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Association between vitamin levels and obesity in the national health and nutrition examination surveys 2017 to 2018

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Original Article

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Abstract

In recent years, the rapidly increasing incidence of obesity is becoming a worldwide public health problem. Obesity is a chronic disease which may have a major negative effect on the people's quality of life. Previous studies on the comprehensive effects of multivitamins on central obesity and general obesity are relatively few. The aim of this study was to evaluate association of vitamins exposure with obesity risk and obesity-related indicators. We fitted three statistical models (linear regression model, logistic regression model, and Bayesian kernel machine regression model) to evaluate the correlation between vitamin levels and obesity in the study population. The vitamin score represents the overall level of vitamin in serum, which was mutually verified with the results obtained from statistical model. The vitamin (A, C, and D) levels were significantly higher among non-obesity group compared to the obesity group. Using the lowest quartile of vitamin level as a referent, vitamin A, C, and D levels showed significantly negative correlation with the obesity risk in both adjusted and unadjusted models. When considering all vitamin as a mixed exposure, we found a generally negative relationship between vitamin mixtures with binary outcome (obesity) and continuous outcome (BMI, waist circumference, and hsCRP). Reduced levels of vitamins (A, C and D) increased the risk of obesity. Increased levels of vitamin mixtures can significantly reduce obesity risk and obesity-related indicators. Vitamins may reduce the risk of obesity by suppressing inflammatory responses.

Introduction

Obesity is a complex metabolic disease characterized by excessive weight gain, which is the main influencing factors of various disorders including hypertension, diabetes, atherosclerosis, and dyslipidemia. In recent years, the COVID-19 pandemic has forced people to stay at home and restrict daily activities, which has greatly increased the likelihood of obesity. Annually, at least 2.8 million deaths globally can be attributed to overweight or obesity.[1] It is estimated that 650 million adults are overweight or obese, and the number of people living with obesity in the world continues to increase.[2] There is an urgently need to understand obesity etiologies in the cause of developing preventable strategies and treatment.

Obesity is caused by numerous factors including heredity, diet, lifestyle, societal determinants, environment, and infectious agents, the above factors will lead to the increase of fat storage in the body.[3,4] However, the link between obesity and vitamin deficiency has been discussed and reviewed in the literature for a long time.[5,6] Vitamins represent a group of biologically active compounds that exert multiple functions in maintaining normal of the human body. Vitamin deficiency is common in people suffering from obesity, which may be linked to the involvement of vitamins in antioxidant, redox, and anti-inflammatory processes.[7,8] Previous animal studies suggest that vitamin supplementation can significantly reduce body fat content, reduce body weight gain or inhibit the development of obesity.[9,10] In vitro experiments, vitamin decreases obesity by promoting fatty acid oxidation in adipocytes and other tissues[11].

At present, there are few studies examining the relationship between multivitamins and obesity. Therefore, we used three statistical models including linear regression model, logistic regression model and Bayesian kernel machine regression (BKMR) model to evaluate the correlation between vitamins and obesity and obesity-related indicators (BMI, waist circumference).

Methods

Study population

The National Health and Nutrition Examination Survey (NHANES) is an ongoing program to assess the health and nutritional status of Americans, respondent data are released every two years. Survey participants were required to complete a series of questionnaires, then participants

underwent physical examination at the Mobile Examination Center (MEC), where biological samples were collected for laboratory tests. In this cross-sectional analysis, we utilized publicly available data covering the period 2017–2018. Participants were excluded if they were <20 years and did not complete a vitamin measurement. Among 9254 subjects, 7435 subjects completed the assessment of serum vitamin concentration at baseline, and 8704 had completed measurements of BMI and waist circumference. After excluding participants did not meet the inclusion criteria, and those with any missing variables, a total of 3059 participants were included in the final analysis. The protocol for NHANES was approved by the National Center for Health Statistics Research Ethics Review Board.

Outcomes variables

The body measures data (BMI and waist circumference) were gathered by trained health technicians in MEC. The height of the subject was measured using a stadiometer by fixing the back of the head, shoulder blades, hips and heels with the backboard. The weight was determined by a digital weight scale, and the waist circumference is measured at the uppermost lateral border of the right ilium with a tape measure. Based on the above measurements, we calculated BMI (kg/m^2). The mediating variable was serum high-sensitivity C-reactive protein (hsCRP), measured using a two reagent, immunoturbidimetric system (Centers for Disease Control and Prevention & National Center for Health Statistics).

Measurement of serum vitamin

After fasting for 12 hours, blood samples of all subjects were collected via venipuncture. Blood samples were stored under appropriate frozen conditions until they are shipped to National Center for Environmental Health for testing.[12] The sample volume required for analysis is 500 uL to allow sufficient material for initial analysis and repeat. Vitamin A (retinol), vitamin C (ascorbic acid), vitamin E (alpha-tocopherol), vitamin D (25-hydroxyvitamin D_2 + 25-hydroxyvitamin D_3) were measured in serum samples. Vitamin A and Vitamin E were determined by high-performance liquid chromatography with photodiode array detection method. Vitamin C is measured using isocratic ultra-high-performance liquid chromatography. Vitamin D is measured using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Critical quality control measures were taken to the analyses, including the uses of quality control specimen, blind separation of samples and random repeated testing of 2% of all samples. Detail information of the NHANES laboratory procedure is available at https://www.cdc.gov/nchs/nhanes/index.htm. For the values lower than the limit of detection (LOD), we used an imputed value of LOD/$\sqrt{2}$.

Covariates

The following covariates were included in this study: age, gender, race, education levels, family income-poverty ratio, serum cotinine, past-year alcohol drinking, history of diabetes and hypertension. Age was entered as a continuous variable. The remaining categorical variables as follow: gender (male, female), race (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Asian, Other Race), education levels (Less than 9th grade, 9–11th grade, High school graduate/GED or equivalent, Some college or AA degree, College graduate or above), family income-poverty ratio (≤1.30, 1.31–3.50, >3.50), serum cotinine (<LOD, LOD-10, >10), past-year alcohol drinking(0 times, >0 times), history of diabetes (yes, no), history of hypertension (yes, no).

Statistical analyses

Mean and standard deviation (SD) are used for describing the characteristics of continuous variables, classification variables are expressed in frequency or percentage. Vitamins (A, C, D and E) did not follow normal distribution according to the results of the Kolmogorov-Smirnov and Shapiro-Wilks tests (all $P < 0.001$). In our study, subjects were divided into two categories according to BMI levels (<30 kg/m^2, control group and ≥30 kg/m^2, general obesity). Vitamin score was calculated in the present study. For the four vitamins (A, C, D and E), each participant was assigned a score between one and ten, corresponding to the participant's decile of the vitamin levels, ten represents the highest level of each vitamin. The vitamin score was obtained by adding the scores of the participants' four vitamins. Linear regression models were used to assess the individual impact of vitamin score on obesity-related indicators. Logistic regression analysis was conducted to examine the association between serum vitamin level and obesity with the lowest quartile vitamin level as the referent category. The BKMR model was used to assess the overall impact of all vitamins on obesity and obesity-related indicators. The total effect of vitamin level on the outcomes was decomposed into direct and intermediary effects through mediation analysis. All statistical analyses were performed using SPSS (Version 22) and RStudio (Version 4.1.3). $P < 0.05$ was considered statistically significant.

Results

Participants' characteristics

The demographic characteristics of 3059 NHANES participants collected from 2017 to 2018 were presented in Table 1. More women were observed in the case group, and the opposite trend occurred in the control group, men were predominant in the control group ($P < 0.001$). The prevalence of obesity among the study participants was 43.35%. The mean (SD) BMI were 36.47 (6.04) kg/m^2 in the obesity group and 24.96 (3.14) kg/m^2 in the non-obesity group ($P < 0.001$). The obesity group tended to have a larger waist circumference (115.73 ± 13.26 cm vs. 89.96 ± 10.38 cm, $P < 0.001$). Significant differences were observed in race, education levels, family income-poverty ratio, hsCRP, the history of hypertension, and the history of diabetes between cases and controls (all $P < 0.05$). There was no significant difference in age, serum cotinine and drinking history between the two groups.

Vitamin levels comparison

None of study subjects had a vitamin level lower than its LOD (vitamin A: 1 μg/dL; vitamin C: 0.03 mg/dL; vitamin E: 40 μg/dL). The concentrations of vitamin A, C, and D in obesity group were significantly lower than that in control group (all $P < 0.001$). The mean (SD) concentration of vitamin score was 20.94 (7.67) in the obesity group and 22.90 (7.65) in the non-obesity group ($P < 0.001$). There was no statistical difference in vitamin E levels between the two groups (Table 2).

Table 1. Participant characteristics ($N = 3059$) in NHANES 2017-2018

Characteristics	Control $n = 1733$	Case $n = 1326$	P value
Age, years	49.74 ± 17.60	49.28 ± 16.00	0.458
Gender			<0.001*
Male	940 (54.2)	633 (47.7)	
Female	793 (45.8)	693 (52.3)	
Body mass index, kg/m^2	24.96 ± 3.14	36.47 ± 6.04	<0.001*
Waist circumference, cm	89.96 ± 10.38	115.73 ± 13.26	<0.001*
Race			<0.001*
Mexican American	206 (11.9)	208 (15.7)	
Other Hispanic	162 (9.3)	111 (8.4)	
Non-Hispanic White	630 (36.4)	499 (37.6)	
Non-Hispanic Black	343 (19.8)	374 (28.2)	
Non-Hispanic Asian	304 (17.5)	48 (3.6)	
Other Race	88 (5.1)	86 (6.5)	
Education levels			<0.001*
Less than 9th grade	113 (6.5)	72 (5.4)	
9–11th grade	189 (10.9)	151 (11.4)	
High school graduate	418 (24.1)	346 (26.1)	
Some college/AA degree	534 (30.8)	502 (37.9)	
College graduate	479 (27.6)	255 (19.2)	
Family income-poverty ratio			0.008*
≤1.30	469 (27.1)	388 (29.3)	
1.31–3.50	699 (40.3)	575 (43.4)	
>3.5	565 (32.6)	363 (27.4)	
Serum cotinine			0.060
<LOD	561 (32.4)	433 (32.7)	
LOD-10	684 (39.5)	567 (42.8)	
>10	488 (28.2)	326 (24.6)	
Past-year alcohol drinking			0.351
0	389 (22.4)	279 (21.0)	
>0	1344 (77.6)	1047 (79.0)	
hsCRP, mg/L	2.56 ± 5.07	5.67 ± 8.17	<0.001*
Diabetes			<0.001*
Yes	191 (11.0)	257 (19.4)	
No	1542 (89.0)	1069 (80.6)	
Hypertension			<0.001*
Yes	498 (28.7)	607 (45.8)	
No	1235 (71.3)	719 (54.2)	

*$P < 0.05$; Data presented are mean ± SD or n (%).

Linear regression analysis

We used linear regression to assess the association between vitamin score and obesity-related indicators (Fig. 1). When the model did not adjust the confounding factors, the vitamin score was negatively associated with BMI ($\beta = -0.13$, 95% CI: −0.16, −0.09), waist circumference ($\beta = -0.18$, 95% CI: −0.26, −0.11), and hsCRP ($\beta = -0.13$, 95% CI: −0.16, −0.10). After adjusting for confounding factors, the correlation stayed significant [BMI ($\beta = -0.16$, 95% CI: −0.20, −0.13), waist circumference ($\beta = -0.37$, 95% CI: −0.45, −0.29), and hsCRP ($\beta = -0.15$, 95% CI: −0.18, −0.11)].

Table 2. Comparison of concentrations of vitamins in all subjects

	Control		Case		
Vitamin	Median ± IQR	Mean ± SD	Median ± IQR	Mean ± SD	*P* value [a]
vitamin A	51.90 ± 19.50	53.39 ± 15.04	49.25 ± 19.50	51.68 ± 16.40	<0.001*
vitamin C	0.95 ± 0.61	0.94 ± 0.49	0.76 ± 0.62	0.79 ± 0.44	<0.001*
vitamin D	66.70 ± 36.60	70.08 ± 29.87	60.05 ± 37.40	64.18 ± 31.15	<0.001*
vitamin E	1130.00 ± 455.00	1227.35 ± 461.75	1150.00 ± 461.00	1223.87 ± 401.18	0.284
vitamin score	23.00 ± 12.00	22.90 ± 7.65	21.00 ± 11.00	20.94 ± 7.67	<0.001*

IQR, interquartile range.
*$P < 0.05$.
[a]the vitamin in the case group and the control group were compared by Mann-Whitney *U* test.

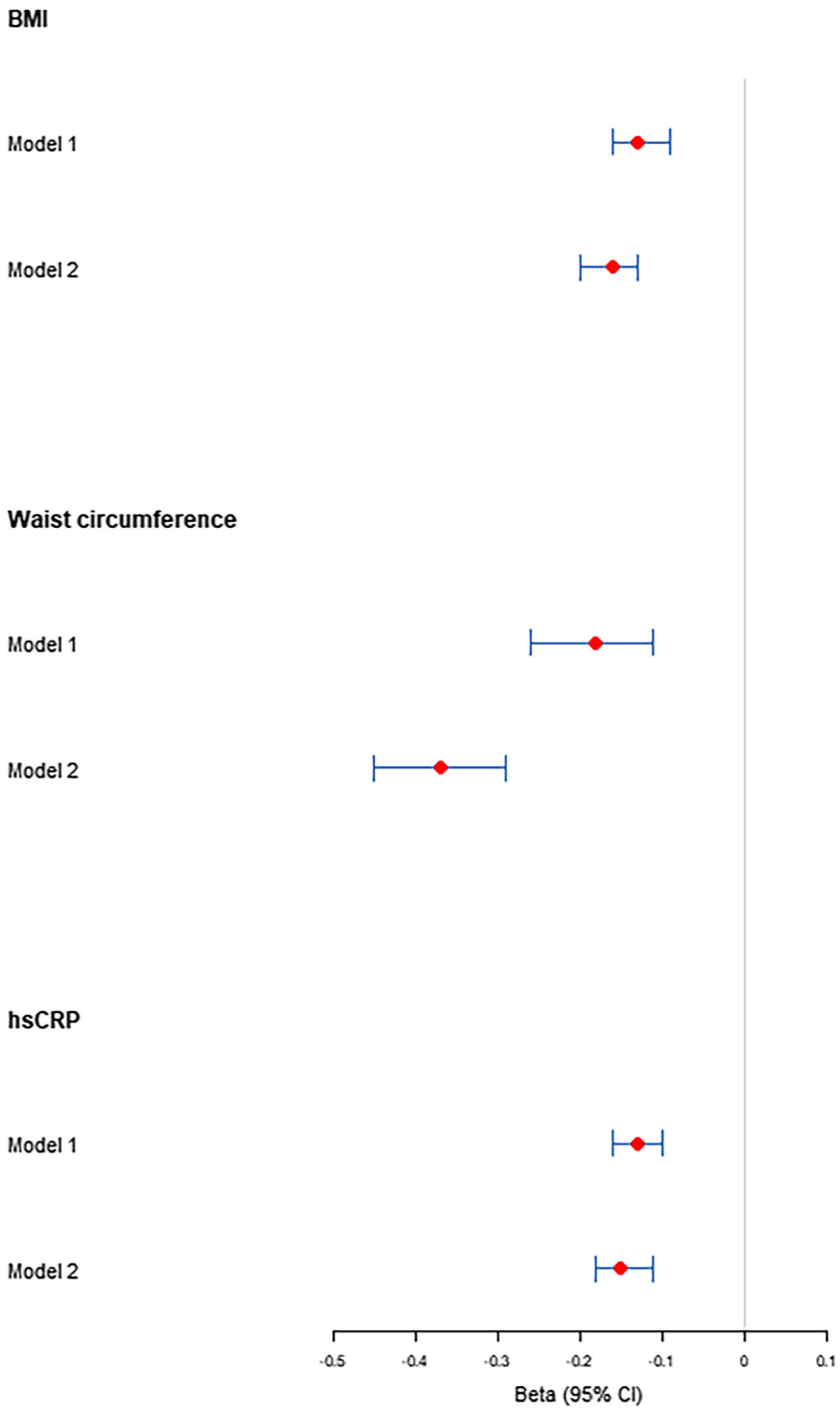

Figure 1. Association between vitamin score and obesity-related indicators based on linear regression model. Model 1 was unadjusted, whereas model 2 adjusted for age, gender, race, education levels, family income-poverty ratio, serum cotinine, past-year alcohol drinking, diabetes, and hypertension.

Logistic regression analysis

The results of logistic regression model are shown in Table 3. When the model did not adjust the confounding factors (Model 1), we compared the highest concentration group with the lowest concentration group. It was found that there was a negative association between vitamin A [OR (95% CI): 0.69 (0.57, 0.85), *P-t* < 0.001], vitamin C [OR (95% CI): 0.39 (0.32, 0.48), *P-t* < 0.001], vitamin D [OR (95% CI): 0.56 (0.46, 0.69), *P-t* < 0.001] with obesity. The adjusted logistic regression analysis (Model 2) also revealed a statistically significant association between obesity and vitamin A [OR (95% CI): 0.64 (0.51, 0.80), *P-t* < 0.001], vitamin C [OR (95% CI): 0.35 (0.28, 0.44), *P-t* < 0.001], vitamin D [OR (95% CI): 0.48 (0.38, 0.60), *P-t* < 0.001]. No correlation between vitamin E level and obesity was found in both adjusted and unadjusted models.

BKMR analysis

When we compared all the predictors fixed at different levels with their 50th percentiles, we found that mixed exposure was negatively correlated with obesity-related indicators. BMI and waist circumference decreased significantly with the increase of vitamin mixture level (Fig. 2a, b). The overall association between the vitamin mixtures and the binomial outcome is shown in Fig. 2c, with the increase of vitamin mixture level, the risk of obesity is significantly reduced. Although no statistically significant difference was found, they revealed a negative association of the mixed exposures with the level of hsCRP (Fig. 2d).

Mediation analysis

The results of mediation analysis are shown in Table 4, we found that hsCRP mediated the effect of vitamins on obesity [vitamin A (ACME: −0.12, 95% CI: −0.18, −0.07); vitamin C (ACME: −0.09, 95% CI: −0.16, −0.05); vitamin D (ACME: -0.03, 95% CI: −0.05, −0.02)]. The proportion of total vitamin effects mediated by hsCRP are as follows: vitamin A (51%), vitamin C (15%), and vitamin D (14%). Compared with vitamin A, the total effect of vitamin C and vitamin D were more mediated through unknown mechanisms. The relationship between vitamin E and obesity cannot be explained by hsCRP (ACME: −0.03, 95% CI: −0.06, 0.00).

Discussion

We observed that the contents of vitamin A, vitamin C, and vitamin D in person living with obesity were relatively lower than the control group. Higher concentrations of vitamins (vitamin A, vitamin C, and vitamin D) were associated with lower risk of obesity. Results from the BKMR models were consistent with the estimates from the linear regression models, suggesting that the level of vitamin mixture is negatively correlated with obesity risk and obesity-related indicators. The results from mediation analysis suggest that hsCRP mediated the effect of vitamins on obesity.

Obesity is a chronic metabolic disease due to the accumulation of excess dietary calories into visceral fat and the release of high concentrations of free fatty acids into various organs.[13] The etiologies of obesity are complex and multifactorial. One of the hypotheses suggests that obesity may represent a state of chronic oxidative stress and low-grade inflammation.[7,14] The results are in agreement with the previous studies, we also found that the level of hsCRP in obesity participants were significantly higher than non-obesity group,[15,16] and vitamins may reduce the risk of obesity by

Table 3. Association between vitamin and obesity in all subjects

Vitamin	Q1	Q2		Q3		Q4		*P-t*
		OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value	
vitamin A								
Model 1	Reference	0.82 (0.67, 1.00)	0.048*	0.71 (0.58, 0.87)	0.001*	0.69 (0.57, 0.85)	<0.001*	<0.001*
Model 2	Reference	0.86 (0.70, 1.07)	0.172	0.70 (0.57, 0.87)	0.002*	0.64 (0.51, 0.80)	<0.001*	<0.001*
vitamin C								
Model 1	Reference	0.86 (0.70, 1.05)	0.137	0.60 (0.49, 0.73)	<0.001*	0.39 (0.32, 0.48)	<0.001*	<0.001*
Model 2	Reference	0.83 (0.67, 1.03)	0.084	0.56 (0.45, 0.70)	<0.001*	0.35 (0.28, 0.44)	<0.001*	<0.001*
vitamin D								
Model 1	Reference	0.76 (0.62, 0.93)	0.008*	0.59 (0.48, 0.72)	<0.001*	0.56 (0.46, 0.69)	<0.001*	<0.001*
Model 2	Reference	0.76 (0.62, 0.94)	0.011*	0.55 (0.45, 0.68)	<0.001*	0.48 (0.38, 0.60)	<0.001*	<0.001*
vitamin E								
Model 1	Reference	0.92 (0.75, 1.12)	0.393	1.12 (0.92, 1.37)	0.260	1.02 (0.83, 1.25)	0.857	0.428
Model 2	Reference	0.96 (0.77, 1.18)	0.674	1.16 (0.94, 1.44)	0.177	1.08 (0.86, 1.35)	0.514	0.254

Q, quartile.
Model 1: unadjusted model; Model 2: adjusted for age, gender, race, education levels, family income-poverty ratio, serum cotinine, past-year alcohol drinking, diabetes, and hypertension.
*$P < 0.05$; *P-t*, *p* value for trend.

Table 4. Estimates of the mediation analysis for the association between vitamin and obesity

Treatment variable[a]	Total effect	ADE	ACME	% mediated
vitamin A	− 0.23 (−0.24, −0.17)	− 0.11 (−0.15, −0.01)	− 0.12 (−0.18, −0.07)	0.51
	$P < 0.001$*	$P = 0.024$*	$P < 0.001$*	$P < 0.001$*
vitamin C	− 0.57 (−0.64, −0.48)	− 0.48 (−0.57, −0.37)	− 0.09 (−0.16, −0.05)	0.15
	$P < 0.001$*	$P < 0.001$*	$P < 0.001$*	$P < 0.001$*
vitamin D	− 0.22 (−0.22, −0.19)	− 0.19 (−0.20, −0.15)	− 0.03 (−0.05, −0.02)	0.14
	$P < 0.001$*	$P < 0.001$*	$P < 0.001$*	$P < 0.001$*
vitamin E	0.05 (−0.07, 0.08)	0.07 (−0.04, 0.11)	− 0.03 (−0.06, 0.00)	− 0.50
	$P = 0.408$	$P = 0.180$	$P = 0.055$	$P = 0.457$

ACME, average causal mediated effect; ADE, average direct effect.
The model was adjusted for age, gender, race, education levels, family income-poverty ratio, serum cotinine, past-year alcohol drinking, diabetes, and hypertension.
*$P < 0.05$.
[a]vitamin data were transformed to log(x + 1).

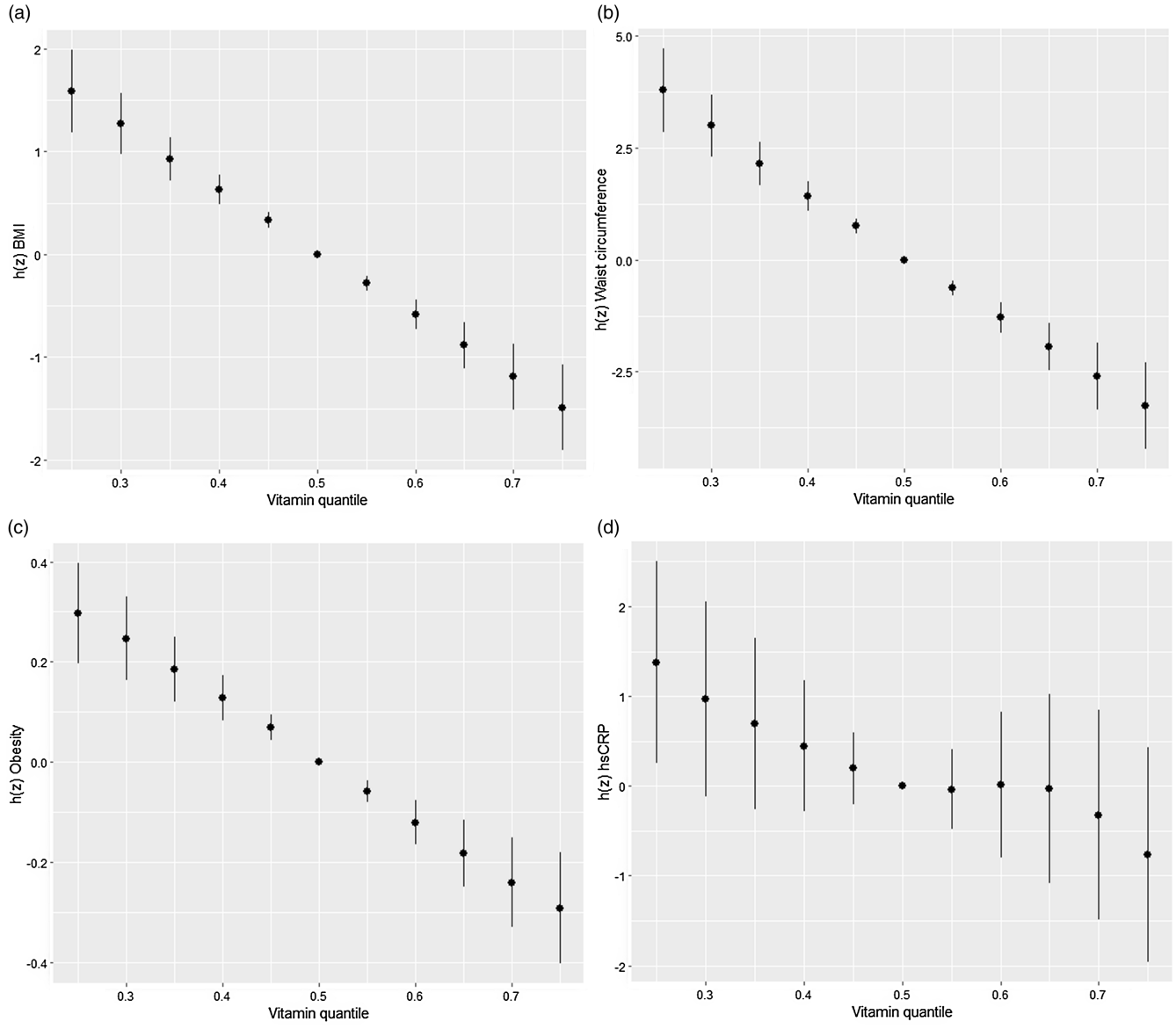

Figure 2. Overall risk (95% credible intervals) of vitamin exposures on BMI (a), waist circumference (b), obesity (c), and hsCRP (d) when comparing all the vitamins at different percentiles with their median level. Models were adjusted for age, gender, race, education levels, family income-poverty ratio, serum cotinine, past-year alcohol drinking, diabetes, and hypertension.

suppressing inflammatory responses. After weight loss, the concentration of inflammatory markers in blood decreased.[17] It is well established that excessive fat accumulation promotes a state of a systemic chronic low-grade inflammation, while inflammatory responses can in turn stimulate oxidative stress reactions in adipocytes, affecting their biological processes such as proliferation, differentiation, and insulin sensitivity, ultimately leading to further fat accumulation.[18,19] Interestingly, antioxidants are thought to improve diseases caused by inflammation and oxidative stress.

Vitamin A is necessary to maintain the normal growth and development of human body, immunity, barrier integrity, male and female reproduction, and vision.[20] A large amount of evidence has been accumulated in the literature, indicating that vitamin A plays a role in the development of obesity and obesity-related diseases.[21,22] In this study, we found a significant negative correlation between vitamin A levels and obesity risk, which is consistent with previous research conclusions.[23,24] Bento[25] concluded that vitamin A participated in the regulation of body fat, proposing that the absence of vitamin A leads to an increase in the recruitment of pre-adipocytes to adipocytes, causing a suppression of apoptosis and an upregulation of adaptive thermogenesis, ultimately promoting fat accumulation. Vitamin A inhibits lipid peroxidation by trapping free radicals in cell membranes, regulates leptin mRNA in adipose tissue and also exerts an inhibitory effect on adipogenesis.[26,27]

As an essential dietary vitamin derived from fruits and vegetables, vitamin C can protect healthy cells from oxidative insults and function as a scavenger of free radicals in the body.[28] Vitamin C deficiency is a common feature of person living with obesity.[29] In agreement with previous study results, we found that person living with obesity had lower levels of vitamin C.[30] Part of the reason may be the decreased consumption of fruits and vegetables in obese individuals.[31] Previous studies found a negative relationship between vitamin C level and BMI, waist-to-height ratio, and leptin concentrations.[7] Potential systemic oxidative stress associated with obesity has been proposed to explain the inverse relationship between obesity and plasma vitamin C concentration.[32,33] Some studies have shown that vitamin C is an important free radical scavenger and protects tissues from ROS reducing inflammation.[34]

The main source of vitamin D in human body is the production from the action of ultraviolet-B light on cholesterol in skin. In fact, vitamin D deficiency has been linked to many chronic diseases and conditions, including obesity and several cancers.[35,36] Multiple population studies showed that low vitamin D levels are increasingly common in people as their BMI increases,[37,38] our study also confirmed the negative correlation between vitamin D and obesity. According to the results of a meta-analysis, increased parathyroid hormone levels in individuals with vitamin D deficiency can promote adiposity by influx of calcium into adipocytes, thereby enhancing lipogenesis. Additionally, the deficiency of vitamin D may lead to a reduction in leptin secretion, ultimately resulting in increased appetite and a higher risk of obesity.[39] The vitro experiments have demonstrated that vitamin D_3 has anti-inflammatory effects on adipocytes by reducing the chemokines and cytokines released by adipocytes and reducing the chemotaxis of monocytes.[40] Vitamin D is fat-soluble and could be stored in adipose tissue, and there is some evidence that muscle may store 25(OH)D, thereby reducing the amount of 25(OH)D available in the circulation for measurement.[41] Another explanation is that higher body weight may limit their outdoor exercise time, resulting in decreased exposure to sunlight and ultimately leading to a reduction in vitamin D biosynthesis.[42]

Vitamin E is a strong fat-soluble antioxidant, most commonly in the form of α-tocopherol, found most frequently in dark chocolate, nuts and vegetable oils, whose main role is to protect lipids from oxidative damage.[43] Although no association was observed between vitamin E levels with obesity risk in this study. In previous studies, it was found that obesity was inversely related to serum vitamin E levels, obese people with metabolic syndrome require more vitamin E than normal people.[7] The primary causes for the increased production of ROS in obese individuals are the heightened blood glucose levels, increased tissue lipid levels, inadequate antioxidant defenses, and chronic inflammation.[44] However, previous studies also found that vitamin E supplementation had no effect on body weight and BMI.[45] Longitudinal prospective studies are needed to better understand the role of vitamin E in the pathogenesis of obesity.

The strength of the present study is using three statistical models to study the effects of single and mixed vitamin exposure on obesity, and discussed the possible indirect mechanisms of vitamin effects on obesity. This study also has the following limitations. First, although this analysis adjusted for a large number of potential confounding factors, there are still some possible confounders (such as dietary habit and physical activity) were not considered. Second, reverse causality is an inherent defect in case-control studies. Third, vitamin levels were determined from serum sample at baseline and may not reflect long-term exposure.

Conclusion

Our study uses three statistical models to analyze the vitamins exposure with obesity. Vitamin A, vitamin C, and vitamin D were found to have a significant association with the outcome. Our study confirms that the exposure to all mixed vitamins was negatively associated with the development of obesity and obesity-related indicators. Vitamins may reduce the risk of obesity by suppressing inflammatory responses. More mechanistic studies and prospective cohort studies are needed to verify the dose-response associations of vitamins in the onset and progression of obesity.

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Author contribution. Xiaomin Lu: Validation, Formal analysis, Writing – original draft. Zhongyou Sun: Conceptualization, Methodology, Validation, Writing – review & editing, Supervision.

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