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Original Research

Associations of dietary vitamin A and C intake with asthma, allergic rhinitis, and allergic respiratory diseases

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ABSTRACT

BACKGROUND/OBJECTIVES: Asthma and allergic rhinitis (AR) are closely related and considered as allergic respiratory diseases (ARD), and their prevalence has recently increased. Data on the association of dietary antioxidant vitamin intake with asthma and AR in adults are limited. The present study aimed to investigate the associations of vitamin A and C intake with asthma, AR, and all cases of both diseases in young adults who participated in a cross-sectional national survey, with the use of high-sensitivity C-reactive protein (hs-CRP) level as an effect modifier.
SUBJECTS/METHODS: This study included 6,293 male and female adults aged 20–49 years from the Korea National Health and Nutrition Examination Survey (KNHANES) conducted between 2016 and 2018. The questionnaire-based reports on asthma and AR diagnosis were used to determine outcome variables. Further, 24-h recall data on dietary vitamin A and C, carotene, and retinol intake were acquired. Logistic regression analysis was performed to calculate odds ratios (ORs) and 95% confidence interval (CI).
RESULTS: Dietary vitamin C intake was inversely associated with asthma prevalence among participants with hs-CRP levels (≥ 1 mg/L); the OR of asthma prevalence was 0.27 (95% CI, 0.08–0.84) for participants with vitamin C consumption ≥ 75 mg/day compared with those consuming < 20 mg/day. Similar association analyses limiting to non-users of dietary supplements were performed to rule out the potential effects of supplement intake on the outcomes; results showed a stronger association. However, the association between vitamin C and asthma was not significant in participants with hs-CRP levels < 1 mg/L; the OR of asthma was 1.44 (95% CI, 0.66–3.16) for participants with vitamin C consumption ≥ 75 mg/day compared with those consuming < 20 mg/day. Vitamin C intake was not associated with AR. Moreover, there was no association between vitamin A intake and neither asthma nor AR.
CONCLUSIONS: These findings suggest that higher vitamin C intake may play a potential role in reducing asthma prevalence. Nevertheless, further studies should be conducted to evaluate whether this association is causal.

Keywords: Vitamin A; ascorbic acid; asthma; rhinitis, allergic

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Conflict of Interest
The authors declare no potential conflicts of interests.

Author Contributions
Conceptualization: García-García C, Kim M, Baik I; Formal analysis: García-García C, Kim M; Investigation: García-García C, Kim M, Baik I; Supervision: Baik I; Writing - original draft: García-García C, Baik I; Writing - review & editing: García-García C, Kim M, Baik I.

INTRODUCTION

The prevalence of allergic respiratory diseases (ARD) such as allergic rhinitis (AR) and asthma has markedly increased worldwide. Approximately, 20–30% of the world's population has one or more allergic diseases, of which ARD is the major contributor [1,2]. In a previous study, which analyzed the 10-yrs prevalence of ARD in the Korean population, a similar increasing trend in the AR prevalence was observed among adults whereas the asthma prevalence was steady, or it has been decreasing gradually among all age groups [3]. Additionally, to health risks, the increased incidence of these respiratory diseases implies an economic burden. In Korea, the total annual expenses for medications and health care provision and the indirect costs were approximately $273 million for AR and $646 million for asthma [4,5].

The development of asthma and AR, which are common comorbidities, is related to several environmental risk factors including air pollution and urbanization with the disappearance of rural environment and better hygiene [6,7]. Dietary factors, particularly antioxidant vitamin intake, can possibly have protective effects. Some epidemiological studies have revealed an inverse association between dietary vitamin A and C intake and asthma prevalence and the protective effects of these antioxidants on pulmonary function [8-10]. However, data on AR are limited and still contrasting. Vitamin C intake was found to be inversely associated with the prevalence of AR and its symptoms among children [11]. Nevertheless, the plasma vitamin A and C levels were not associated with AR among adults [12]. Due to the effects of early-life exposure to allergen (allergic sensitization) on the prognosis of AR [13], data on young and old populations may be inconsistent. In fact, younger individuals may be more affected by AR than elderly ones [3]. Information on the associations between vitamin A and C intake and asthma and AR among young adults is limited, and there are only few studies investigating both diseases. Further, the impact of high-sensitivity C-reactive protein (hs-CRP), an indicator of systemic inflammation and asthma severity [14], on the association is unclear.

The present study aimed to investigate the association of dietary intake of antioxidant vitamins including vitamin A and C with individual and combined prevalence of asthma and AR among young Korean adults who participated in the Korea National Health and Nutrition Examination Survey (KNHANES). In further analysis, serum hs-CRP was considered to be an effect modifier.

SUBJECTS AND METHODS

Participants

This study used data from the 7th survey period (year 2016–2018) of KNHANES, which is a population-based cross-sectional survey study (https://knhanes.kdca.go.kr/knhanes/sub03/sub03_02_05.do) conducted by the Korea Disease Control and Prevention Agency. The participants of KNHANES were noninstitutionalized Korean citizens residing in South Korea who signed an informed consent form [15]. The KNHANES questionnaires differed slightly across the survey periods. However, identical variables such as exposures and outcomes of interest were included in the 7th survey period data, which were utilized in this study. Of 24,269 participants included in the complex stratified sampling design (n = 8,150 in year 2016, n = 8,127 in year 2017, and n = 7,992 in year 2018), only young adults (aged 20−49 years) were included in this research. Thus, the data of 6,293 participants (2,635 men and 3,658 women) were used in the analysis after excluding those with missing data regarding

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the medical diagnosis of asthma and AR and those with hs-CRP values > 10 mg/L, which indicated a possible infection. The present study was approved by the Institutional Review Board of Kookmin University (approval number: KMU-202102-HR-260).

Definition of asthma, AR, and ARD

The main outcomes were asthma and AR, and the presence of these conditions was determined using the survey question ("Have you ever been diagnosed with asthma [or AR] by a doctor?") and was used as prevalent cases [3]. ARD included all cases of allergic asthma and AR. However, KNHANES did not provide detailed information on either allergic or non-allergic asthma. Thus, this study analyzed all cases of asthma and AR.

Dietary antioxidant vitamin intake and potential confounding variables

Information on the dietary intake of antioxidant vitamins was collected via 1-day 24-h recall, and only data on vitamin A and C, carotene, and retinol intake were available.

Data on demographic and health-related characteristics including age, sex, body mass index (BMI, kg/m^2), residential district, household income level, educational level, type of residence, smoking status, alcohol consumption, perceived depressive mood, and emotional stress, sleep duration, use of dietary supplements (vitamins and minerals and functional foods), total calorie intake, atopic dermatitis diagnosis, and serum hs-CRP level, which was determined using a chemistry analyzer, were collected as potential confounding variables based on previous studies [8,12].

Statistical analysis

Descriptive statistics were obtained with consideration of sampling weight and were presented as mean ± standard error or percentage. Statistical differences between groups were evaluated using the Student's *t*-test for continuous variables and the χ^2 test for categorical variables. To analyze the association between vitamin intake and the prevalence of asthma, AR, and ARD, logistic regression analysis was performed with consideration of sampling weight and potential confounding variables to obtain odds ratios (ORs) and 95% confidence interval (CI). Vitamin A and C consumption was categorized with consideration of the estimated average requirements (450 µg RAE/day for vitamin A and 75 mg/day for vitamin C) based on the 2020 Dietary Reference Intakes for Koreans (https://www.mohw.go.kr/react/jb/sjb030301vw.jsp?PAR_MENU_ID=03&MENU_ID=032901&CONT_SEQ=362385) and the distribution of cases and non-cases across the categories. The estimated average intake requirement of carotene and retinol was not established. Hence, its consumption was categorized by rounding off quartile cutoff points. In the models, sex, residential district (urban, rural), household income level (low and lower-middle, upper middle, and high), educational level (middle school, high school, and above university level), type of residence (detached house, apartment, and others), smoking status (abstainer, former smoker, and current smoker [2 categories: < 0.5, ≥ 0.5 pack/day]), alcohol consumption (abstainer, former drinker, and current drinker [3 categories: ≤ 1 glass/day in women or ≤ 2 glasses/day in men, 1–3 glasses/day in women or 2–4 glasses/day in men, and > 3 glasses/day in women or > 4 glasses/day in men]), perceived depressive mood (yes, no), perceived emotional stress (low, high), average sleep duration (< 7, 7–9, and > 9 h), and use of dietary supplements (no, yes), and atopic dermatitis diagnosis were considered as categorical covariates and age, BMI, total calorie intake, and hs-CRP levels as continuous variables. Similar association analyses limited to non-users of dietary supplements (restriction method to control confounding) were performed to rule out the potential effects of supplement intake on the outcomes.

Statistical analyses were performed with SAS v.9.4 software (SAS Institute Inc., Cary, NC, USA). P-values of < 0.05 were considered statistically significant.

RESULTS

Characteristics of the study participants

Among the study participants, 158 (2.5%) were diagnosed with asthma and 1,296 (20.6%) with AR. In total, 1,372 participants presented one of these diseases. According to asthma or AR diagnosis, the characteristics of the study participants were compared (**Table 1**). Participants with asthma or AR were more likely to be women, younger, have a greater BMI, non-smokers (abstainers or former smokers), have a lower household income and a higher perceived emotional stress or depressive mood, and not use dietary supplements.

Associations between vitamin intake and asthma and AR

Table 2 shows the associations between dietary vitamin A and C intake and asthma and AR. There was no significant association between vitamin A and C intake and asthma, AR, and all cases of these diseases. Further, there was an increase in the multivariate OR of the association between the upper category of vitamin A intake and asthma. Nevertheless, the result was not significant (OR, 1.21; 95% CI, 0.72–2.02).

Associations stratified according to hs-CRP levels

Table 3 shows the associations stratified according to hs-CRP levels. The results showed no significant associations between vitamin A intake and asthma, AR, and all cases of these diseases. However, among the participants with elevated hs-CRP levels (≥ 1 mg/L), a higher vitamin C intake was significantly associated with a lower asthma prevalence. The OR of asthma prevalence was 0.27 (95% CI, 0.08–0.84; $P < 0.05$) in participants with vitamin C consumption ≥ 75 mg/day compared with those consuming vitamin C < 20 mg/day. No significant association between vitamin C intake and asthma was observed in participants with hs-CRP levels < 1 mg/L; multivariate OR was 1.44 (95% CI, 0.66–3.16). Vitamin C intake was not associated with AR prevalence regardless of hs-CRP levels.

Associations stratified according to hs-CRP levels in non-users of dietary supplements

Table 4 shows the results of further analyses limited to participants who did not use dietary supplements. Similar to the results depicted in **Table 3**, no significant association was observed between vitamin A intake and asthma. However, a significant association was observed between vitamin C intake and a lower asthma prevalence in non-users of dietary supplements who had elevated hs-CRP levels (≥ 1 mg/L).

DISCUSSION

This cross-sectional study analyzed the associations between dietary vitamin A and C intake and asthma, AR, and all cases of these diseases among young adults. In the analyses by stratified according to serum hs-CRP levels, a significant inverse association was found between dietary vitamin C intake (≥ 75 mg/day) and asthma prevalence among participants with elevated serum hs-CRP levels, which reflect asthma severity.

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Table 1. Comparison of participant characteristics according to self-reports on asthma or AR diagnosis

Characteristics	Diagnosed with asthma or AR	Not diagnosed	*P*-value
Number of participants	1,372	4,921	
Sex, female	878 (64.0)	2,780 (56.5)	< 0.001
Age (yrs)	34.32 ± 0.27	35.86 ± 0.17	< 0.001
Body mass index (kg/m^2)	25.57 ± 0.12	23.95 ± 0.07	< 0.05
Residential district			0.78
Urban	1,198 (87.32)	4,288 (87.1)	
Rural	174 (12.7)	633 (12.9)	
Type of residence			0.49
Detached house	309 (22.5)	1,167 (23.7)	
Apartment and others[1)]	1,063 (77.5)	3,754 (76.3)	
Income level			< 0.05
Low and lower-middle	442 (32.2)	1,461 (29.7)	
Upper-middle and high	930 (67.8)	3,460 (70.3)	
Education level			0.36
High school or below	531 (38.7)	1,963 (39.9)	
University or above	841 (61.3)	2,958 (60.1)	
Smoking status			< 0.001
Abstainer	889 (64.8)	3,007 (61.1)	
Former smoker	52 (3.8)	139 (2.8)	
Current smoker, < 0.5 pack/d	339 (24.7)	1,228 (24.9)	
Current smoker, ≥ 0.5 pack/d	92 (6.7)	547 (11.1)	
Alcohol consumption status[2)]			< 0.05
Abstainer	36 (2.6)	194 (3.9)	
Former drinker	181 (13.2)	569 (11.6)	
Current light drinker	928 (67.6)	3,283 (66.7)	
Current moderate drinker	156 (11.37)	640 (13.0)	
Current heavy drinker	71 (5.2)	235 (4.8)	
Perceived emotional stress			< 0.001
Low	841 (61.3)	3,405 (69.2)	
High	531 (38.7)	1,516 (30.8)	
Perceived depressive mood			< 0.05
No	1,305 (95.1)	4,779 (97.1)	
Yes	67 (4.9)	142 (2.9)	
Average sleep duration			0.66
< 7 h	546 (39.8)	1,830 (37.2)	
7–9 h	780 (56.8)	1,937 (59.7)	
> 9 h	46 (3.4)	154 (3.1)	
Use of dietary supplements			< 0.05
No	732 (53.3)	2,303 (46.8)	
Yes	640 (46.7)	2,618 (53.2)	
hs-CRP level (mg/L)	0.90 ± 0.04	0.97 ± 0.02	0.07
Total calorie intake (kcal)	1,569.2 ± 37.4	1,549.5 ± 21.7	0.65
Dietary intake of antioxidant vitamins			
Vitamin A (μg RAE)	402.87 ± 13.94	405.80 ± 9.75	0.86
Carotene (μg)	2,644.66 ± 99.98	2,697.434 ± 80.19	0.63
Retinol (μg)	181.80 ± 10.48	180.44 ± 6.75	0.91
Vitamin C (mg)	65.26 ± 2.49	62.76 ± 1.35	0.36

Values are presented as mean ± standard error or number (%). Statistical significance was evaluated using the χ^2 test or the Student's *t*-test.
AR, allergic rhinitis; hs-CRP, high-sensitivity C-reactive protein; RAE, retinol activity equivalents.
[1)]Include apartment, villa, and multiplex housing.
[2)]Light drinker (≤ 1 glass/day in women or ≤ 2 glasses/day in men), moderate drinker (1–3 glasses/day in women or 2–4 glasses/day in men), and heavy drinker (> 3 glasses/day in women or > 4 glasses/day in men) were defined according to the average daily alcohol consumption.

The co-occurrence of asthma and rhinitis is often observed and ARD are specified according to the allergic origin of these diseases. Asthma is associated with atopic march, which describes the evolvement of atopic (or allergic) affections, from atopic dermatitis at an early age to the later onset of allergic respiratory disorders including AR and asthma.

Table 2. Associations between dietary vitamin A and C intake and asthma and AR

Antioxidant vitamins	Asthma			AR			All cases[1]		
	No.[2]	Age-adjusted	Multivariate[3]	No.[2]	Age-adjusted	Multivariate[3]	No.[2]	Age-adjusted	Multivariate[2]
Vitamin A (μg RAE)									
< 250	56/2,434	Reference	Reference	522/2,434	Reference	Reference	548/2,434	Reference	Reference
250–349	28/1,225	1.08 (0.65–1.77)	0.99 (0.59–1.66)	235/1,225	0.94 (0.78–1.12)	0.92 (0.77–1.11)	250/1,225	0.97 (0.82–1.16)	0.92 (0.77–1.11)
350–449	20/864	1.10 (0.61–1.98)	1.05 (0.56–1.97)	152/864	0.83 (0.67–1.04)	0.84 (0.66–1.06)	161/864	0.87 (0.71–1.07)	0.84 (0.66–1.06)
≥ 450	54/1,770	1.35 (0.88–2.08)	1.21 (0.72–2.02)	387/1,770	1.06 (0.89–1.26)	1.03 (0.85–1.25)	413/1,770	1.08 (0.92–1.28)	1.03 (0.85–1.25)
Carotene (μg)									
< 1,000	35/1,289	Reference	Reference	293/1,289	Reference	Reference	310/1,289	Reference	Reference
1,000–1,999	43/1,830	0.87 (0.53–1.43)	0.85 (0.52–1.39)	382/1,830	0.93 (0.76–1.13)	0.95 (0.78–1.17)	400/1,830	0.89 (0.74–1.08)	0.95 (0.78–1.17)
2,000–2,999	27/1,238	0.95 (0.53–1.70)	0.88 (0.47–1.62)	224/1,238	0.79 (0.62–1.00)	0.80 (0.62–1.04)	239/1,238	0.81 (0.65–1.00)	0.80 (0.62–1.04)
≥ 3,000	53/1,936	1.12 (0.65–1.94)	0.96 (0.53–1.73)	397/1,936	0.97 (0.79–1.19)	1.00 (0.80–1.25)	423/1,936	0.98 (0.80–1.83)	1.00 (0.80–1.25)
Retinol (μg)									
< 40	30/1,516	Reference	Reference	300/1,516	Reference	Reference	314/1,516	Reference	Reference
40–99	46/1,601	0.99 (0.57–1.72)	0.94 (0.54–1.63)	315/1,601	0.99 (0.81–1.21)	0.96 (0.78–1.18)	330/1,601	1.04 (0.86–1.25)	0.96 (0.78–1.18)
100–199	46/1,672	1.41 (0.86–2.30)	1.30 (0.77–2.19)	355/1,672	1.10 (0.90–1.33)	1.05 (0.86–1.29)	379/1,672	1.18 (0.99–1.42)	1.05 (0.86–1.29)
≥ 200	45/1,504	1.17 (0.67–2.02)	1.05 (0.58–1.90)	326/1,504	1.07 (0.87–1.31)	1.00 (0.80–1.25)	349/1,504	1.10 (0.91–1.34)	1.00 (0.80–1.25)
Vitamin C (mg)									
< 20	28/1,214	Reference	Reference	252/1,214	Reference	Reference	267/1,214	Reference	Reference
20–39	48/1,769	1.14 (0.68–1.90)	1.02 (0.59–1.74)	374/1,769	1.08 (0.89–1.31)	1.09 (0.89–1.34)	395/1,769	1.08 (0.89–1.30)	1.09 (0.89–1.34)
40–74	46/1,724	1.10 (0.64–1.90)	0.88 (0.50–1.58)	332/1,724	0.93 (0.76–1.14)	0.91 (0.73–1.13)	355/1,724	0.94 (0.79–1.17)	0.91 (0.73–1.14)
≥ 75	36/1,586	1.12 (0.64–1.96)	0.92 (0.50–1.69)	338/1,586	1.14 (0.93–1.41)	1.10 (0.88–1.38)	355/1,586	1.17 (0.96–1.42)	1.10 (0.88–1.38)

Values are presented as odds ratio (95% confidence interval).
AR, allergic rhinitis; RAE, retinol activity equivalents; hs-CRP, high-sensitivity C-reactive protein.
[1]Include all cases of asthma and AR.
[2]Number of cases/total number of participants in each cell.
[3]The multivariate models include age, sex, body mass index,, residential district (urban, rural), household income level (low and lower-middle, upper middle, and high), educational level (middle school, high school, and above university), type of residence (detached house, apartment, and others), smoking status (abstainer, former smoker, and current smoker [2 categories: < 0.5, ≥ 0.5 pack/day]), alcohol consumption (abstainer, former drinker, and current drinker [3 categories: ≤ 1 glass/day in women or ≤ 2 glasses/day in men, 1–3 glasses/day in women or 2–4 glasses/day in men, and > 3 glasses/day in women or > 4 glasses/day in men]), perceived depressive mood (yes, no), perceived emotional stress (low, high), average sleep duration (< 7, 7–9, and > 9 h), use of dietary supplements (no, yes), total calorie intake, atopic dermatitis diagnosis, and serum hs-CRP levels.

The development of asthma and rhinitis is influenced by genetic and environmental factors and may persist for several years [16]. Asthma is a chronic airway inflammation syndrome caused by T-lymphocytes and eosinophils. These cells are associated with airway remodeling after releasing cytotoxic products that damage the epithelial wall. Thus, it is important to monitor and control inflammatory changes during asthma management [17]. Among all inflammatory biomarkers, hs-CRP, a sensitive biomarker of low-grade systemic inflammation, is positively associated with asthma severity [14,18]. Airway inflammation in asthma increases the production of reactive oxygen species, such as superoxide anion, hydroxyl radical, and hydrogen peroxide molecules, which are commonly produced by eosinophils and neutrophils. In particular, eosinophil peroxidase released during allergic inflammatory responses provokes oxidative damage in resident lung proteins [19]. To decrease oxidative damage, enzymatic elements, such as superoxide dismutase, catalase and glutathione peroxidase, and non-enzymatic compounds, such as vitamins A and C, play a role in the antioxidant defense mechanisms of the lung [19,20]. AR and asthma have similar immunopathological features [21]. Hence, both conditions can occur together.

Several epidemiological studies investigated the association between antioxidant vitamin intake and asthma among adults [8]. Adults with asthma, specifically those with severe asthma, had a lower dietary vitamin A intake than those without asthma. However, both groups had similar serum vitamin A levels regardless of asthma. In addition, there was no associations between carotene and retinol intake and asthma. Data on the association between dietary vitamin C intake and asthma were inconsistent.

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Table 3. Multivariate associations between dietary vitamin A and C intake and asthma and AR stratified according to serum hs-CRP levels

Antioxidant vitamins	Asthma						AR						All cases[1]					
	hs-CRP < 1 mg/L			hs-CRP ≥ 1 mg/L			hs-CRP < 1 mg/L			hs-CRP ≥ 1 mg/L			hs-CRP < 1 mg/L			hs-CRP ≥ 1 mg/L		
	OR	95% CI	No.	OR	95% CI	No.	OR	95% CI	No.	OR	95% CI	No.	OR	95% CI	No.	OR	95% CI	No.
Number of cases	111			47			1,000			296			1,061			311		
Vitamin A (μg RAE)																		
< 250	Reference		36[2]	Reference		20	Reference		397	Reference		125	Reference		418	Reference		130
250–349	1.29	0.71–2.34	22	0.48	0.16–1.40	6	0.95	0.77–1.16	188	0.86	0.55–1.35	47	0.95	0.77–1.16	200	0.86	0.55–1.35	50
350–449	1.14	0.53–2.44	15	0.79	0.28–2.27	5	0.90	0.69–1.16	124	0.63	0.37–1.07	28	0.90	0.69–1.16	132	0.63	0.37–1.07	29
≥ 450	1.49	0.78–2.86	38	0.70	0.29–1.70	16	1.03	0.83–1.29	291	0.98	0.65–1.49	96	1.03	0.83–1.29	311	0.98	0.65–1.49	102
Carotene (μg)																		
< 1,000	Reference		24	Reference		11	Reference		223	Reference		70	Reference		237	Reference		73
1,000–1,999	0.74	0.39–1.39	29	1.08	0.45–2.61	14	0.96	0.76–1.22	304	0.83	0.54–1.28	78	0.96	0.76–1.22	317	0.83	0.54–1.28	83
2,000–2,999	0.88	0.42–1.85	19	0.74	0.25–2.15	8	0.78	0.59–1.04	173	0.82	0.49–1.38	51	0.78	0.59–1.04	185	0.82	0.49–1.38	54
≥ 3,000	1.00	0.49–2.06	39	0.69	0.25–1.88	14	0.95	0.74–1.21	300	1.14	0.71–1.81	97	0.95	0.74–1.21	322	1.14	0.71–1.81	101
Retinol (μg)																		
< 40	Reference		19	Reference		11	Reference		234	Reference		66	Reference		245	Reference		69
40–99	0.98	0.50–1.93	26	1.00	0.37–2.71	11	0.91	0.72–1.15	236	1.20	0.76–1.89	79	0.91	0.72–1.15	247	1.20	0.76–1.89	83
100–199	1.66	0.91–3.00	34	0.82	0.30–2.29	12	1.04	0.83–1.32	273	1.15	0.75–1.78	82	1.04	0.83–1.32	294	1.15	0.75–1.78	85
≥ 200	1.28	0.62–2.63	32	0.83	0.29–2.40	13	1.03	0.81–1.32	257	0.91	0.53–1.55	69	1.03	0.81–1.32	275	0.91	0.53–1.55	74
Vitamin C (mg)																		
< 20	Reference		16	Reference		12	Reference		190	Reference		62	Reference		200	Reference		67
20–39	1.39	0.69–2.83	35	0.50	0.22–1.17	13	1.05	0.82–1.33	285	1.22	0.78–1.92	89	1.05	0.82–1.33	305	1.22	0.78–1.92	90
40–74	1.32	0.62–2.78	31	0.37	0.13–1.03	15	0.90	0.70–1.16	259	0.92	0.58–1.46	73	0.90	0.70–1.16	277	0.92	0.58–1.46	78
≥ 75	1.44	0.66–3.16	29	0.27	0.08–0.84	7	1.08	0.83–1.40	266	1.13	0.69–1.84	72	1.08	0.83–1.40	279	1.13	0.69–1.84	76

The multivariate models include age, sex, body mass index,, residential district (urban, rural), household income level (low and lower-middle, upper middle, and high), educational level (middle school, high school, and above university), type of residence (detached house, apartment, and others), smoking status (abstainer, former smoker, and current smoker [2 categories: < 0.5, ≥ 0.5 pack/day]), alcohol consumption (abstainer, former drinker, and current drinker [3 categories: ≤ 1 glass/day in women or ≤ 2 glasses/day in men, 1–3 glasses/day in women or 2–4 glasses/day in men, and > 3 glasses/day in women or > 4 glasses/day in men]), perceived depressive mood (yes, no), perceived emotional stress (low, high), average sleep duration (< 7, 7–9, and > 9 h), use of dietary supplements (no, yes), total calorie intake, and atopic dermatitis diagnosis.
AR, allergic rhinitis; hs-CRP, high-sensitivity C-reactive protein; OR, odds ratio; CI, confidence interval; RAE, retinol activity equivalents.
[1]Include all cases of asthma and AR.
[2]Number of cases in each category.

One case-control study showed a significant positive association between low dietary vitamin C intake and asthma among adults. Nevertheless, other cross-sectional and prospective studies found a null association [8]. Our study revealed an inverse trend between dietary vitamin A, carotene, and retinol intake and asthma among participants with elevated hs-CRP levels. Meanwhile, a significant inverse association was observed between carotene at a dose of 1,000–1,999 μg and asthma among non-users of dietary supplements with low hs-CRP levels. No significant association was observed between total vitamin A intake and asthma regardless of hs-CRP levels. However, a strong association between dietary vitamin C intake and asthma prevalence was observed among participants with elevated hs-CRP levels. This inverse association was still robust among non-users of dietary supplements after confounding effects of supplement intake was ruled out. Such associations between vitamin C intake, hs-CRP levels, and asthma prevalence were not reported in previous studies. A few epidemiological reports presented the association between vitamin C intake and asthma [8] or hs-CRP levels [22]. However, data on the association between vitamin C intake and both asthma and hs-CRP levels are limited.

The strengths of this study include analysis of national population-based survey data, a large sample size, consideration of a broad range of potential confounding variables, and a detailed analysis on the coexisting outcomes. However, the study limitations should be considered when interpreting the results. The study outcomes were determined based on the participants' self-report, and information on allergic asthma was unavailable. Therefore,

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Table 4. Multivariate associations between dietary vitamin A and C intake and asthma and AR stratified according to serum hs-CRP levels among non-users of dietary supplements

Antioxidant vitamins	Asthma						AR						All cases[1)]					
	hs-CRP < 1 mg/L			hs-CRP ≥ 1 mg/L			hs-CRP < 1 mg/L			hs-CRP ≥ 1 mg/L			hs-CRP < 1 mg/L			hs-CRP ≥ 1 mg/L		
	OR	95% CI	No.	OR	95% CI	No.	OR	95% CI	No.	OR	95% CI	No.	OR	95% CI	No.	OR	95% CI	No.
Number of cases	61			30			459			136			495			145		
Vitamin A (μg RAE)																		
< 250	Reference		21[2)]	Reference		16	Reference		193	Reference		70	Reference		208	Reference		74
250–349	1.29	0.56–2.98	13	0.49	0.12–2.07	3	1.13	0.83–1.53	90	0.89	0.47–1.69	23	1.11	0.83–1.50	97	0.98	0.53–1.80	26
350–449	1.26	0.47–3.37	10	0.53	0.19–1.47	3	0.95	0.63–1.43	56	0.77	0.38–1.58	11	0.91	0.61–1.36	60	0.68	0.35–1.33	11
≥ 450	1.18	0.48–2.88	17	0.51	0.16–1.54	8	1.03	0.74–1.42	120	0.71	0.37–1.34	32	1.02	0.75–1.37	130	0.67	0.36–1.25	34
Carotene (μg)																		
< 1,000	Reference		17	Reference		6	Reference		116	Reference		40	Reference		127	Reference		42
1,000–1,999	0.43	0.19–0.96	13	1.24	0.43–3.57	8	0.91	0.65–1.27	135	0.72	0.39–1.30	36	0.83	0.60–1.16	141	0.69	0.39–1.21	38
2,000–2,999	0.59	0.22–1.58	10	1.58	0.41–6.11	7	0.99	0.66–1.48	91	0.64	0.32–1.29	23	0.95	0.64–1.39	97	0.72	0.36–1.43	26
≥ 3,000	0.75	0.31–1.82	21	1.18	0.30–4.15	9	0.89	0.61–1.28	117	0.96	0.48–1.93	37	0.88	0.62–1.25	130	0.91	0.46–1.79	39
Retinol (μg)																		
< 40	Reference		12	Reference		10	Reference		109	Reference		42	Reference		116	Reference		45
40–99	0.89	0.39–2.02	14	1.00	0.35–2.86	10	0.94	0.66–1.34	106	1.01	0.56–1.84	42	0.93	0.66–1.32	115	1.05	0.59–1.87	46
100–199	1.75	0.83–3.71	21	0.52	0.15–1.76	6	1.21	0.85–1.71	118	0.94	0.51–1.75	31	1.24	0.89–1.73	131	0.89	0.50–1.59	33
≥ 200	1.02	0.41–2.54	14	0.30	0.08–1.17	4	1.32	0.93–1.87	126	0.55	0.23–1.29	21	1.25	0.88–1.77	133	0.47	0.21–1.05	21
Vitamin C (mg)																		
< 20	Reference		9	Reference		9	Reference		104	Reference		36	Reference		109	Reference		41
20–39	1.33	0.53–3.35	19	0.61	0.20–1.80	9	1.20	0.87–1.67	141	1.32	0.74–2.35	48	1.22	0.90–1.64	152	0.98	0.56–1.72	48
40–74	1.25	0.47–3.35	15	0.41	0.13–1.31	8	0.94	0.65–1.35	113	1.01	0.51–2.02	28	0.97	0.69–1.37	123	0.80	0.42–1.52	30
≥ 75	1.58	0.56–4.51	18	0.25	0.06–0.92	4	1.10	0.76–1.59	101	1.12	0.55–2.26	24	1.12	0.78–1.60	111	0.89	0.46–1.75	26

The multivariate models include age, sex, body mass index,, residential district (urban, rural), household income level (low and lower-middle, upper middle, and high), educational level (middle school, high school, and above university), type of residence (detached house, apartment, and others), smoking status (abstainer, former smoker, and current smoker), alcohol consumption (abstainer, former drinker, and current drinker), perceived depressive mood (yes, no), perceived emotional stress (low, high), average sleep duration (< 7, 7–9, and > 9 h), total calorie intake, and atopic dermatitis diagnosis.
AR, allergic rhinitis; hs-CRP, high-sensitivity C-reactive protein; OR, odds ratio; CI, confidence interval; RAE, retinol activity equivalents.
[1)]Include all cases of asthma and AR.
[2)]Number of cases in each category.

nondifferential misclassification of the outcomes resulting in a null association might have existed. Our findings was limited for causal inference due to the cross-sectional nature of the study. Dietary vitamin A and C intake might be overestimated or underestimated because dietary data were obtained via 1-day 24-h recall. Moreover, information on vitamin E, an antioxidant vitamin, was not available. The use of OR might have overestimated the strength of the association between vitamin intake and the prevalent outcomes (with a rate of > 10%) such as AR. Residual confounding caused by unmeasured variables might have existed, and the generalization of study results is limited because of the characteristics of the study participants, who were Koreans aged 20–49 yrs.

In summary, no associations were found between dietary vitamin A and C intake and asthma and AR in all participants. However, the association between a higher vitamin C intake and a lower asthma prevalence among participants with high serum hs-CRP levels, which reflect inflammatory condition, is significant. Nevertheless, in the future, further epidemiologic studies should be conducted to provide evidence on causal inference. Thus, the implication of high vitamin C intake as a preventive strategy against asthma is still unclear.

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