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Association between dietary zinc intake and asthma in overweight or obese children and adolescents: A cross-sectional analysis of NHANES

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ABSTRACT

Background: Asthma, characterized by recurrent wheezing, breathlessness, chest tightness, and coughing, is a major health concern among children and adolescents worldwide, currently affecting more than 5 million children. The increasing prevalence of obesity and overweight among the pediatric population has made the issue of childhood respiratory health more complex. Compared with children of healthy weight, the risk of asthma is higher in overweight and obese children. Zinc, a nutrient that regulates the oxidant-antioxidant balance, has been studied for its potential protective effects against asthma in adults and children. However, the results are controversial, with some studies reporting a beneficial effect and others showing no effect. Therefore, our objective was to assess the correlation between zinc intake from diet and asthma occurrence among children and adolescents who are overweight or obese.

Methods: The National Health and Nutrition Examination Survey (NHANES) (2011–2020) provided data on individuals aged $\leq$20 who were overweight or obese, had asthma, and consumed zinc in their diet. The association between dietary zinc and asthma was evaluated using a variety of statistical methods, including multivariate logistic regression, restricted cubic spline analysis, and subgroup analysis.

Results: A total of 4597 pediatrics and adolescents were enrolled, with 20.9% (963/4597) suffering from asthma. After adjusting for all covariates in the multivariate logistic regression, compared with the lowest zinc intake group Q1($\leq$5.68 mg/day), the adjusted OR values for zinc intake and asthma in Q2 (5.69–8.36 mg/day), Q3 (8.37–11.95 mg/day), and Q4 ($\geq$11.96 mg/day) were 0.78 (95% CI: 0.62–0.98, p = 0.03), 0.76 (95% CI: 0.6 ~ 0.98, p = 0.032), 0.71 (95% CI: 0.53 ~ 0.95, p = 0.022), respectively. Stratified analysis showed no interactive role for dietary zinc intake and asthma in overweight or obese children and adolescents.

Conclusions: Dietary zinc intake is inversely associated with asthma in overweight or obese children and adolescents.

Keywords: Asthma, Zinc, Child, Adolescent, Cross-sectional study

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INTRODUCTION

Asthma, which is marked by ongoing airway inflammation and redox imbalance, is the most prevalent chronic respiratory condition during childhood. According to the Global Asthma Report, current asthma symptom prevalence in GAN Phase I was 9.1% in children and 11.0% in adolescents.[1] In 2021, the United States Centers for Disease Control and Prevention (CDC) reported that asthma affected approximately 4.6 million children (6%) in the United States.[2] Concern should be expressed about the alarming rise in the incidence of asthma in children and adolescents worldwide as well as the shifting patterns of its burden. In addition, asthma attacks impose a significant burden on families and healthcare systems, resulting in increased healthcare visits and the administration of systemic corticosteroids and antibiotics.[3]

With economic development and improvements in living standards, the proportion of overweight and obesity among children and adolescents exhibits an alarming upward trend. Childhood obesity has become a major public health challenge of the 21st century, with approximately 41 million children age <5 years and over 340 million children and adolescents aged between 5 and 19 affected by overweight or obesity in 2016, which represents a more than tenfold increase from 1976.[4,5] These individuals typically face an increased likelihood of developing asthma, exhibit reduced lung function, are more prone to asthma exacerbation, and respond less effectively to conventional asthma treatments compared to their peers of normal weight.[6–8] Thus, there is an urgent need to figure out ways to ease the asthmatic symptoms among this specific population.

In recent years, the impact that various nutrients play in asthma has been the subject of an increasing number of research reports, highlighting the dietary factors that may contribute to the development and management of asthma. An abundant diet of fruits and vegetables has already been advised for those suffering from asthma, according to the Global Strategy for Asthma Management and Prevention,[1] while the guidelines have not yet included the recommendation to consume a diet rich in other nutrients. Among those factors, micronutrients are of interest because of their unique role in oxidative stress and inflammatory responses.[9,10] Zinc, the second most prevalent trace metal in mammals, assumes a crucial function in the regulation of inflammation and immune response. Moreover, zinc also contributes to oxidant/antioxidant equilibrium by acting as a co-factor for superoxide dismutase, an enzyme with antioxidant properties.[11] As a result, insufficiency of zinc may contribute to pulmonary impairment, exacerbating symptoms of asthma. Prior research that attempted to establish an association between zinc and asthma mostly evaluated its levels in body fluids and their correlation with asthma, yielding inconsistent findings. Several studies have shown that asthmatic patients have a decrease in zinc concentration in their serum, hair, or sputum.[12–14] However, it has not been shown to be significantly associated with asthma in other studies.[15,16]

Therefore, further research is necessary to comprehend the association between dietary zinc consumption and asthma in overweight or obese children and adolescents. Data from the National Health and Nutrition Examination Survey (NHANES) were drawn upon in this present study. We hypothesized that among overweight or obese children and adolescents, those with asthma exhibit a diminished dietary intake of zinc compared to their healthy counterparts within this demographic.

METHODS

Data source

NHANES, conducted by CDC,[17] was designed to evaluate the health or nutrition status of the noninstitutionalized US population. Each year, approximately 5000 persons are examined as a nationally representative sample. The individuals surveyed were chosen using a multistage, stratified probability design.[18] The NHANES acquires demographic data and a wide array of health-related information by means of household visits, screening assessments, and laboratory analyses administered via a mobile examination center (MEC). NHANES received approval from the Ethics Review Committee at the National Center for Health Statistics (NCHS), and written informed

consent was obtained from all participants before their inclusion. For the secondary analysis, no additional institutional review board approval was required.[19] The NHANES data can be obtained from the NHANES website (http://www.cdc.gov/nchs/nhanes.htm).

Inclusion and exclusion criteria

Data from 4 survey cycles (2011–2012, 2013–2014, 2015–2016, 2017–2020) were extracted from NHANES for this study. Participants under the age of 20 who completed the survey were incorporated. Individuals who had incomplete data regarding questionnaire responses for asthma, dietary zinc intake, and Body mass index (BMI) Category were eliminated from the study, as well as those who were either underweight or of normal weight.

Asthma assessment

To identify participants with asthma, we assessed their answers to the question, "Has a doctor or other health professional ever told you that you have asthma?" in the medical condition questionnaire. Those who replied "yes" were classified as asthmatic, whereas those who responded "no" were classified as non-asthmatic.

Responses to the question "During the past 12 months, have you had an episode of asthma or an asthma attack?" were reviewed for persons who had had an asthma attack in the past year. Those who answered "yes" were classified as having had an asthma attack in the past year, and the others were not.

Dietary zinc intake

Dietary survey participants in NHANES were asked to report their consumption of food and beverages within a 24-h period. Data on dietary intake were collected between 2011 and 2020 using the Automated Multiple Pass Method (AMPM). These data were utilized to accurately calculate the nutrient values for participants based on the food and beverages they consumed.[20] The NHANES Dietary Interviewers Procedure Manuals provide a comprehensive outline of the methodology employed in the dietary survey.[17] The subjects were divided into 4 groups based on their dietary zinc consumption.

Overweight or obese

We selected individuals for this study who were overweight or obese. The data on BMI Category were derived from the examination data and there were 4 categories:[21] underweight (BMI$<$5th percentile), normal weight (BMI 5th to 85th percentile), overweight (BMI 85th to 95th percentile), and obese (BMI$\geqslant$95th percentile).

Covariates

Several potential covariates were evaluated according to previous literature requirements,[22] including age, sex, race and ethnicity, family income, onset age of asthma, family history of asthma, second-hand smoking, laboratory parameters (white blood cell count [WBC], eosinophils percent [EOPC], hemoglobin [HGB]), consumption of calorie, protein, carbohydrate, sugar, fiber, and fat, and use of dietary supplements. The classifications for race and ethnicity specifically included Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other race. According to a US government report,[23] the poverty income ratio (PIR) was used in the classification of family income. This ratio was instrumental in dividing family incomes into 3 distinct categories: low (PIR $\leqslant$ 1.3), medium (1.3–3.5), and high (PIR $>$3.5). Complete blood counts (CBC) and blood cell distribution of blood samples were measured for all subjects with the Beckman Coulter DxH 800 instrument at the NHANES MEC, including WBC, EOPC, and HGB. A dietary recall interview was conducted prior to an interview at MEC to collect participants' nutritional data for a 24-h period, including calories, protein, carbohydrates, sugar, fiber, and fat consumption. The use of dietary supplements by the subjects was determined by their answer to the question "Any Dietary Supplements taken in the past 24 h?".

A multivariate single imputation method for missing data was implemented using an iterative imputer. At each step of the round-robin imputation, a Bayesian Ridge model was used as the estimator.[24]

Statistical analysis

This is a secondary analysis of data sets available in the public domain. Mean (standard deviation) and median (interquartile range, 25–75%) were used to present normally distributed and skewed variables, respectively. Categorical variables were presented as proportions. The comparison of continuous data employed t tests, while categorical data were assessed through the $\chi 2$ test.

The variable of interest was the dietary intake of zinc, and all analyses were performed according to quartiles of zinc intake. The odds ratios (OR) and 95% confidence intervals (CIs) for the correlation between consumption of dietary zinc and asthma were calculated using logistic regression models. Sociodemographic variables such as age, sex, race, ethnicity, and PIR were taken into account while adjusting Model 1. In Model 2, additional factors, including family asthma, secondhand smoking, EOPC, WBC, and HGB, were further adjusted. The consumption of calories, protein, carbohydrates, sugar, fiber, and fat was then taken into consideration while making additional adjustments to Model 3.

We employed restricted cubic splines (RCS) utilizing 4 knots to assess the correlation between zinc consumption and asthma while controlling for variables in Model 3.

Furthermore, we utilized multivariate logistic regression analysis, incorporating likelihood ratio tests for interactions, to evaluate any potential modifications in the association between dietary zinc and asthma according to factors including sex, age (<13 vs. 13–19 years), PIR, and family history of asthma.

Finally, we performed several sensitivity analyses. First, we excluded participants with missing covariates to ascertain if the patterns of the single imputation analysis were consistent with the trends found; multivariable logistic regression modeling and RCS were employed. Next, to further examine the association between dietary zinc intake and asthma, we investigated the relationship between dietary zinc intake and asthma attack in the past year. Finally, we included the presence or absence of asthma treatment in a multivariate regression analysis model for the 2011–2012 cycle to determine whether the association between dietary zinc intake and asthma remained consistent.

Statistical power calculations were not performed prior to the study, as the sample size was solely determined by the existing data. The statistical analyses were conducted utilizing R software (version 4.2.1; R Foundation for Statistical Computing; http://www.R-project.org), along with the R survey package (version 4.1–1) and Free Statistics software version 1.9.[25] A two-tailed p-value <0.05 was utilized to signify statistical significance in all analyses.

RESULTS

Study population

Data from 4 NHANES cycles (2011–2012, 2013–2014, 2015–2016, and 2017–2020) were utilized in this analysis. Out of the 45,462 respondents who finished the poll, 26,280 were 20 years of age or older. Among the remaining 19,182 participants under 20, those with incomplete asthma questionnaires (n = 1793) and those who did not provide complete dietary zinc intake information (n = 3396) were not included. The study eliminated those who did not have BMI information (n = 1112) and those who were underweight or of normal weight (n = 8284). In all, the present study included 4597 individuals in total, of which 963 reported having asthma (Fig. 1).

Baseline characteristics

Table 1 demonstrates the baseline characteristics of the entire participant cohort, categorized by quartiles of dietary zinc intake. There were no significant differences between the 4 survey cycles in dietary zinc intake. The median age of the subjects was 11 years, with 2280 individuals (49.6%) identified as male. Among the participants, 963 individuals (20.9%) were diagnosed with asthma. The median onset age of asthma was 3 years. Notably, those who consumed higher amounts of zinc predominantly included males, of non-Hispanic white ethnicity, reported a reduced household income, were without a familial asthma background, and did not use dietary supplements. Additionally, this group showed lower exposure to passive smoking and a higher intake of nutrients, including calories, proteins, carbohydrates, sugars, dietary fiber, and fats.

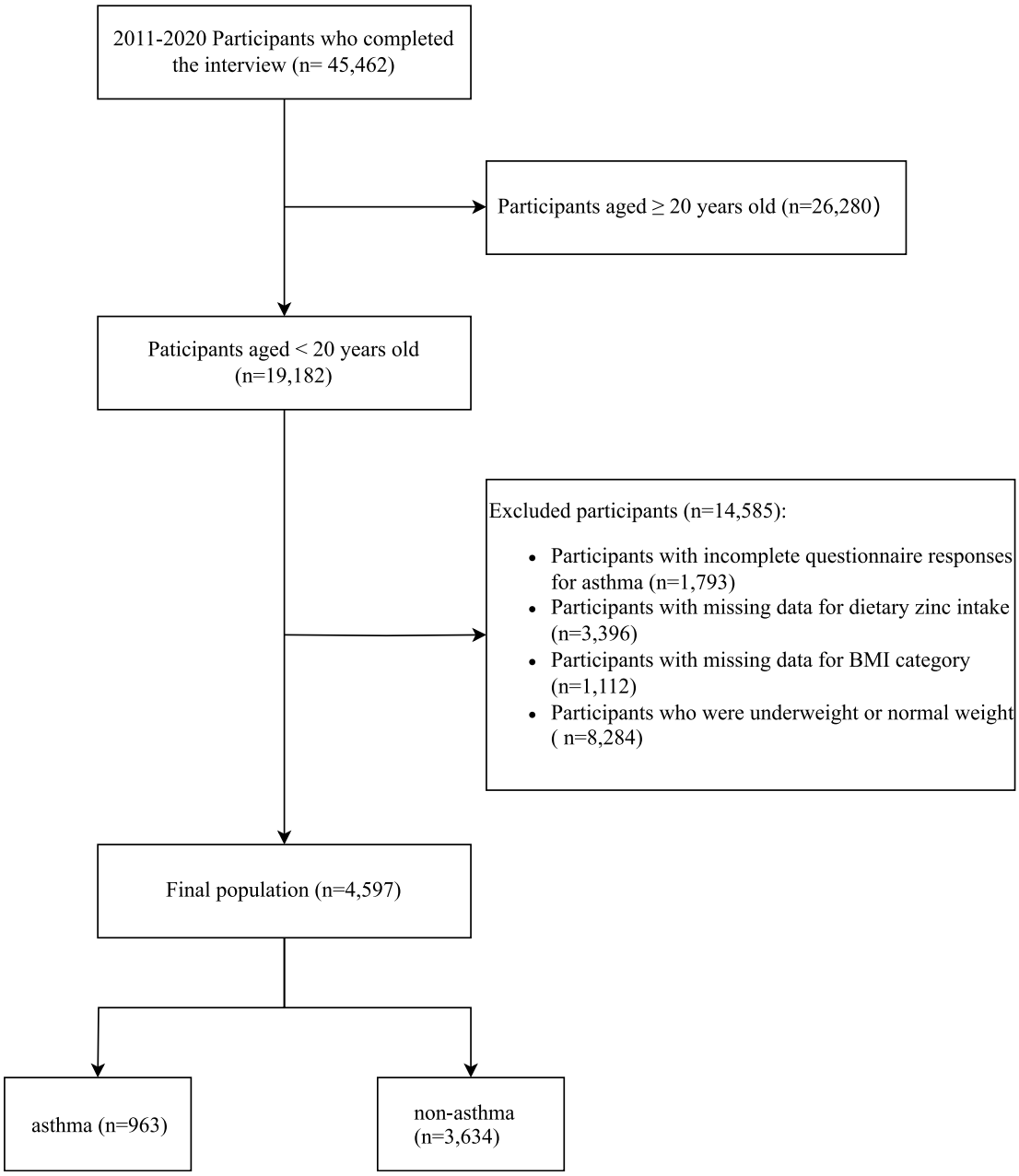

Fig. 1 Flowchart of this study.

Association between dietary intake of zinc and asthma

The univariate analysis revealed significant associations between asthma and several factors, including age, sex, race and ethnicity, family history of asthma, second-hand smoking, EOPC, calorie, protein, carbohydrate, sugar, and fat intake. (Table 2).

Upon examining zinc dietary intake categorized into quartiles, a notable inverse correlation emerged between zinc consumption and asthma, after adjusting for all the potential covariates. In comparison to individuals with the lowest zinc intake (Q1, ⩽5.68 mg/day), participants in Q2 (5.69–8.36 mg/day), Q3(8.37–11.95 mg/day), and Q4 (⩾11.96 mg/day) exhibited adjusted ORs for

Variables	Zinc intake (mg/day)					p-Value
	Total (n = 4597)	Q[a]1(≤5.68) (n = 1141)	Q[a]2(5.69-8.36) (n = 1156)	Q[a]3(8.37-11.95) (n = 1147)	Q[a]4(≥11.96) (n = 1153)	
Release cycle, n (%)						0.013
2011–2012	983 (21.4)	205 (18)	268 (23.2)	255 (22.2)	255 (22.1)	
2013–2014	1045 (22.7)	256 (22.4)	261 (22.6)	262 (22.8)	266 (23.1)	
2014–2016	1053 (22.9)	251 (22)	253 (21.9)	273 (23.8)	276 (23.9)	
2017–2020	1516 (33.0)	429 (37.6)	374 (32.4)	357 (31.1)	356 (30.9)	
Age(years)	11.0 (7.0, 15.0)	12.0 (6.0, 15.0)	10.0 (6.0, 14.0)	10.0 (7.0, 14.0)	12.0 (8.0, 15.0)	<0.001
Sex, n (%)						<0.001
Male	2280 (49.6)	436 (38.2)	527 (45.6)	591 (51.5)	726 (63)	
Female	2317 (50.4)	705 (61.8)	629 (54.4)	556 (48.5)	427 (37)	
Race and ethnicity, n (%)						<0.001
Mexican American	1111 (24.2)	258 (22.6)	252 (21.8)	315 (27.5)	286 (24.8)	
Other Hispanic	529 (11.5)	137 (12)	150 (13)	115 (10)	127 (11)	
Non-Hispanic White	1163 (25.3)	276 (24.2)	281 (24.3)	301 (26.2)	305 (26.5)	
Non-Hispanic Black	1233 (26.8)	350 (30.7)	336 (29.1)	274 (23.9)	273 (23.7)	
Other/Multi-Racial	561 (12.2)	120 (10.5)	137 (11.9)	142 (12.4)	162 (14.1)	
PIR[b], n (%)						0.323
Low(<1.3)	2212 (48.1)	570 (50)	567 (49)	527 (45.9)	548 (47.5)	
Median(1.3–3.5)	1664 (36.2)	400 (35.1)	422 (36.5)	418 (36.4)	424 (36.8)	
High(>3.5)	721 (15.7)	171 (15)	167 (14.4)	202 (17.6)	181 (15.7)	
Family asthma, n (%)						0.451
Yes	1644 (35.8)	430 (37.7)	401 (34.7)	403 (35.1)	410 (35.6)	
No	2953 (64.2)	711 (62.3)	755 (65.3)	744 (64.9)	743 (64.4)	
Second-hand smoking, n (%)						0.513
No	3332 (72.5)	826 (72.4)	843 (72.9)	845 (73.7)	818 (70.9)	
Yes	1265 (27.5)	315 (27.6)	313 (27.1)	302 (26.3)	335 (29.1)	
WBC[c](1000 cells/uL)	7.6 ± 2.2	7.5 ± 2.2	7.7 ± 2.3	7.7 ± 2.1	7.6 ± 2.2	0.064

(continued)

Variables	Zinc intake (mg/day)					p-Value
	Total (n = 4597)	Q[a]1(≤5.68) (n = 1141)	Q[a]2(5.69-8.36) (n = 1156)	Q[a]3(8.37-11.95) (n = 1147)	Q[a]4(≥11.96) (n = 1153)	
EOPC[d](%)	13.3 ± 1.3	13.2 ± 1.3	13.2 ± 1.2	13.3 ± 1.3	13.5 ± 1.3	<0.001
HGB[e](g/dL)	2.5 (1.5, 4.1)	2.4 (1.5, 3.8)	2.5 (1.6, 4.1)	2.5 (1.6, 4.2)	2.5 (1.5, 4.1)	0.215
Calorie consumption(kcal/day)	1745.0 (1324.0, 2284.0)	1183.0 (912.0, 1478.0)	1623.5 (1348.0, 1940.2)	1971.0 (1604.5, 2400.5)	2458.0 (1928.0, 3152.0)	<0.001
Protein consumption (gm/day)	61.8 (44.5, 84.2)	35.9 (27.4, 45.2)	54.9 (47.4, 64.7)	71.5 (60.3, 85.4)	97.4 (77.0, 121.1)	<0.001
Carbohydrate consumption (gm/day)	226.7 (166.9, 295.4)	160.5 (121.9, 205.2)	214.5 (167.1, 264.8)	247.5 (199.2, 312.7)	297.5 (232.2, 385.4)	<0.001
Sugar consumption (gm/day)	98.4 (67.7, 141.3)	73.3 (48.5, 101.9)	94.3 (67.2, 129.2)	107.2 (76.9, 147.2)	129.7 (89.6, 180.5)	<0.001
Fiber consumption (gm/day)	12.2 (8.4, 17.4)	8.0 (5.5, 10.8)	11.6 (8.6, 15.1)	14.2 (10.1, 18.9)	17.2 (12.6, 23.2)	<0.001
Fat consumption (gm/day)	66.0 (46.4, 93.3)	42.0 (29.5, 57.1)	60.3 (47.6, 77.3)	75.5 (57.1, 97.4)	99.6 (70.4, 132.9)	<0.001
Dietary supplements taken, n (%)						0.249
Yes	666 (14.5)	150 (13.1)	170 (14.7)	184 (16)	162 (14.1)	
No	3931 (85.5)	991 (86.9)	986 (85.3)	963 (84)	991 (85.9)	
Onset age of asthma(years)	3.0 (1.0, 6.0)	2.0 (1.0, 6.0)	3.0 (1.0, 6.0)	3.0 (1.0, 6.0)	3.0 (1.0, 6.0)	0.276
Asthma, n (%)						0.018
Yes	963 (20.9)	208 (18.2)	240 (20.8)	243 (21.2)	272 (23.6)	
No	3634 (79.1)	933 (81.8)	916 (79.2)	904 (78.8)	881 (76.4)	

Table 1. (Continued) Baseline characteristics categorized by dietary zinc intake. *[a]Quartiles based on dietary zinc consumption. [b]Ratio of income to poverty. [c]White blood cell count. [d]Eosinophils percent. [e]Hemoglobin*

asthma of 0.78 (95% CI: 0.62–0.98, p = 0.03), 0.76 (95% CI: 0.6–0.98, p = 0.032), and 0.71 (95% CI: 0.53–0.95, p = 0.022), respectively (Table 3). Furthermore, the relationship between asthma and zinc intake demonstrated a consistent negative linear trend (nonlinear, p = 0.602), as illustrated in the RCS analysis (Fig. 2).

Stratified analyses based on additional variables and sensitivity analysis

A stratified analysis has been conducted across multiple subgroups in order to assess any potential alterations in the correlation between zinc consumption in the diet and asthma. When stratified

Variable	OR[a] (95% CI[b])	*p*-Value
Age(years)	0.96 (0.94～0.97)	<0.001
Sex, n(%)		
Male	Reference	
Female	1.3 (1.12～1.5)	<0.001
Race and ethnicity, n(%)		
Mexican American	Reference	
Other Hispanic	0.78 (0.6～1.02)	0.068
Non-Hispanic White	0.78 (0.63～0.97)	0.026
Non-Hispanic Black	0.52 (0.42～0.63)	<0.001
Other/Multi-Racial	0.7 (0.54～0.91)	0.007
PIR[c], n(%)		
Low(<1.3)	Reference	
Median(1.3–3.5)	1.14 (0.97～1.33)	0.106
High(>3.5)	1.1 (0.89～1.35)	0.37
Family asthma, n(%)		
No	Reference	
Yes	3.42 (2.95～3.96)	<0.001
Second-hand smoking, n(%)		
Yes	Reference	
No	0.79 (0.68～0.93)	0.004
WBC[d](1000 cells/uL)	1.02 (0.99～1.05)	0.267
EOPC[e](%)	0.9 (0.88～0.92)	<0.001
HGB[f](g/dL)	0.98 (0.93～1.04)	0.489
Dietary supplements taken, n(%)		
Yes	Reference	
No	1.1 (0.91～1.35)	0.329
Calorie consumption(kcal/day)	1 (1～1)	<0.001
Protein consumption (gm/day)	1 (1～1)	0.015
Carbohydrate consumption (gm/day)	1 (1～1)	0.007
Sugar consumption (gm/day)	1 (1～1)	0.017

(continued)

Variable	OR[a] (95% CI[b])	*p*-Value
Fiber consumption (gm/day)	1 (0.99∼1.01)	0.679
Fat consumption (gm/day)	1 (0.99∼1)	<0.001
Zinc intake (mg/day)	0.98 (0.97∼1)	0.007

Table 2. (Continued) Association of covariates and asthma risk. [a]*Odds ratio.* [b]*Confidence interval.* [c]*Ratio of income to poverty.* [d]*White blood cell count.* [e]*Eosinophils percent.* [f]*Hemoglobin*

by PIR, sex, age, and family history of asthma, no significant interactions were observed (Fig. 3). Subsequently, we performed sensitivity analyses by excluding the subjects whose variables were missing. After modifying the model for restricted cubic spline analyses and multivariate logistic regression, our results remained constant. A consistent negative linear connection (nonlinear, $p = 0.248$) was observed between dietary zinc intake and asthma (Supplementary Material, Table S1-S3, Figure S1-S2).

Additionally, we investigated the correlation between dietary zinc intake and asthma attack in the past year. After adjusting for all covariates, the adjusted OR for asthma in Q4 (≥11.96 mg/day) was 0.6 (95% CI: 0.37–0.99, $p = 0.046$) compared to the lowest zinc intake (Q1, ⩽5.68 mg/day) (Supplementary Material, Table S4).

The data regarding asthma treatment was only available for the 2011–2012 cycle, and therefore could only be included in the multivariate regression analysis model for that cycle. After adding asthma treatment to the multivariate analysis model, the adjusted OR values for zinc intake and asthma in Q4 (≥12.15 mg/day) were 0.3 (95%CI: 0.11–0.84, $p = 0.022$) compared to the lowest zinc intake group Q1(≤5.96 mg/day), which means that dietary zinc intake is still inversely associated with asthma (Supplementary Material, Table S5).

DISCUSSION

In this cross-sectional analysis, an inverse association between dietary zinc intake and asthma in the overweight or obese pediatric population was observed. Further scrutiny through stratified and sensitivity analyses unveiled a substantial and robust correlation between dietary zinc intake and asthma in overweight or obese children and adolescents.

Compared to children who are of a healthy weight, those who are overweight or obese have a greater chance of developing asthma.[6] Besides, these children tend to be more severely ill and potentially less likely to respond to inhaled corticosteroids, resulting in a poorer quality of life.[26] Thus, it is important to look for ways to improve symptoms in obese or overweight asthmatics.

Several studies have investigated the correlation between zinc levels and asthma at varying stages of life, ranging from fetal to adulthood. Nevertheless, consistent conclusions have not been reached in these studies, with most focusing on zinc levels in body fluids instead of dietary zinc intake. Previous research has indicated that individuals with asthma tend to have lower serum zinc levels compared to those without the condition.[12,27,28] Additionally, asthmatics with low serum zinc levels appear to have a higher likelihood of experiencing wheezing symptoms and have worse lung function.[29] Sanguansak et al found a significant reduction in asthma severity in the first 48 h after hospital admission when children with acute asthma were treated with zinc bis-glycinate from admission to discharge.[30] Ghaffari et al reported that supplementation with 50 mg/day of zinc was associated with significant improvement in clinical symptoms and lung function in zinc-deficient children with moderate asthma.[31] In a British case-control study, no association was discovered between severe asthma and micronutrient deficiencies, including zinc.[16] It is important to note that, in contrast to our study, the study population in this investigation consisted of British adults. Additionally, while investigating the association between zinc and asthma, potential confounders that might have contributed were not taken into account, potentially yielding different findings than in our study. Unlike these previous studies, our study

Quartile	OR[a] (95% CI[b])									
	No.	n(%)	Crude	*p*-Value	Model 1	*p*-Value	Model 2	*p*-Value	Model 3	*p*-Value
Zinc intake (mg/day)										
Q[c]1(≤5.68)	1141	933 (81.8)	1(Ref)		1(Ref)		1(Ref)		1(Ref)	
Q[c]2(5.69～8.36)	1156	916 (79.2)	0.85 (0.69～1.05)	0.126	0.84 (0.68～1.03)	0.097	0.79 (0.64～0.99)	0.037	0.78 (0.62～0.98)	0.03
Q[c]3(8.37～11.95)	1147	904 (78.8)	0.83 (0.67～1.02)	0.076	0.8 (0.65～0.99)	0.041	0.79 (0.63～0.98)	0.032	0.76 (0.6～0.98)	0.032
Q[c]4(≥11.96)	1153	881 (76.4)	0.72 (0.59～0.88)	0.002	0.76 (0.62～0.93)	0.009	0.74 (0.6～0.92)	0.007	0.71 (0.53～0.95)	0.022
Trend. test	4597			0.002		0.01		0.012		0.03

Table 3. Association between dietary zinc intake and asthma. *Model 1 was adjusted for age, sex, race and ethnicity, PIR; Model 2 was adjusted for Model 1+family asthma, second-hand smoking, EOPC, WBC, HGB; Model 3 was adjusted for Model 2+calorie consumption, protein consumption, carbohydrate consumption, sugar consumption, fiber consumption, fat consumption.* [a]*Odds ratio.* [b]*Confidence interval.* [c]*Quartiles based on dietary zinc consumption*

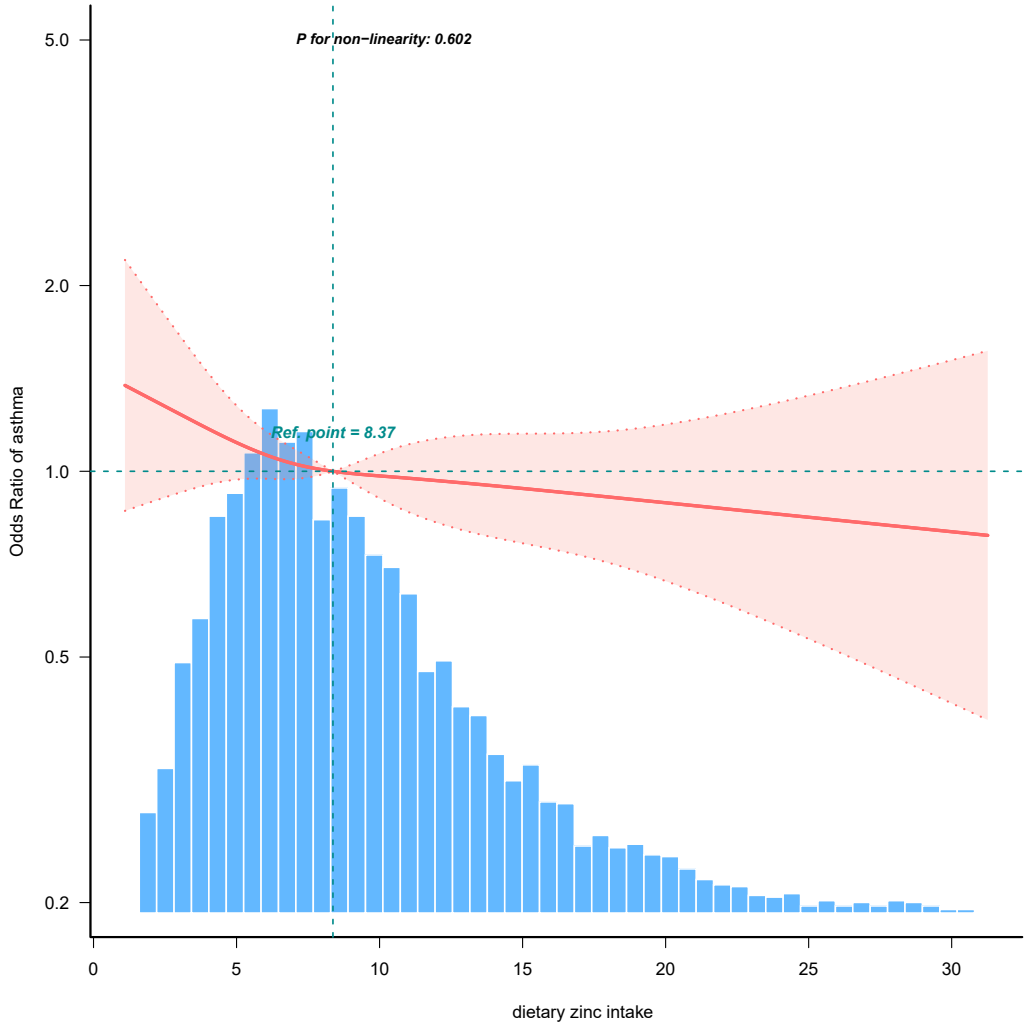

Fig. 2 Association between dietary zinc intake and asthma odds ratio. Solid and dashed lines represent the predicted value and 95% confidence intervals. They were adjusted for age, sex, race and ethnicity, PIR, WBC, EOPC, HGB, family asthma, second-hand smoking, calorie consumption, protein consumption, carbohydrate consumption, sugar consumption, fiber consumption, fat consumption. Only 99% of the data is shown.

evaluated the relationship between dietary zinc intake and asthma, with a focus on children and adolescents who were overweight or obese. In addition, our study has examined a much larger population. The study demonstrated that increased dietary zinc intake correlates with a reduced risk of asthma (OR: 0.71; 95% CI: 0.53–0.95). This correlation remained significant after adjusting for age, sex, race and ethnicity, PIR, family asthma, second-hand smoking, EOPC, WBC, HGB, as well as intake of calorie, protein, carbohydrate, sugar, fiber, and fat. It is necessary to do more prospective research and multicenter randomized controlled trials in the future to examine the impact of zinc consumption on asthma in children and adolescents who are overweight or obese. Nuts, nutritious grains, poultry, seafood such as shellfish, and red meat are among the foods high in zinc.[32]

Our findings align with existing research, even if the precise mechanisms by which zinc influences asthma in overweight or obese individuals remain incompletely known. Zinc, recognized for its anti-oxidant properties, contributes to diminishing oxidative stress through a variety of mechanisms. It suppresses the generation of reactive oxygen species by impeding pro-oxidant enzymes such as

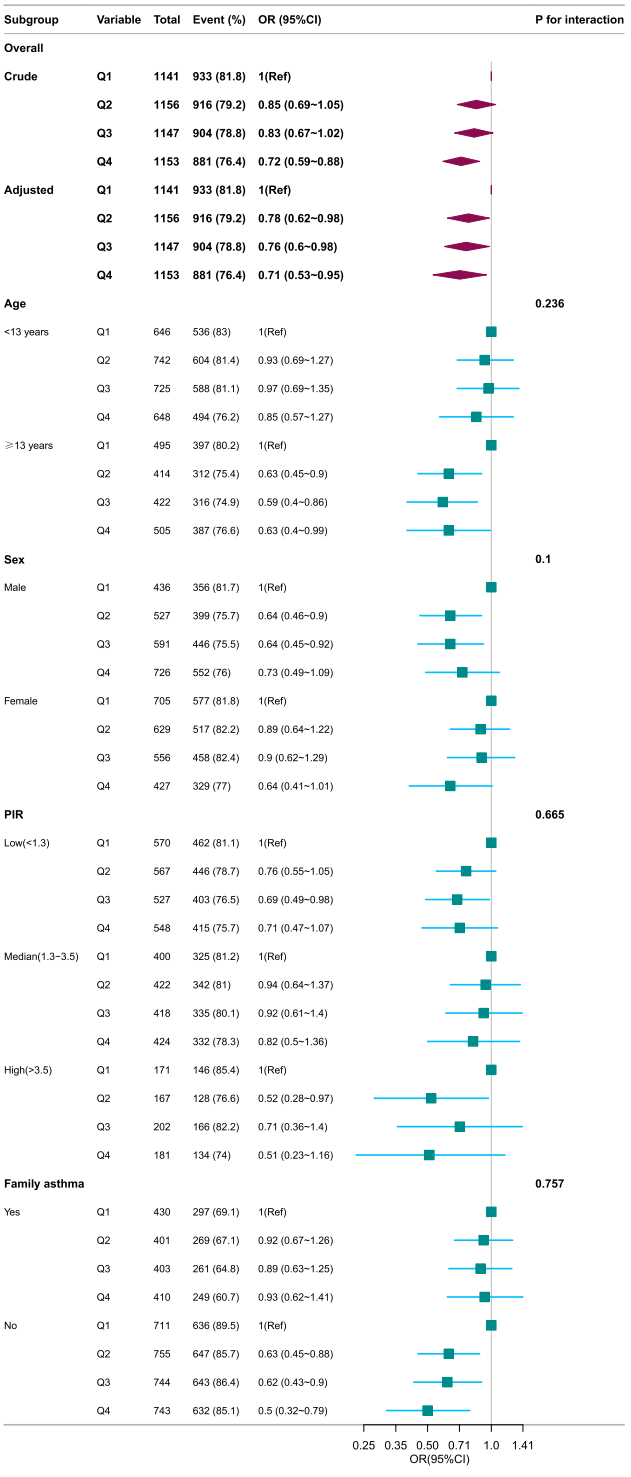

Fig. 3 Forest plot of multivariable logistics analysis between dietary zinc and asthma. Except for the stratification component itself, each stratification factor was adjusted for age, sex, race and ethnicity, PIR, WBC, EOPC, HGB, family asthma, second-hand smoking, calorie consumption, protein consumption, carbohydrate consumption, sugar consumption, fiber consumption, fat consumption.

NADPH oxidase and iNOS. Additionally, zinc activates antioxidant enzymes, including those related to glutathione, as well as catalase and superoxide dismutase.[11,33] Zinc also has immunomodulatory and anti-inflammatory effects. These effects are exerted primarily by maintaining the proper balance of Th1/Th2 cells and inhibiting the nuclear factor-kappa B pathway, a central regulator of inflammation. By doing so, zinc may attenuate the release of pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha.[34-36] In the case of asthma, which is acknowledged as a long-term inflammatory respiratory disease, the main feature is the excessive production of pro-inflammatory cytokines.[37] Similarly, obesity and overweight conditions are associated with a state of chronic low-grade inflammation, involving the release of pro-inflammatory cytokines from adipose tissue.[26] Furthermore, a lack of zinc makes the airway epithelium highly vulnerable to damage and cell apoptosis both in laboratory settings[38] and in living organism,[39] and, as a result, aggravates airway inflammation.[40] In conclusion, this multifaceted role of zinc in mitigating oxidative stress, modulating immune response, and an-inflammatory effects highlight its potential as a therapeutic target for alleviating symptoms in overweight or obese asthmatics.

Strengths and limitations

Our study boasts several strengths, foremost among them being the utilization of data from multiple survey cycles. This approach contributes to a substantial sample size, enhancing the statistical power and generalizability of our findings. Another notable strength is our specific focus on the overweight or obese population. This targeted approach allows for a more nuanced examination of the relationship between our variables within this demographic, providing valuable insights that may have particular relevance to this subgroup. Furthermore, our study employed a diverse set of statistical methods, including multivariate logistic regression and stratified analysis. This methodological diversity enhances the comprehensiveness of our analysis, enabling a thorough examination of the association between zinc intake and asthma. Nevertheless, it is essential to acknowledge certain

limitations within our study. First, although rigorous statistical procedures were implemented, it is important to note that potential residual confounding effects may still exist. For example, data related to allergens, specific asthma-control medications, and asthma endotypes were not included in the 2011–2020 NHANES database and may have an impact on the results. Second, the 24-h recall technique imposed inherent limitations that hindered the reliability and validity of the nutritional assessment. Third, the self-proclaimed diagnosis of asthma may affect the reliability. However, during the interview process, the interviewer emphasized to the participant that self-diagnosed asthma or asthma diagnosed by someone other than a doctor or health professional was not acceptable,[41] which greatly ensures the accuracy of asthma diagnosis. Fourth, since the study population in this research was overweight or obese children and adolescents, the diagnosis of asthma in this population may be due to respiratory-related issues caused by obesity itself rather than asthma. Furthermore, as asthma and food allergies may often coincide,[42] and since zinc-rich foods like nuts and seafood are common allergens, the lower dietary zinc intake observed in this study may be an attempt to avoid allergens. In addition, because of the limitations of the NHANES database, which does not provide data on the progression of asthma, we were unable to further assess the relationship between zinc intake and asthma. Finally, the cross-sectional design of the study also prevents the establishment of causal inferences. Future large-scale prospective cohort studies and multicenter randomized controlled trials are needed to investigate the cause-and-effect relationship between dietary zinc intake and asthma in overweight or obese children and adolescents.

CONCLUSIONS

This study revealed an inverse association between dietary zinc intake and asthma in overweight or obese US pediatric populations. Our findings suggest the potential significance of zinc as a crucial nutrient with implications for asthma.

Abbreviations

NHANES, National Health and Nutrition Examination Survey; CDC, the Centers for Disease Control and Prevention; MEC, mobile examination center; NCHS, National Center for Health Statistics; BMI, Body mass index; AMPM, Automated Multiple Pass Method; WBC, white blood cell count; EOPC, eosinophils percent; HGB, hemoglobin; PIR, the poverty income ratio; OR, odds ratios; Cis, confidence intervals; RCS, restricted cubic splines.

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Availability of data and materials

Public datasets used in this study are available online. The repository names and accession numbers are available at https://www.cdc.gov/nchs/nhanes/index.htm (accessed: March 6, 2024).

Author contributions

(1) Conception and design: Chuhan Cheng and Liyan Zhang.
(2) Data curation: Chuhan Cheng, Jing Lin, and Zihan Zhang.
(3) Data analysis and interpretation: Chuhan Cheng.
(4) Writing - Original Draft: Chuhan Cheng.
(5) Writing - Review & Editing: All authors.
(6) Final approval of manuscript: All authors.

Ethics statement

The NHANES obtained authorization from the National Center for Health Statistics (NCHS) Ethics Review Committee. For the secondary analysis, no additional institutional review board approval was required.

Authors' consent for publication

All authors have read the manuscript and approved it for publication.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2024.100900.

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REFERENCES

1. The Global Asthma Report 2022. http://globalasthmareport.org/burden/burden.php (accessed 2023-12-07).
2. Most Recent National Asthma Data | CDC. https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm (accessed 2023-12-07).
3. Zhang X, Han Y, Tian Q, et al. The association between N-3 polyunsaturated fatty acid intakes and asthma in US children and adolescents: a cross-sectional study from NHANES. *Pediatr Allergy Immunol*. 2023;34(9):e14024. https://doi.org/10.1111/pai.14024.
4. The WHO Child Growth Standards. https://www.who.int/tools/child-growth-standards (accessed 2023-12-07).
5. Children: new threats to health. https://www.who.int/news-room/fact-sheets/detail/children-new-threats-to-health (accessed 2023-12-18).
6. Reyes-Angel J, Kaviany P, Rastogi D, Forno E. Obesity-related asthma in children and adolescents. *Lancet Child Adolesc Health*. 2022;6(10):713–724. https://doi.org/10.1016/S2352-4642(22)00185-7.
7. Wong M, Han Y-Y, Rosser F, et al. Persistent overweight or obesity, lung function, and asthma exacerbations in Puerto Rican youth. *Ann Allergy Asthma Immunol*. 2022;128(4):408–413.e2. https://doi.org/10.1016/j.anai.2022.01.004.
8. Juel CT-B, Ulrik CS. Obesity and asthma: impact on severity, asthma control, and response to therapy. *Respir Care*. 2013;58(5):867–873. https://doi.org/10.4187/respcare.02202.
9. Brustad N, Bønnelykke K, Chawes B. Dietary prevention strategies for childhood asthma. *Pediatr Allergy Immunol*. 2023;34(7), e13984. https://doi.org/10.1111/pai.13984.
10. Knebusch N, Mansour M, Vazquez S, Coss-Bu JA. Macronutrient and micronutrient intake in children with lung disease. *Nutrients*. 2023;15(19):4142. https://doi.org/10.3390/nu15194142.
11. Zajac D. Mineral micronutrients in asthma. *Nutrients*. 2021;13(11):4001. https://doi.org/10.3390/nu13114001.
12. Khanbabaee G, Omidian A, Imanzadeh F, Adibeshgh F, Ashayeripanah M, Rezaei N. Serum level of zinc in asthmatic patients: a case-control study. *Allergol Immunopathol*. 2014;42(1):19–21. https://doi.org/10.1016/j.aller.2012.07.008.
13. Tahan F, Karakukcu C. Zinc status in infantile wheezing. *Pediatr Pulmonol*. 2006;41(7):630–634. https://doi.org/10.1002/ppul.20413.
14. Jayaram L, Chunilal S, Pickering S, Ruffin RE, Zalewski PD. Sputum zinc concentration and clinical outcome in older asthmatics. *Respirology*. 2011;16(3):459–466. https://doi.org/10.1111/j.1440-1843.2011.01932.x.
15. Uysalol M, Uysalol EP, Yilmaz Y, et al. Serum level of vitamin D and trace elements in children with recurrent wheezing: a cross-sectional study. *BMC Pediatr*. 2014;14:270. https://doi.org/10.1186/1471-2431-14-270.
16. Bishopp A, Sathyamurthy R, Manney S, Webbster C, Krishna MT, Mansur AH. Biomarkers of oxidative stress and antioxidants in severe asthma: a prospective case-control study. *Ann Allergy Asthma Immunol*. 2017;118(4):445–451. https://doi.org/10.1016/j.anai.2017.02.004.
17. NHANES survey methods and analytic guidelines. https://wwwn.cdc.gov/nchs/nhanes/analyticguidelines.aspx (accessed 2023-12-07).
18. Zipf G, Chiappa M, Porter KS, Ostchega Y, Lewis BG, Dostal J. National health and nutrition examination survey: plan and operations, 1999-2010. *Vital Health Stat 1*. 2013;(56):1–37.
19. Nhanes - NCHS research Ethics review board approval. https://www.cdc.gov/nchs/nhanes/irba98.htm (accessed 2023-12-07).
20. Food Surveys Research Group : USDA ARS. https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/food-surveys-research-group/(accessed 2023-12-07).
21. Growth charts - homepage. https://www.cdc.gov/growthcharts/index.htm (accessed 2023-12-07).
22. Nurmatov U, Nwaru BI, Devereux G, Sheikh A. Confounding and effect modification in studies of diet and childhood asthma and allergies. *Allergy*. 2012;67(8):1041–1059. https://doi.org/10.1111/j.1398-9995.2012.02858.x.
23. WWEIA data tables : usda ars. https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/food-surveys-research-group/docs/wweia-data-tables/(accessed 2023-12-07).
24. Buuren SV, Groothuis-Oudshoorn K. Mice : multivariate imputation by chained equations in *R*. *J Stat Software*. 2011;45(3). https://doi.org/10.18637/jss.v045.i03.
25. Yang Q, Zheng J, Chen W, et al. Association between preadmission metformin use and outcomes in intensive care unit patients with sepsis and type 2 diabetes: a cohort study. *Front Med*. 2021;8, 640785. https://doi.org/10.3389/fmed.2021.640785.
26. Peters U, Dixon AE, Forno E. Obesity and asthma. *J Allergy Clin Immunol*. 2018;141(4):1169–1179. https://doi.org/10.1016/j.jaci.2018.02.004.
27. Siripornpanich S, Chongviriyaphan N, Manuyakorn W, Matangkasombut P. Zinc and vitamin C deficiencies associate with poor pulmonary function in children with persistent asthma. *Asian Pac J Allergy Immunol*. 2022;40(2):103–110. https://doi.org/10.12932/AP-100620-0878.
28. Ariaee N, Farid R, Shabestari F, Shabestari M, Jabbari Azad F. Trace elements status in sera of patients with allergic asthma. *Rep Biochem Mol Biol*. 2016;5(1):20–25.
29. de Cássia Ribeiro-Silva R, Fiaccone RL, Barreto ML, da Silva LA, Santos LFP, Alcantara-Neves NM. The prevalence of wheezing and its association with serum zinc concentration in children and adolescents in Brazil. *J Trace Elem Med Biol*. 2014;28(3):293–297. https://doi.org/10.1016/j.jtemb.2014.02.007.

30. Rerksuppaphol S, Rerksuppaphol L. Zinc supplementation in children with asthma exacerbation. *Pediatr Rep*. 2016;8(4):6685. https://doi.org/10.4081/pr.2016.6685.

31. Ghaffari J, Khalilian A, Salehifar E, Khorasani E, Rezaii MS. Effect of zinc supplementation in children with asthma: a randomized, placebo-controlled trial in northern Islamic Republic of Iran. *East Mediterr Health J*. 2014;20(6):391–396.

32. Institute of Medicine (US) Panel on Micronutrients. *Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Washington (DC): National Academies Press (US); 2001.

33. Prasad AS. Zinc: an antioxidant and anti-inflammatory agent: role of zinc in degenerative disorders of aging. *J Trace Elem Med Biol*. 2014;28(4):364–371. https://doi.org/10.1016/j.jtemb.2014.07.019.

34. Sprietsma JE. Modern diets and diseases: NO–zinc balance. *Med Hypotheses*. 1999;53(1):6–16. https://doi.org/10.1054/mehy.1999.0867.

35. Kahmann L, Uciechowski P, Warmuth S, Malavolta M, Mocchegiani E, Rink L. Effect of improved zinc status on T helper cell activation and TH1/TH2 ratio in healthy elderly individuals. *Biogerontology*. 2006;7(5–6):429–435. https://doi.org/10.1007/s10522-006-9058-2.

36. Wessels I, Maywald M, Rink L. Zinc as a gatekeeper of immune function. *Nutrients*. 2017;9(12):1286. https://doi.org/10.3390/nu9121286.

37. Lambrecht BN, Hammad H, Fahy JV. The cytokines of asthma. *Immunity*. 2019;50(4):975–991. https://doi.org/10.1016/j.immuni.2019.03.018.

38. Bao S, Knoell DL. Zinc modulates airway epithelium susceptibility to death receptor-mediated apoptosis. *Am J Physiol Lung Cell Mol Physiol*. 2006;290(3):L433–L441. https://doi.org/10.1152/ajplung.00341.2005.

39. Truong-Tran AQ, Ruffin RE, Foster PS, et al. Altered zinc homeostasis and caspase-3 activity in murine allergic airway inflammation. *Am J Respir Cell Mol Biol*. 2002;27(3):286–296. https://doi.org/10.1165/rcmb.2001-0014OC.

40. Roscioli E, Hamon R, Lester S, Murgia C, Grant J, Zalewski P. Zinc-rich inhibitor of apoptosis proteins (IAPs) as regulatory factors in the epithelium of normal and inflamed airways. *Biometals*. 2013;26(2):205–227. https://doi.org/10.1007/s10534-013-9618-2.

41. NHANES 2015-2016 Questionnaire Instruments. https://wwwn.cdc.gov/nchs/nhanes/ContinuousNhanes/questionnaires.aspx?BeginYear=2015 (accessed 2024-02-18).

42. Emons JAM, Gerth van Wijk R. Food allergy and asthma: is there a link? *Curr Treat Options Allergy*. 2018;5(4):436–444. https://doi.org/10.1007/s40521-018-0185-1.