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RESEARCH

High ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 increases the risk of asthma attack in American asthma adults: a population study

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Abstract

Objective The relationship between vitamin D3 and asthma remains controversial. However, previous studies have largely overlooked the impact of epi-25-(OH)-vitamin D3. This study aims to investigate the effects of different forms of vitamin D3 on asthma attack in adults.

Methods In this cross-sectional study, a total of 3,873 eligible adult participants were extracted from the national health and nutrition examination survey (NHANES) database from 2007 to 2018. Based on quartiles method, different levels of vitamin D were divided into four groups (Quartile 1–4). Bivariate correlation analysis was performed for vitamin D and covariates to avoid multicollinearity. Multivariate logistic regression was used to investigate the association between serum levels of vitamin D3 (epi-25-(OH)-vitamin D3 and 25-(OH)-vitamin D3) and asthma attack, adjusting for covariates including age, gender, race, length of time in the U.S., house poverty income ratio (PIR), education level, smoking history, hypertension history, and diabetes history. The ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 was used for secondary analysis of its association with asthma attack. The outcomes were assessed by odds ratios (ORs) and 95% confidence intervals (CIs).

Results Among the 3,873 eligible adults American with asthma, 1,508 (38.94%) had experienced at least one acute asthma attack in the past year. There was no significant correlation between vitamin D and covariates. After adjusting for covariates including age, gender, race, length of time in the U.S., house poverty income ratio (PIR), education level, smoking history, hypertension history and diabetes history, we found a positive correlation between the ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 and asthma attack. Additionally, a high ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 was more common among elder, male, of normal weight, non-Hispanic American, have a long time stay in the U.S., a high house PIR, and a history of hypertension individuals.

Conclusion Our findings suggest that attention should be given to asthma attack associated with a high ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 in American adults who are elderly, male, of normal weight, non-Hispanic Americans, have long-term residence in the U.S., a high house PIR, and a history of hypertension.

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Keywords Asthma, Attack, Vitamin, NHANES

Background

Asthma is a non-infectious disease affecting both children and adults, characterized by bronchial hyperresponsiveness, reversible obstruction, and chronic airway inflammation. The Global Initiative for Asthma (GINA) 2024 guidelines reported [1] that asthma affects approximately 300 million people worldwide and causes around 1,000 deaths daily. Additionally, the World Health Organization (WHO) [2] predicted that the number of people with asthma would increase by 100 million by 2025. The high costs of acute attacks, hospitalization, and comorbidity management make asthma a significant public health problem, and the variety of allergens complicates prevention efforts [3]. Therefore, exploring other risk factors to improve the quality of life for asthma patients and reduce healthcare costs is beneficial for asthma management.

Vitamins are one of the nutrients that make up the human body and play an important role in maintaining normal metabolism and bodily functions. Vitamin D, an essential trace element, is primarily sourced from dietary intake, particularly from eggs and milk [4]. Additionally, the body can synthesize vitamin D3 when the skin is exposed to ultraviolet (UV) light, converting 7-dehydrocholesterol to vitamin D3, which is subsequently hydroxylated by liver 25-hydroxylase and kidney 1α-hydroxylase to form the active 1,25-dihydroxyvitamin D3 [5]. Growing evidences suggested that vitamin D may influence the development of asthma. A case-control study from northern Jordan [6] found a positive correlation between serum 25-(OH)-vitamin D3 levels and asthma control in female asthma patients. A meta-analysis [7] indicated that low levels of vitamin D3 in both adults and children were associated with a decreased lung function (FEV1, FEV1%, FVC, FEV1/FVC). Moreover, Adam-Bonci TI and colleagues [8] concluded that vitamin D supplementation exhibited protective effects against oxidative stress related to OVA-induced acute airway inflammation in asthma mice. However, several clinical studies [9–11] have reported that vitamin D3 supplementation does not significantly reduce the risk of asthma attack.

Epi-25-(OH)-vitamin D3 is an intermediate metabolite of vitamin D, and its synthesis depends on the enzyme 3-epimase in the liver [5]. Epi-25-(OH)-vitamin D3 has the same molecular weight as 25-(OH)-vitamin D3, but the different spatial configuration of the hydroxyl group on the third carbon atom renders it biologically inactive [5]. Therefore, epi-25-(OH)-vitamin D3 can affect the conversion of biologically active vitamin D and lead to an overestimation of vitamin D storage levels. Despite nationwide surveys measuring epi-25-(OH)-vitamin D3 in some developed countries and regions being conducted for less than 15 years [12, 13], a cross-sectional case-control study [14] have confirmed its involvement in various diseases, including those affecting the endocrine and skeletal systems. This suggests that there is significant potential in exploring the role of epi-25-(OH)-vitamin D3 in asthma. In this study, we aim to utilize high-quality data from the NHANES database to investigate the association between epi-25-(OH)-vitamin D3 and asthma attack.

Methods

Data sources

The NHANES is a research initiative crafted to evaluate the health and nutritional status of both adults and children within the United States. NHANES gathers a wide spectrum of data, encompassing demographics, socioeconomic factors, dietary habits, and health information, all for the betterment of the American populace. These invaluable datasets are readily accessible to researchers and internet users on www.cdc.gov/nchs/nhanes/. The NHANES study received ethical approval from the Ethics Review Board of the National Center for Health Statistics. Throughout our study, we meticulously adhered to the NHANES data usage policy, ensuring that no sensitive matters such as gender or racial discrimination were implicated.

Study population

The study used six cycles of NHANES (2007–2008, 2009–2010, 2011–2012, 2013–2014, 2015–2016, 2017–2018) for a cross-sectional survey. The exclusion criteria were as follows: (a) participants below 18 years old and (n=29126); (b) Participants were in pregnancy (n=236); (c) missing or incomplete data for epi-25-(OH)-vitamin D3 and 25-(OH)-vitamin D3 (n=3870); (d) had never been told have asthma (n=22737). Finally, a representative national sample of 3873 participants was recruited for this survey. The data selection process is shown in Fig. 1.

Define of current asthma

Asthma attack status is determined based on information obtained from questionnaires of the NHANES. If a participant answers "Yes" to the question "Has a doctor or other health professional ever told you that you have asthma?" and also responds affirmatively to any of the following questions: "During the past 12 months, have you had an episode of asthma or an asthma attack?", "During the past 12 months, have you had to visit an emergency room or urgent care center because of asthma?", "During

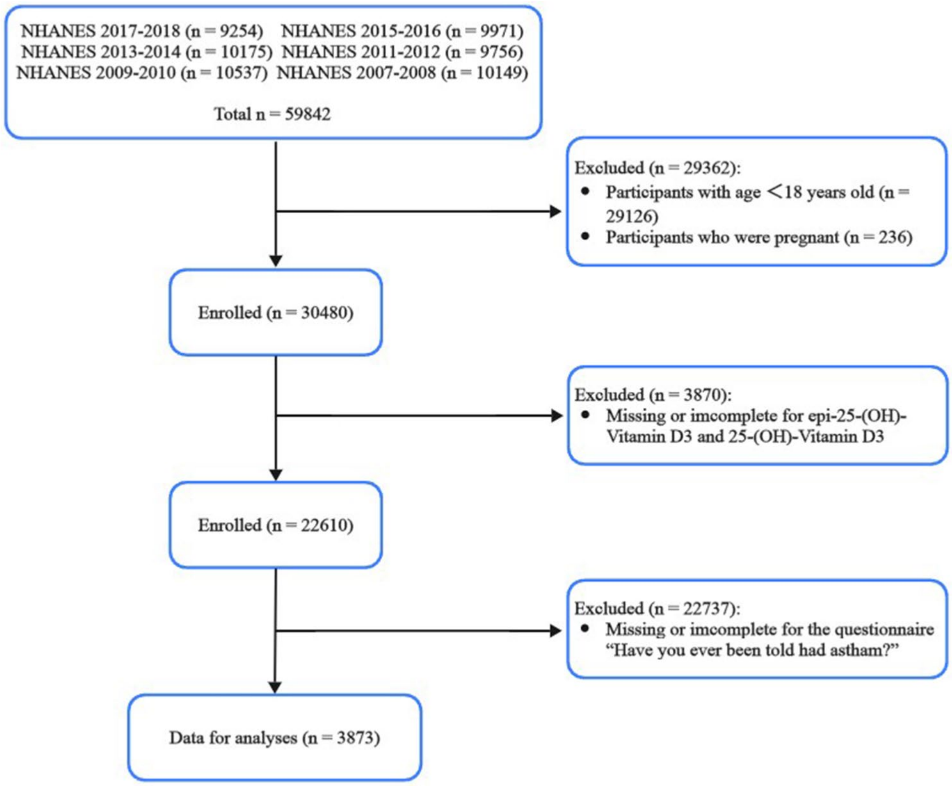

Fig. 1 The flow chart of participants selection

the past 3 months, have you taken medication prescribed by a doctor or other health professionals for asthma?", "In the past 12 months, have you had wheezing or whistling in your chest?" or "In the past 12 months, have you taken medication, prescribed by a doctor, for wheezing or whistling?", they are regarded as asthma attack.

Measurement of Vitamin D

The serum levels of 25-(OH)-vitamin D3 and epi-25-(OH)-vitamin D3 in participants from 2008 to 2018 NHANES were measured using a standardized liquid chromatography-tandem mass spectrometry (LC-MS/MS) method. In this study, we calculated the ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 for secondary analysis of the association between epi-25-(OH)-vitamin D and asthma exacerbations. This ratio can indirectly reflect the percentage of bioactive vitamin D.

Evaluation of covariates

According to previous literatures [15, 16], we identified 10 confounding factors related to vitamin D3 and asthma exacerbations, including age, gender, race, body mass index (BMI), length of time in the US, education level, smoking history, diabetes history, hypertension history, and house poverty income ratio (PIR). To facilitate comparative analysis, we performed secondary processing on some covariates as follows:

a) **Gender**: Classified as male and female.
b) **Age**: Represented as a continuous variable in the baseline characteristics table of the study population. To explore the correlation between vitamin D levels and current asthma exacerbations across different age groups, participants were categorized into three groups according to WHO standards [17]: youth (< 45 years old), middle-aged (≥ 45 and <60 years old), and elderly (≥ 60 years old).
c) **BMI**: Participants were classified into four groups based on WHO standards [18]: underweight (< 18.5 kg/m^2), normal weight (18.50–24.99 kg/m^2), overweight (25.00–29.99 kg/m^2), and obesity (≥ 30.00 kg/m^2).
d) **Race/Ethnicity**: Classified into Mexican American, non-Hispanic White, non-Hispanic Black, and other races.
e) **Education level**: Categorized as high school or less, some college, and college graduate or above.
f) **Length of time in the US**: Classified into less than 10 years, 10–29 years, and 30 years or more.
g) **House PIR**: Reflects the ratio of family income to the national poverty line, classified into below poverty line (< 1.00) and equal to or above the national poverty line (≥ 1.00).
h) **Smoking history**: Classified into three different frequencies groups based on the participant's

response to the survey question "Do you now smoke cigarettes?", including every day, some days, and not at all.

i) **Hypertension history**: Categorized as having or not having a history of hypertension based on the participant's affirmative or negative response to the survey question "Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?"

j) **Diabetes history**: Categorized as having or not having a history of diabetes based on the participant's affirmative or negative response to the survey question "Have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?"

Table 1 Characteristics of the study population based on the presence of asthma attack

Characteristics	Asthma attack(*n* = 1508)	Non-asthma attack (*n* = 2365)	*P* Value
Age(Year)			<0.001
<45	616 (40.85)	1240 (52.43)	
≥45&<60	403 (26.72)	474 (20.04)	
≥60	489 (32.43)	651 (27.53)	
Gender(%)			<0.001
Male	523 (34.68)	1128 (47.40)	
Female	985 (65.32)	1237 (52.30)	
BMI(kg/m2)			<0.001
<18.50	18 (1.20)	52 (2.23)	
18.50-24.99	318 (21.31)	613 (26.29)	
25.00-29.99	381 (25.54)	690 (29.59)	
≥30.00	775 (51.94)	977 (41.90)	
Race(%)			0.083
Mexican American	140 (9.28)	260 (10.99)	
Non-Hispanic White	734 (48.67)	1004 (42.45)	
Non-Hispanic Black	351 (23.28)	546 (23.09)	
Other	283 (18.77)	555 (23.47)	
Education levels(%)			<0.001
High school or below	709 (49.79)	931 (42.59)	
Some college	470 (33.01)	742 (33.94)	
College graduate or above	245 (17.21)	513 (23.47)	
Length of time in US(%)			0.175
less than 10 year	29 (13.12)	82 (18.89)	
10 year to 29 year	102 (46.15)	185 (42.63)	
30 year or more	90 (40.72)	167 (38.48)	
PIR(%)			<0.001
<1.00	436 (31.17)	500 (23.10)	
≥1.00	963 (68.84)	1665 (76.91)	
Hypertension(%)			<0.001
Yes	703 (46.65)	852 (36.04)	
No	804 (53.35)	1512 (63.96)	
Diabetes(%)			<0.001
Yes	300 (20.49)	309 (13.43)	
No	1164 (79.51)	1992 (86.57)	
Smoke			0.020
Every day	357 (44.29)	399 (38.07)	
Some days	72 (8.93)	94 (8.97)	
Not at all	377 (46.77)	555 (52.96)	
Epi-25-OH-D3 (nmol/L)	3.50±2.81	3.88±2.91	<0.001
25-OH-D3 (nmol/L)	57.99±27.81	61.51±29.57	<0.001
Epi-25-OH-D3/25-OH-D3	0.060±0.029	0.072±0.026	0.031

BMI: body Mass Index. PIR: poverty income ratio

Statistical analysis

We performed all statistical analyses using IBM SPSS Statistics 26.0 and EmpowerStats. In this study, continuous variables were described as means±standard errors (for continuous variable) or interquartile ranges (IQR, for discontinuous variable) and were compared between groups using the Student's t-test and one-way anova (for continuous variable), and the Mann-Whitney U test (for discontinuous variable). Categorical variables were described as frequencies and percentages and were compared using the Chi-square test. Statistical significance was defined at a P value <0.05. Survey weights, strata, and primary sampling units were applied to all analyses to account for the NHANES complex and multi-stage survey design.

Bivariate correlation analysis was performed for vitamin D and covariates to avoid multicollinearity. Multivariate logistic regression was used to determine the adjusted odds ratios (ORs) and 95% confidence intervals (CIs) between serum vitamin D3 [epi-25-(OH)-vitamin D3, 25-(OH)-vitamin D3, and the ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3)] and asthma attack in U.S. adults. The crude model was unadjusted. Model 1 was adjusted for age, gender, and race. Model 2 further adjusted for education level, length of time in the U.S., PIR, BMI, smoking history, diabetes history, and hypertension history.

Result

Population characteristics

In this study, 3873 eligible adult participants were divided into asthma attack group ($n=1508$) and non-asthma attack group ($n=2365$). In participants with asthma, the probability of experiencing at least one acute asthma exacerbation within one year is approximately 38.94%. Table 1 shows the baseline characteristics of all included participants. Compared to American adults without asthma attack, those with asthma attack were more likely to be middle-aged and elderly, female, obese, lower education level, lower household PIR, higher frequency of smoking history, and a history of diabetes and hypertension. However, serum levels of epi-25-(OH)-vitamin D3 and 25-(OH)-Vitamin D3 appear to be lower in asthma attack group, as well as the ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3.

Table 2 Weighted multivariate logistic regression of serum vitamin D3 levels for people with asthma attack

	Cut-off (nmol/L)	Crude Model		Model 1		Model 2	
		OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Epi-25-(OH)-VitaminD3							
Quarttile 1	<1.93	1.912 (1.908-1.916)	<0.001	1.726 (1.720-1.727)	<0.001	3.998 (3.926-4.072)	<0.001
Quarttile 2	≥1.93&<2.98	1.560 (1.557-1.562)	<0.001	1.516 (1.514-1.519)	<0.001	0.521 (0.513-0.529)	<0.001
Quarttile 3	≥2.98&<4.24	1.490 (1.488-1.492)	<0.001	1.465 (1.463-1.467)	<0.001	2.818 (2.788-2.847)	<0.001
Quarttile 4	≥4.24	Ref		Ref		Ref	
25-(OH)-VitaminD3							
Quarttile 1	<41.50	0.880 (0.879-0.882)	<0.001	1.051 (1.049-1.053)	<0.001	0.913 (0.900-0.927)	<0.001
Quarttile 2	≥41.50&<55.00	0.933 (0.932-0.935)	<0.001	1.159 (1.158-1.161)	<0.001	2.516 (2.489-2.543)	<0.001
Quarttile 3	≥55.00&<70.10	0.963 (0.962-0.964)	<0.001	1.131 (1.130-1.132)	<0.001	1.233 (1.222-1.243)	<0.001
Quarttile 4	≥70.10	Ref		Ref		Ref	
Epi-25-(OH)-VitaminD3/25-(OH)-VitaminD3							
Quarttile 1	<0.043	1.023 (1.022-1.024)	<0.001	0.976 (0.975-0.977)	<0.001	0.167 (0.165-0.170)	<0.001
Quarttile 2	≥0.043&<0.056	0.928 (0.927-0.929)	<0.001	0.928 (0.927-0.929)	<0.001	0.187 (0.185-0.189)	<0.001
Quarttile 3	≥0.056&<0.070	1.026 (1.025-1.027)	<0.001	1.012 (1.011-1.013)	<0.001	0.420 (0.416-0.424)	<0.001
Quarttile 4	≥0.070	Ref		Ref		Ref	

ref, reference; ORs, odds ratio; CIs, confidence interval; crude model, unadjusted Model; model 1, adjustment for age, gender, race; Model 2, adjustment for age, gender, BMI, race, education level, length of time in U.S., house PIR, smoking history, diabetes and hypertension

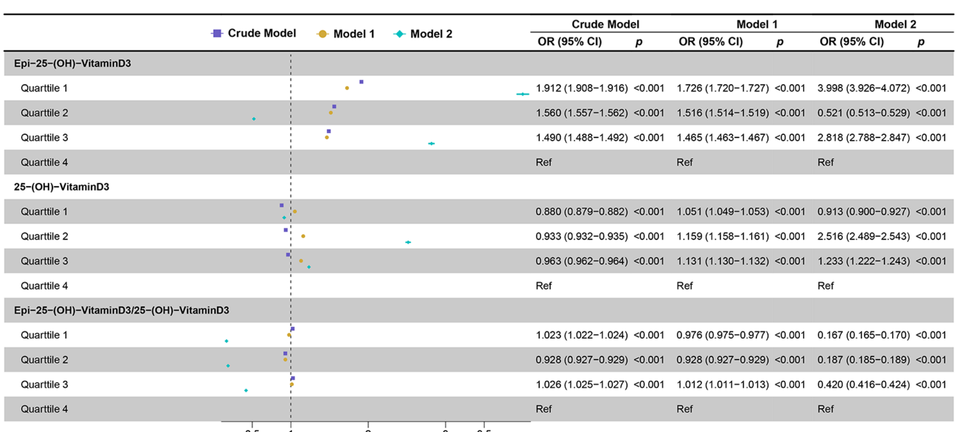

Fig. 2 Forest plot of weighted multivariate logistic regression

The association between vitamin D3 and current asthma attack

To explore the association between serum epi-25-(OH)-vitamin D3 and 25-(OH)-vitamin D3 with asthma attack in American adults, weighted multinomial logistic regression was performed, as shown in Tables 2 and Fig. 2. Elevated serum levels of epi-25-(OH) -vitamin D3 increased asthma attacks in both the crude model and Model 1. Serum 25-(OH) -Vitamin D3 levels were negatively associated with acute asthma attacks in the crude model, whereas positively associated in the model 1 after adjusting for age, gender, and race. However, the association of different ratios of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 with asthma attacks was inconsistent between the crude model and Model 1.

In Model 2, adjusted for all covariates, serum levels of epi-25-(OH)-vitamin D3 and 25-(OH)-vitamin D3 showed different correlations with asthma exacerbation. Compared to the Quartile 4 level, epi-25-(OH)-vitamin

D3 at Q1 [OR 3.998, 95%CI (3.926–4.072)]and Q3 [OR 2.818, 95%CI (2.788–2.847)] levels had a higher risk of asthma attack, whereas at Q2 [OR 0.521, 95%CI (0.513–0.529)] level, the risk was lower. For 25-(OH)-vitamin D3, the risk of asthma attack was significantly higher at Q2 [OR 2.516, 95%CI (2.489–2.543)] and Q3 [OR 1.233, 95%CI (1.222–1.243)] levels, and lower at Q1 [OR 0.913, 95%CI (0.900-0.927)] level. Therefore, further secondary analysis of the ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 in relation to asthma exacerbation is necessary. Although crude models and model 1 were unstable, results in model 2 showed that a lower ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 was significantly associated with a decreased risk of asthma attack.

Serum vitamin D3 in different population

Table 3 shows the level of serum epi-25-(OH)-vitamin D3, 25-(OH)-vitamin D3, and the ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-Vitamin D3 among different populations of American adults. Serum levels of epi-25-(OH)-vitamin D3 and 25-(OH)-vitamin D3 are higher in individuals who are of normal weight, non-Hispanic White, highly educated, long-term U.S. residents, with

Table 3 The population differences of serum vitamin D3 levels

	epi-25-OH-D3		25-OH-D3		epi-25-OH-D3/25-OH-D3	
	Mean±MD	*P* value	Mean±MD	*P* value	Mean±MD	*P* value
Age		<0.001		<0.001		<0.001
<45	3.60±2.31		61.51±26.31		0.062±0.024	
≥45&<60	4.85±3.45		65.79±28.97		0.061±0.026	
≥60	4.39±3.11		73.91±34.55		0.067±0.030	
Gender		0.577		0.003		<0.001
Male	3.76±2.59		58.56±26.17		0.063±0.025	
Female	3.71±3.07		61.31±30.80		0.059±0.028	
BMI(kg/m2)		<0.001		<0.001		<0.001
<18.50	3.60±2.31		63.00±28.37		0.057±0.021	
18.50-24.99	4.85±3.45		72.28±31.47		0.065±0.028	
25.00-29.99	4.39±3.11		68.43±27.85		0.062±0.027	
≥30.00	3.72±2.71		59.68±28.29		0.061±0.025	
Race		<0.001		<0.001		<0.001
Mexican American	3.27±2.52		52.86±21.89		0.061±0.024	
Non-Hispanic White	4.67±3.18		71.45±29.20		0.064±0.027	
Non-Hispanic Black	2.67±2.05		45.40±26.01		0.060±0.024	
Other	3.69±2.76		60.27±26.12		0.060±0.026	
Education levels		<0.001		<0.001		0.959
High school or below	4.01±3.04		62.67±28.81		0.062±0.027	
Some college	4.14±3.02		65.14±29.55		0.062±0.026	
College graduate or above	4.47±3.03		70.25±30.38		0.062±0.025	
Length of time in US		<0.001		<0.001		0.008
less than 10 year	3.12±2.43		55.48±20.77		0.056±0.027	
10 year to 29 year	3.36±1.93		56.09±21.75		0.060±0.023	
30 year or more	4.39±3.95		63.80±29.14		0.065±0.034	
PIR		<0.001		<0.001		0.012
<1.00	3.26±2.83		54.73±27.34		0.059±0.028	
≥1.00	3.90±2.90		62.08±29.27		0.062±0.027	
Hypertension		0.001		<0.001		<0.001
Yes	3.93±3.60		61.98±32.00		0.063±0.029	
No	3.60±2.72		58.89±26.63		0.060±0.025	
Diabetes		0.793		0.733		0.128
Yes	3.69±2.70		59.55±29.99		0.063±0.030	
No	3.72±2.90		59.99±28.65		0.060±0.026	
Smoke		<0.001		<0.001		0.088
Every day	3.80±2.80		60.18±26.03		0.062±0.026	
Some days	3.88±2.95		59.67±31.89		0.065±0.028	
Not at all	4.54±3.32		68.79±30.11		0.064±0.028	

BMI: body Mass Index. PIR: poverty income ratio high family PIR, a history of hypertension, and non-smokers. 25-(OH)-vitamin D3 is higher in middle-aged individuals, while epi-25-(OH)-vitamin D3 is higher in females and the elderly. Moreover, higher ratios of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 are found in the elderly, males, non-Hispanic Whites, highly educated individuals, long-term U.S. stay, those with high family PIR, and those with a history of hypertension.

Discussion

Asthma is a chronic inflammatory disease of the airways, characterized by wheezing, shortness of breath, coughing, and chest tightness [19]. The neglect of treatment and management makes asthma one of the significant challenges faced by the healthcare system, especially in low-income developing countries [20]. Due to the complex pathogenesis of asthma, its prevalence varies among different populations. Age and gender are closely related to asthma. Before puberty, the prevalence of asthma is higher in boys, while after puberty, women become the primary group affected by asthma, and this trend continues into old age [21]. Obesity is an independent risk factor for asthma. A prospective study [22] has shown that the risk of daily or near-daily asthma symptoms is higher in obese populations [OR 1.81, 95% CI 1.10–2.96]. Income is also a potential factor influencing asthma. A survey of adults in 17 countries [23] revealed that the prevalence of asthma in high-income developed countries reached a remarkable 10.6%, significantly higher than in low-income developing countries. Additionally, several national surveys from different countries [24–26] have confirmed a positive correlation between hypertension, diabetes, and asthma prevalence. Our study found that asthma attacks are more concentrated in American asthma populations with characteristics such as youth, female gender, obesity, low education level, long-term residence in the U.S., high smoking frequency, and a history of diabetes or hypertension.

Vitamin D is one of the essential vitamins for daily activities in the human body. In clinical practice, vitamin D is commonly used to predict systemic bone density and plasma calcium and phosphorus levels, particularly in elderly patients with osteoporosis [27, 28]. It is also an important medication for preventing rickets in children [29]. Previous studies have investigated the correlation between vitamin D3 and asthma, but their conclusions vary. Al-Thagfan et al. [30] found that serum vitamin D3 levels were lower in asthma patients and were moderately to strongly correlated with disease severity. A large sample study from the UK [31] showed that vitamin D deficiency was associated with a higher likelihood of asthma and current wheezing, as well as lower lung function. Another high-quality meta-analysis [32] indicated that vitamin D3 supplementation could reduce the rate of asthma exacerbations, especially in patients with vitamin D deficiency. However, results from the ViDiAs and VIDA randomized controlled trials [9, 33] in the US did not support the benefit of vitamin D supplementation for asthma patients. Therefore, we believe that different forms of vitamin D contributed to these discrepancies. In this study, we independently explored the correlation between epi-25-(OH)-vitamin D3 and 25-(OH)-vitamin D3 with acute asthma exacerbations. The results indicated that different plasma levels of vitamin D3 were correlated differently with acute asthma exacerbations in American adults. Considering that the ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 can indirectly reflect biological activity, a secondary analysis of this ratio with acute asthma exacerbations was necessary. We found that, compared to North American asthma adults with a high ratio, those with a lower ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 had a significantly reduced risk of acute exacerbations. Additionally, a high ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 was more common in older adults, males, individuals with normal weight, non-Hispanic Americans, those with long-term residence in the US, high PIR, and a history of hypertension.

To our knowledge, this study is the first to explore the correlation between the ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 and the risk of acute asthma exacerbations based on the high-quality NHANES database. Additionally, this study investigated the differences in vitamin D3 levels among different populations. The study confirmed that a higher ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 is associated with an increased frequency of acute asthma exacerbations in American asthma adults. However, the study also has some limitations: (a) asthma diagnosis was based on NHANES interview reports, which may involve recall bias; (b) some potential confounding factors were not controlled; (c) the study population was limited to Americans and may not be generalizable; (d) a cross-sectional study cannot establish causation, and further research is needed to explain these findings.

Conclusion

Our findings suggest that attention should be given to asthma attack associated with a high ratio of epi-25-(OH)-vitamin D3 to 25-(OH)-vitamin D3 in American adults who are elderly, male, of normal weight, non-Hispanic Americans, have long-term residence in the U.S., a high PIR, and a history of hypertension.

Abbreviations

BMI	Body mass index
Cis	Confidence intervals
GINA	Global initiative for asthma
IQR	Interquartile ranges

NHANES	National health and nutrition examination survey
ORs	Odds ratios
PIR	Poverty income ratio
UV	Ultraviolet
WHO	World health organization

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Author contributions
Project design: Biao Peng. Data screening and verification: Biao Peng, Zhi-chao Yang and Da Liu. Statistical analysis: Biao Peng and Zhi-chao Yang. Manuscript writing: Biao Peng. Manuscript revision: Yi Xiong, Ting Ouyang, Qin He, Ling He and Shuo Qi.

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Data availability
All the data in our study was obtained from the open, public NHANES database (http://www.cdc.gov/nchs/nhanes/).

Declarations

Ethics approval and consent to participate
The NCHS Ethics Review Board protects the rights and welfare of NHANES participants. The NHANES protocol complies with the U.S. Department of Health and Human Services Policy for the Protection of Human Research Subjects. NCHS IRB/ERC Protocol number: 2005-06; 2011-17. Ethical review and approval were waived for this study as it solely used publicly available data for research and publication. Informed consent was obtained from all subjects involved in the NHANES.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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