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Background: In recent years, the incidence of asthma in children has been increasing. As a chronic disease, in addition to drug treatment, dietary management is also important. However, studies of carotenoids and asthma have shown mixed results. This study aimed to evaluate whether the relationship between carotenoid intake and current asthma holds significant importance.

Methods: We studied 9,118 children aged 6–16 years in the National Health and Nutrition Examination Survey (NHANES) of US from 2007 to 2016, and the relationship of dietary carotenoid and its subgroup with pediatric asthma. Current asthma was assessed by parent-reported, doctor-diagnosed, asthma using a standardized questionnaire. We used multivariate logistic regression to calculate the odds ratio (OR) for current asthma with a 95% confidence interval (CI).

Results: Total carotenoid intake was not associated with the risk of current asthma. Compared with the first quantile, the second quantile of β-cryptoxanthin intake was positively correlated with current asthma (Q2: 1.227; 95% CI: 1.025–1.470; P=0.03). The test of trend showed that, as the α-carotene intake increased, the risk of current asthma showed a decreasing trend, which was very close to the statistic confidence cutoff (Model I: P for trend =0.001; Model II: P for trend =0.003; Model III: P for trend =0.08). In subgroup analysis, family history of asthma interacted with carotenoid intake (P=0.005). The population without a family history of asthma, there were significant negative associations between carotenoid intakes and asthma (quartile 4: Model III: 0.720; 95% CI: 0.549–0.943; P=0.02).

Conclusions: In this study, pediatric current asthma was not related to total carotenoids in our total participants. Total dietary carotenoid intake has a protective effect on children without a family history of asthma. Meanwhile, β-cryptoxanthin intake is positively correlated with asthma.

Keywords: Pediatric asthma; dietary carotenoid; epidemiology; National Health and Nutrition Examination Survey (NHANES)

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Introduction

Asthma is a highly complex, immune-mediated, inflammatory disease (1). In recent years, the prevalence of asthma has increased gradually. Asthma affects as many as 339 million people (2), and poses a public health problem worldwide. In the United States (US), an estimated 24.6 million people, including 6.2 million children, have asthma (3). In 1980, the asthma prevalence in children, was

reported to be 3.5%; 30 years later, that figure had jumped to 9.5% of children aged 0–17 years (4). Asthma is currently among the top 5 chronic conditions contributing to the global burden of disease among children aged 5–14 years. Unfavorable changes in diet have been hypothesized to increase the susceptibility to asthma (5).

In the human diet, carotenoids are found in fruits and vegetables (6), and are described to have anti-oxidant effects that can reduce the incidence of asthma by reducing oxidative stress. Epidemiological studies have shown that total fruit and vegetable intake is inversely associated with the risk of asthma (7). Another study found that the antioxidants found in plant foods contribute to reduced airway inflammation and resulting improvements in forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and lung function (4). Contrastingly, a study from Finland showed that there was a positive, although insignificant, relationship between total intake of dietary carotenoids (α and β) from food and childhood asthma (8).

The relationship between dietary carotenoids and current asthma is controversial. Our objective was to investigate the association of diet carotenoid intake and current asthma in children and adolescents, using data from the National Health and Nutrition Examination Survey (NHANES) [2007–2016], which provided a representative sample of the US population. Consequently, we aimed to determine whether dietary carotenoids are beneficial or detrimental to decreasing the disease burden of asthma.

Highlight box

Key findings

- β-cryptoxanthin intake is positively correlated with pediatric current asthma in the United States.
- In the population without a family history of asthma, there were significant negative associations between total dietary carotenoid intake and pediatric current asthma.

What is known and what is new?

- Dietary carotenoids are related to the occurrence of asthma.
- Our study found that total dietary carotenoid intake has a protective effect on children without a family history of asthma.

What is the implication, and what should change now?

- The balance of carotenoid intake could be of importance to asthma.
- It is important for parents and children to understand the role of dietary carotenoids in asthma and that they need to be included in the management of pediatric current asthma.

We present this article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-24-117/rc).

Methods

Data source

The United States National Health and Nutrition Examination Survey (NHANES) is a continuous cross-sectional survey of the US non-institutionalized civilian population conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) (9). Information about the NHANES cross-sectional study design and the methods of participant selection are publicly available through the CDC.gov website.

NHANES protocols were approved by the Institutional Review Boards of the NCHS and CDC and informed consent was obtained from all participants' parents/legal guardians (10). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Details of the International Review Board (IRB) approval are available on http://www.cdc.gov/nchs/nhanes/irba98.htm.

Participants

In the present study, we have analyzed the participants from 5 cycles of NHANES (including 2007–2008, 2009–2010, 2011–2012, 2013–2014, and 2015–2016). A total of 10,838 children and adolescents aged 6–16 years participated in the study. We excluded 11 participants who had missing data on the asthma questionnaire, 1,391 participants who had missing carotenoid intake, and 152 participants with missing data for self-reported family history of asthma. Additionally, 166 participants within the extreme 1% percentiles of total carotenoid intake were excluded to reduce the effects of implausible extreme values of carotenoid intake. After exclusions, our study contained a total of 9,118 children and adolescents (4,624 males and 4,494 females) (*Figure 1*).

Asthma assessment

Current asthma was defined as a positive response to both of the following questions: MCQ010 "Has a doctor or other health professional ever told you that you have asthma: yes/no" and MCQ040 "Had asthma attack in past year: yes/

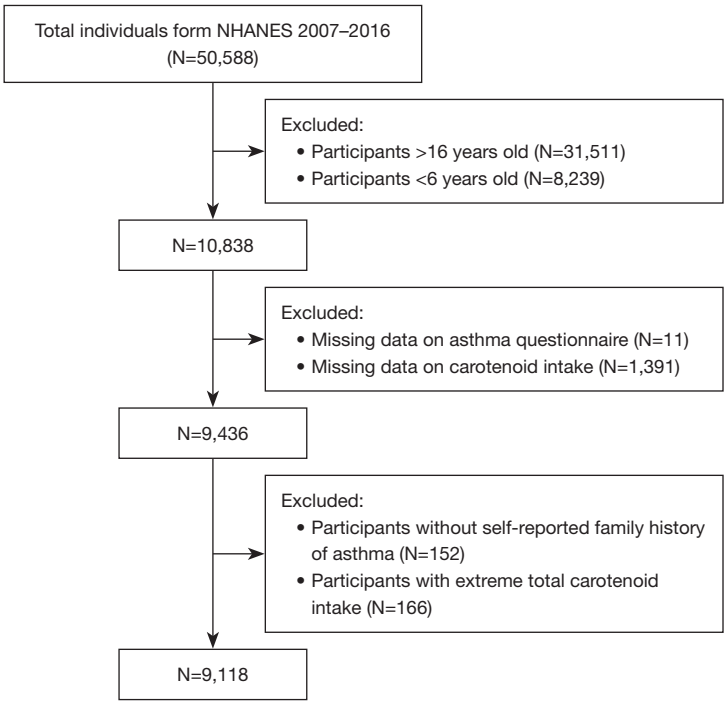

Figure 1 Flow chart of the current study. NHANES, National Health and Nutrition Examination Survey.

no" (11). Participants who had neither an asthma diagnosis nor an asthma attack in the previous year were selected as control cases.

Dietary carotenoid intakes assessment

In cycles of the NHANES 2007–2016, dietary intakes were estimated using data from 2 separate 24-h dietary recalls performed. The first dietary recall was collected in-person during the NHANES visit, whereas the second recall was collected by telephone 3–10 days later (12). Our primary intake of interest was carotenoid, including α-carotene, β-carotene, β-cryptoxanthin, lycopene, and lutein with zeaxanthin. We defined the sum of the aforementioned 5 carotenoids as the total carotenoid. Dietary carotenoid intakes were defined as the average dietary intake data of the 2 separate 24-h dietary recall interviews. Although participants were also queried about supplement use for the these 24-h periods with respect to supplement intake of lycopene and lutein/zeaxanthin, data were available for only 28 participants. Therefore, our analysis focused on dietary intake.

Other covariates

Potential confounders were identified from the existing literature. The following covariates were collected: age (6–11 and 12–16 years), gender (male and female), ethnicity (Mexican American, non-Hispanic White, non-Hispanic Black, other Hispanic, and other race), family poverty-income ratio (PIR), whether the mother smoked when pregnant, tobacco smoke exposure, body mass index standard deviation scores (BMI-Z scores), self-reported family history of asthma, vitamins A, C, and E, and dietary fiber intake.

PIR is computed by the NCHS and is a ratio of family income to the poverty threshold established by the US Census Bureau with a range from 0 to 5. Values from 0 to 1.35 were considered "poor", 1.36–1.85 were considered "nearly poor", and values of 1.86+ were considered "not poor" for classification (13). Tobacco smoke exposure was quantified based on serum cotinine concentration as follows: cotinine level of <0.05 ng/mL was defined as unexposed or non-smoker: 0.05–10 ng/mL was defined as exposed but not an active smoker (AS) [i.e., second-hand smoke (SHS)], whereas >10 ng/mL was defined as an AS (14).

BMI was calculated as body weight (kg) divided by the square of height (m^2). Standard deviations scores, known as BMI-Z scores, of weight, height, and BMI for sex and age were calculated using World Health Organization (WHO) and CDC calculators (15). Vitamins A, C, and E, and dietary fiber intake were also obtained from the average of two individual 24-hour dietary recall interviews.

Statistical analysis

In this study, categorical variables were expressed as frequency (N) and percentage (%), whereas mean ± SD or medians (Q1, Q3) were used to present the continuous variables. Categorical variables were compared using the chi-squared test among the different groups. Continuous variables were compared using the one-way analysis of variance (ANOVA) (normal distribution), Kruskal-Wallis H (skewed distribution) among the different groups. Multivariate logistic regression analysis was used to explore the relationships between dietary carotenoid intake and current asthma. The adjustment of covariate was determined by the following principle: when added to this model, the matched odds ratio changed by at least 10%. Model I was adjusted for none. Model II was adjusted for age, gender, race, and vitamin E. Model III was adjusted for age, gender, race, vitamin E, BMI-Z scores, tobacco smoke exposure, whether the mother smoked when pregnant, and self-reported family history of asthma. Tests for trend (P for trend) were performed by entering the quartiles of carotenoids intake as a continuous variable and rerunning the corresponding regression models. Furthermore, smooth curve fitting was applied to examine linear or non-linear relationship between them. Finally, subgroup analyzes separately stratified on age, gender, and self-reported family history of asthma were also performed with the stratification variable excluded from the model, and examined the interaction between each factor and the relationship of carotenoid intake and the risk of current asthma.

All analyses were performed with the statistical software packages R (http://www.R-proje ct.org; The R Foundation for Statistical Computing, Vienna, Austria) and EmpowerStats (http://www.empowersta ts.com; X&Y Solutions, Inc, USA).

Results

Participant characteristics

A total of 9,118 participants were included in this study. The characteristics of the study population are shown in *Table 1*. All participants were divided into either an asthma group or a non-asthma group according to whether they had current asthma or not.

In the asthma group, there were 971 males (56.16%) and 758 females (43.84%). The prevalence of asthma in boys was significantly higher than that in girls (P<0.001). The prevalence of pediatric asthma varied by race (P<0.001), with the most likely highest prevalence rate of pediatric asthma observed among the non-Hispanic Black race. Among tobacco exposures, ASs had the highest incidence, followed by exposed but not ASs, and unexposed or non-smokers had the lowest prevalence of asthma (P<0.001). In children born to mothers who smoked while pregnant, asthma was more prominent than among those born to non-smoking mothers (P<0.001). The prevalence of asthma with family history was significantly higher than that without family history in this study (P<0.001). Additionally, vitamin E and asthma medication use in the asthma group was higher than that non-asthma group (P<0.001). The BMI-Z scores of the asthma group was lower than the non-asthma group (P<0.001). There were no differences in PIR, dietary fiber, vitamin C, and vitamin A between the asthma group and non-asthma group.

Association between dietary carotenoid intakes and asthma

The relationship between dietary carotenoid intakes and the prevalence of asthma is shown in *Table 2*. Total carotenoids were not associated with the risk of asthma. In Model I, the highest intake of α-carotene was negatively correlated with current asthma [quartile 4: 0.837; 95% confidence interval (CI): 0.720–0.974; P=0.02]. In Model II, the results remained stable and statistically (quartile 4: 0.851; 95% CI: 0.729–0.993; P=0.04). In Model III, α-carotene was not associated with current asthma. At the same time, we conducted a trend test. In Model I and Model II, as the α-carotene intake increased, the risk of current asthma showed a decreasing trend (Model I: P for trend =0.001; model II: P for trend =0.003). In Model III, this trend was still present, but the correlation was weaker (P for trend =0.08). We performed smooth curve fitting and the results showed that no nonlinear relationship was found (*Figure 2*). In Model III, compared with the first quantile, the second quantile of β-cryptoxanthin was positively correlated with current asthma (Q2: 1.227; 95% CI: 1.025–1.470; P=0.03). However, in the trend test, β-cryptoxanthin was not associated with current asthma. β-carotene, lycopene, and lutein/zeaxanthin intakes were not

Table 1 Characteristics of participants by asthma, National Health and Nutrition Examination Survey 2007–2016 (N=9,118)

Characteristics	Without asthma (N=7,389)	With asthma (N=1,729)	P value
Age (years)			0.007
6–11	4,384 (59.33)	965 (55.81)	
12–16	3,005 (40.67)	764 (44.19)	
Gender			<0.001
Male	3,653 (49.44)	971 (56.16)	
Female	3,736 (50.56)	758 (43.84)	
Race			<0.001
Mexican American	1,861 (25.19)	302 (17.47)	
Non-Hispanic Black	1,689 (22.86)	542 (31.35)	
Non-Hispanic White	2,134 (28.88)	466 (26.95)	
Other Hispanic	867 (11.73)	230 (13.30)	
Other race	838 (11.34)	189 (10.93)	
PIR			0.21
≤1.35	3,126 (45.60)	784 (48.01)	
1.36–1.85	850 (12.40)	190 (11.64)	
≥1.86	2,879 (42.00)	659 (40.36)	
Total carotene (mcg)	3,833.00 (1,469.00, 8,476.00)	3,934.00 (1,503.00, 8,957.00)	0.34
α-carotene (mcg)	22.00 (4.00, 76.00)	20.00 (3.00, 62.00)	0.009
β-carotene (mcg)	389.00 (177.00, 1,013.00)	393.00 (180.00, 952.00)	0.61
β-Cryptoxanthin (mcg)	23.00 (5.00, 82.00)	21.00 (5.00, 77.00)	0.042
Lycopene (mcg)	1,980.00 (11.00, 5,200.00)	2,171.00 (10.00, 5,820.00)	0.19
Lutein zeaxanthin (mcg)	471.00 (248.00, 853.00)	484.00 (258.00, 870.00)	0.34
Dietary fiber (gm)	14.17±7.72	13.99±7.73	0.38
Vitamin E (mg)	6.64±4.52	7.21±5.60	<0.001
Vitamin C (mg)	53.50 (21.60, 108.80)	54.50 (21.40, 114.70)	0.450
Vitamin A (mg)	569.33±430.65	565.02±421.92	0.706
BMI-Z scores	−0.84 (−1.18, −0.36)	−0.66 (−1.10, −0.09)	<0.001
Tobacco smoke exposure*			<0.001
Unexposed or non-smoker	3,740 (59.89)	724 (49.39)	
Exposed but not an active smoker	2,394 (38.33)	703 (47.95)	
Active smoker	111 (1.78)	39 (2.66)	
Mother smoked when pregnant*			<0.001
No	5,992 (89.31)	1,309 (84.45)	
Yes	717 (10.69)	241 (15.55)	
Self-reported family history of asthma			<0.001
No	5,504 (74.49)	703 (40.66)	
Yes	1,885 (25.51)	1,026 (59.34)	

Categorical variables were expressed as frequency (N) and percentage (%); continuous variables were expressed as mean ± SD or medians (Q1, Q3). *, 1,407 cases of missing data in the tobacco smoke exposure group, 859 cases of missing data in the mother smoked when pregnant group. PIR, family poverty-income ratio; BMI-Z scores, body mass index standard deviation scores; SD, standard deviation.

Table 2 ORs (95% CIs) for relationship between current asthma and carotenoids intakes in different models among US children and adolescents

Variables	Cut-off (mcg)	Model I		Model II		Model III	
		OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Total carotene							
Quartile 1	69–1,484	Reference		Reference		Reference	
Quartile 2	1,485–3,853	1.011 (0.871, 1.173)	0.88	1.009 (0.868, 1.172)	0.91	1.034 (0.864, 1.239)	0.71
Quartile 3	3,854–8,551	0.997 (0.859, 1.157)	0.97	0.986 (0.848, 1.148)	0.86	0.995 (0.828, 1.194)	0.95
Quartile 4	8,552–45,230	1.076 (0.928, 1.247)	0.33	1.000 (0.857, 1.166)	0.99	0.952 (0.791, 1.146)	0.61
P for trend		0.29		0.96		0.46	
α-carotene							
Quartile 1	0–3	Reference		Reference		Reference	
Quartile 2	4–21	1.032 (0.892, 1.195)	0.67	1.040 (0.897, 1.206)	0.60	1.011 (0.845, 1.211)	0.90
Quartile 3	22–71	1.058 (0.914, 1.224)	0.45	1.060 (0.914, 1.230)	0.44	1.175 (0.982, 1.405)	0.08
Quartile 4	72–12,188	0.837 (0.720, 0.974)†	0.02†	0.851 (0.729, 0.993)†	0.04†	0.917 (0.760, 1.106)	0.36
P for trend		0.001†		0.003†		0.08	
β-carotene							
Quartile 1	0–177	Reference		Reference		Reference	
Quartile 2	178–391	1.017 (0.877, 1.180)	0.82	1.014 (0.873, 1.178)	0.86	1.080 (0.901, 1.295)	0.40
Quartile 3	392–1,005	1.086 (0.937, 1.258)	0.27	1.055 (0.907, 1.226)	0.49	1.067 (0.888, 1.283)	0.49
Quartile 4	1,006–29,383	0.970 (0.836, 1.127)	0.69	0.943 (0.807, 1.101)	0.26	1.063 (0.881, 1.284)	0.79
P for trend		0.44		0.46		0.52	
β-cryptoxanthin							
Quartile 1	0–4	Reference		Reference		Reference	
Quartile 2	5–22	1.088 (0.940, 1.259)	0.26	1.076 (0.928, 1.247)	0.33	1.227 (1.025, 1.470)†	0.03†
Quartile 3	23–80	0.933 (0.803, 1.085)	0.37	0.928 (0.797, 1.080)	0.34	1.031 (0.856, 1.242)	0.75
Quartile 4	81–6,077	0.937 (0.806, 1.089)	0.39	0.919 (0.788, 1.071)	0.28	1.079 (0.895, 1.301)	0.42
P for trend		0.15		0.10		0.86	
Lycopene							
Quartile 1	0–10	Reference		Reference		Reference	
Quartile 2	11–2,014	0.921 (0.793, 1.070)	0.28	0.939 (0.807, 1.092)	0.41	0.926 (0.772, 1.112)	0.41
Quartile 3	2,015–5,282	0.982 (0.847, 1.140)	0.81	0.985 (0.848, 1.144)	0.84	0.917 (0.765, 1.099)	0.35
Quartile 4	5,283–42,734	1.089 (0.941, 1.261)	0.25	1.038 (0.893, 1.207)	0.62	0.978 (0.816, 1.172)	0.81
P for trend		0.06		0.33		0.87	
Lutein zeaxanthin							
Quartile 1	1–249	Reference		Reference		Reference	
Quartile 2	250–472	1.093 (0.942, 1.269)	0.24	1.084 (0.932, 1.261)	0.30	1.161 (0.968, 1.393)	0.11
Quartile 3	473–855	1.075 (0.925, 1.248)	0.34	1.042 (0.895, 1.215)	0.59	1.087 (0.903, 1.309)	0.38
Quartile 4	856–25,000	1.102 (0.949, 1.279)	0.20	1.019 (0.872, 1.192)	0.81	1.054 (0.871, 1.276)	0.59
P for trend		0.33		0.86		0.94	

Model I was adjusted for none. Model II was adjusted for age, gender, race, vitamin E. Model III was adjusted for age, gender, race, vitamin E, BMI-Z scores, tobacco smoke exposure, whether mother smoked when pregnant, and self-reported family history of asthma. †, significant values. OR, odds ratio; CI, confidence interval.

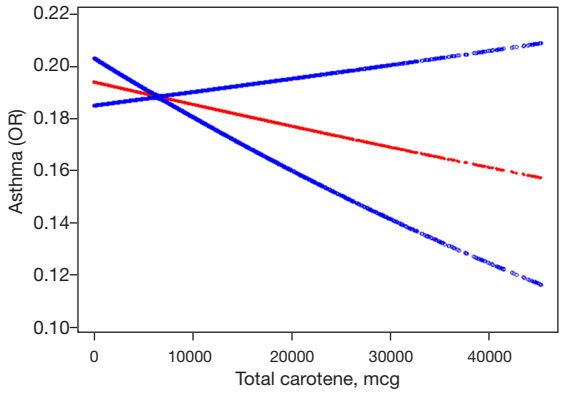

Figure 2 Association between current asthma and total carotene intakes. The red line and blue line represent the estimated values and their corresponding 95% confidence interval. All adjusted for age, gender, race, vitamin E, BMI-Z scores, tobacco smoke exposure, whether mother smoked when pregnant, and self-reported family history of asthma. OR, odds ratio; BMI-Z scores, body mass index standard deviation scores.

associated with asthma risk.

Subgroup analyses

Association between dietary carotenoid intakes and the risk of current asthma by age, gender, and self-reported family history of asthma

Table 3 shows that there was no significant relationship between dietary carotenoid intakes and the risk of asthma in participants of different ages and genders. Family history of asthma was shown to interact with carotenoid intake (P=0.005). In Model II and Model III, the highest intake of total carotenoids was negatively associated with asthma in participants without a family history of asthma (quartile 4: Model II: 0.760; 95% CI: 0.602–0.961; P=0.02, Model III: 0.720; 95% CI: 0.549–0.943; P=0.02). In participants with a family history of asthma, high intake of total carotenoids was positively associated with asthma in Model I and Model II (quartile 4: Model I: 1.398; 95% CI: 1.131–1.728; P=0.002, Model II: 1.301; 95% CI: 1.039–1.629; P=0.02). In Model III, there was no difference (P=0.13).

According to age, gender, and self-reported family history of asthma, stratified analyses were performed to further investigate the relationship between total carotenoid intake and the risk of current asthma in each subgroup, shown in Tables S1-S5. As shown in Table S4, family history of asthma interacted with lycopene (P=0.001). High intake of total lycopene was positively associated with asthma in Model I and Model II (quartile 4: Model I: 1.318; 95% CI: 1.066–1.629; P=0.01, Model II: 1.250; 95% CI: 1.004–1.558; P=0.046). In Model III, lycopene had no association with asthma. Smooth curve fitting revealed no nonlinear relationship, as shown in Figures S1-S5.

Discussion

Asthma is a common chronic disease that is characterized by chronic airway inflammation and airway hyperresponsiveness (16). Physiological damage caused by oxidative stress through reactive oxygen species (ROS) attack plays an important role in the chronic inflammation of asthma (17). Carotenoids are a group of more than 750 pigments that are synthesized organically by plants, algae, and photosynthetic microorganisms (6). The majority of the 40–50 carotenoids found in the human diet are found in fruits and vegetables (18). The most familiar dietary carotenoids comprise α-carotene and β-carotene (oranges, carrots, and green leafy vegetables), zeaxanthin and lutein (corn and green leafy vegetables), β-cryptoxanthin (citrus and watermelon), lycopene (tomato), and zeaxanthin (6,19). Carotenoids have antioxidants that scavenge free radicals in order to prevent oxidative stress and repair the effects of oxidation and cellular damage. The lungs are exposed to endogenous and environmental oxidants, which can result in oxidative stress, pulmonary dysfunction, and asthma (4,20).

In this study, total carotenoids were not associated with the risk of asthma. We found that in children and adolescents, in Model I and Model II, α-carotene intake was negatively correlated with asthma (Model I: P for trend =0.001; Model II: P for trend =0.003). In model III, α-carotene intake was also negative, but weakly correlated with asthma (P for trend =0.08). A national analysis that used data from the NHANES [2007–2012] found that all carotenoid intakes were associated with lower odds of having current asthma (16).

A randomized control trial analysis conducted among 137 adult patients with asthma demonstrated that those assigned to a low versus a high fruit and vegetable (F&V) diet (<3 *vs.* ≥7 serves of F&V per day) for 14 weeks had a 2.26-fold increased risk of an asthma exacerbation (21). Extending these observations, they reported that the high F&V diet group (63.6%) had significantly fewer cases with ≥2 asthma exacerbations than the control group (88%) in children with asthma following a 6-month high F&V dietary intervention. Fruit and vegetables are high in antioxidants and anti-

Table 3 Stratified analyses of the relationship between current asthma and total carotene intakes by age, gender, and self-reported family history of asthma

Variables	Model I		Model II		Model III		P for interaction
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	
Age							0.21
6–11 years							
Quartile 1	Reference		Reference		Reference		
Quartile 2	0.908 (0.745, 1.106)	0.34	0.902 (0.738, 1.102)	0.31	0.914 (0.724, 1.154)	0.45	
Quartile 3	1.000 (0.822, 1.216)	0.99	0.970 (0.795, 1.185)	0.77	0.991 (0.785, 1.252)	0.94	
Quartile 4	0.988 (0.810, 1.204)	0.90	0.901 (0.733, 1.108)	0.32	0.895 (0.703, 1.138)	0.37	
12–16 years							
Quartile 1	Reference		Reference		Reference		
Quartile 2	1.179 (0.940, 1.478)	0.15	1.171 (0.933, 1.471)	0.17	1.257 (0.942, 1.677)	0.12	
Quartile 3	0.995 (0.790, 1.252)	0.96	0.992 (0.786, 1.253)	0.95	0.976 (0.724, 1.315)	0.87	
Quartile 4	1.195 (0.959, 1.491)	0.11	1.140 (0.904, 1.439)	0.27	1.029 (0.765, 1.383)	0.85	
Gender							0.60
Male							
Quartile 1	Reference		Reference		Reference		
Quartile 2	1.052 (0.856, 1.294)	0.63	1.053 (0.854, 1.298)	0.63	1.035 (0.806, 1.328)	0.79	
Quartile 3	1.092 (0.890, 1.338)	0.40	1.100 (0.894, 1.353)	0.37	1.078 (0.841, 1.381)	0.55	
Quartile 4	1.098 (0.897, 1.343)	0.36	1.048 (0.848, 1.294)	0.67	0.950 (0.738, 1.224)	0.69	
Female							
Quartile 1	Reference		Reference		Reference		
Quartile 2	0.958 (0.773, 1.188)	0.70	0.964 (0.777, 1.197)	0.74	1.036 (0.797, 1.347)	0.79	
Quartile 3	0.873 (0.700, 1.089)	0.23	0.866 (0.693, 1.084)	0.21	0.904 (0.687, 1.190)	0.47	
Quartile 4	1.019 (0.819, 1.267)	0.87	0.971 (0.774, 1.218)	0.80	0.973 (0.739, 1.282)	0.85	
Self-reported family history of asthma							0.005†
No							
Quartile 1	Reference		Reference		Reference		
Quartile 2	0.883 (0.707, 1.104)	0.28	0.880 (0.703, 1.101)	0.26	0.871 (0.673, 1.126)	0.29	
Quartile 3	1.033 (0.833, 1.281)	0.77	1.014 (0.815, 1.261)	0.90	0.965 (0.750, 1.242)	0.78	
Quartile 4	0.839 (0.670, 1.052)	0.13	0.760 (0.602, 0.961)†	0.02†	0.720 (0.549, 0.943)†	0.02†	
Yes							
Quartile 1	Reference		Reference		Reference		
Quartile 2	1.223 (0.986, 1.517)	0.07	1.200 (0.965, 1.493)	0.10	1.231 (0.956, 1.585)	0.11	
Quartile 3	1.041 (0.836, 1.297)	0.72	1.005 (0.804, 1.257)	0.96	1.025 (0.790, 1.331)	0.85	
Quartile 4	1.398 (1.131, 1.728)†	0.002†	1.301 (1.039, 1.629)†	0.02†	1.225 (0.944, 1.590)	0.13	

Each subgroup analysis adjusted for all other variables except its own. Model I was adjusted for none. Model II was adjusted for age, gender, race, vitamin E. Model III was adjusted for age, gender, race, vitamin E, BMI-Z scores, tobacco smoke exposure, whether mother smoked when pregnant, and self-reported family history of asthma. †, significant values. OR, odds ratio; CI, confidence interval.

inflammatory phytochemicals, including carotenoids and other biologically active substances (7).

Antioxidant withdrawal resulted in increased airway neutrophils and upregulation of inflammatory and immune response genes in sputum cells, including the innate immune receptors TLR2, IL1R2, CD93, and ANTXR2, the innate immune signaling molecules IRAK2, IRAK3, and MAP3K8, and neutrophil proteases MMP25 and CPD (7). Antioxidants can reduce oxidative stress and potentially reduce asthmatic symptoms (4).

The relationship between β-cryptoxanthin and asthma is exactly the opposite. We found that, compared with the first quantile, the second quantile of β-cryptoxanthin intake is positively correlated with asthma (quartile 2: 1.227; 95% CI: 1.025–1.470; P=0.03). Some studies (6,22,23) found that β-cryptoxanthin is inversely related to current asthma. A study showed that serum β-cryptoxanthin was negatively correlated with asthma in US adults (OR =0.80; 95% CI: 0.65–0.98, P for trend =0.064) (22). A review reported that β-cryptoxanthin can improve pulmonary function, and β-cryptoxanthin was positively related to forced expiratory volume (FEV) and FVC (6). In addition, the increased risk of asthma was been found to be associated with lower serum β-cryptoxanthin levels (23). β-cryptoxanthin may regulate pulmonary function through antioxidant effects, thereby reducing the risk of asthma. However, we found no protective effect of β-cryptoxanthin intake on asthma. As the molecular mechanism is currently unclear, further research is needed on the relationship between β-cryptoxanthin and asthma.

We found that family history of asthma interacts with carotenoid intake (P=0.005). In the population without a family history of asthma, in Model III, there were significant negative associations between the highest total carotenoid intakes and asthma (0.720; 95% CI: 0.549–0.943; P=0.02). In the Avon Longitudinal Study of Parents and Children, evidence was found of a lower risk of asthma with higher intakes of carotenoid intakes in children without a paternal history of atopy, but not in those with one (24). This result may be related to the pathogenesis of asthma. We know that pediatric asthma is accompanied by allergic diseases and increased family history. Total carotenoids mainly play an antioxidant role, so it has no protective effect on children and adolescents with asthma predominantly caused by nonoxidative stress damage.

Strengths and limitations of this study

Our study has several strengths. We had high statistical power (9,118 cases) to study pediatric asthma. A larger, nationally representative NHANES database was used to investigate the association between individual and combined carotenoid intake and asthma risk. We also adjusted for more potential confounders than in previous studies. This study also had some limitations. First, we used a validated food frequency questionnaire (FFQ) and few previous studies have estimated the total intake of carotenoids from foods. Memory biases can occur, and it is not clear whether the reported information was representative of a long-term diet or the diet at the time of the survey; the study lacked more consistent data on participants' serum carotenoid levels. Second, it is not clear whether carotenoid intake increases the risk of asthma or whether carotenoid intake is altered by the disease after an asthma attack. Therefore, we could not establish a causal relationship between carotenoid intake and asthma risk. The molecular and physiological mechanisms behind it need to be further studied and clarified. In addition, similar to other large, national, population-based studies, we used the self-report scale to identify participants with asthma; it cannot be excluded that there were some misclassifications in our asthma diagnosis. Although we adjusted for some confounders, some potential unknown confounders may have influenced our results.

Conclusions

In this study, we found that there was no significant correlation between total dietary carotenoid and asthma in total participants. Total dietary carotenoids intakes have a protective effect on children without a family history of asthma. Meanwhile, we found that β-cryptoxanthin intake is positively correlated with asthma. Thus, the balance of carotenoid intake could be of importance to asthma. This is an appealing strategy, which is likely to be widely accepted and adopted by children and their caregivers. Further longitudinal studies are needed to determine the causal relationship between carotenoid intake and current asthma.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-24-117/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-24-117/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. NHANES protocols were approved by the Institutional Review Boards of the NCHS and CDC and informed consent was provided by all participants' parents/legal guardians. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Details of the IRB approval are available on http://www.cdc.gov/nchs/nhanes/irba98.htm.

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