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Article

Impact of Vitamin B6 Status on the Relationship Between Tobacco Exposure and Central Obesity in Children and Adolescents: A Cross-Sectional Study

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Abstract

Background: The purpose of this research is to explore the relationship between vitamin B6 status (measured by pyridoxal-5′-phosphate, PLP levels) and central obesity in children and adolescents. Additionally, the study seeks to examine how this relationship might influence the link between exposure to tobacco and central obesity in this age group. **Methods:** This cross-sectional study utilized data from the National Health and Nutrition Examination Survey spanning 2005 to 2010. Central obesity was identified by waist circumference measurements that were equal to or exceeded the 90th percentile, with adjustments made for age and gender. To assess the relationship between tobacco exposure and central obesity, both weighted univariate and multivariate logistic regression analyses were applied. An analysis was performed using PLP concentration categories (PLP ≥ 53.74 nmol/L and PLP < 53.74 nmol/L) to determine the impact of tobacco exposure on central obesity in each respective PLP group. **Results:** The final sample included 5,865 participants. Higher tobacco exposure [odds ratio (OR): 1.25, 95% confidence interval (CI): 1.03-1.53, P =0.027] and lower PLP levels (OR: 1.28, 95% CI: 1.05-1.57, P =0.016) were each independently linked to an increased risk of central obesity in children and adolescents. Among children and adolescents with lower PLP levels, cotinine exposure was related to an increased risk of central obesity (OR: 1.36, 95% CI: 1.05-1.76, P =0.022), particularly in specific subgroups: individuals under the age of 12 years, males, and those with six hours or less of daily screen time. **Conclusion:** Our results underscore the critical role of nutritional status, specifically vitamin B6 levels, in modulating the relationship between environmental exposures and obesity risk. Future initiatives aimed at primary prevention could be enhanced by recognizing the link between central obesity and adjustable lifestyle elements.

Keywords: vitamin B6; tobacco exposure; central obesity; children and adolescents

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Introduction

Globally, there is a rising trend in the incidence of obesity among children and teenagers [1]. In 2019, the World Obesity Federation projected that the global number of obese children and adolescents aged 5 to 19 would reach 206 million by 2025, with a further increase to an estimated 254 million by 2030 [2]. In recent years, the prevalence of central obesity in children and adolescents has remained high all over the world [3–5]. Research Indicates higher risks of metabolic disorders, cardiometabolic disease, and depression associated with central obesity compared to general obesity [6,7]. Therefore, attention to central obesity in children and adolescents is crucial.

Childhood tobacco exposure is a significant risk factor for both general and central obesity during childhood and later in adulthood [8,9]. A previous study in adults has shown that smokers are more likely to accumulate abdominal fat compared to non-smokers, even when accounting for increases in body mass index (BMI) [10]. The obesity risk associated with tobacco exposure may be linked to oxidative stress induced by smoking [11]. Studies have found that adequate intake of dietary fiber and antioxidant vitamins may mitigate the risk of obesity and metabolic syndrome associated with tobacco exposure in children and adolescents [12,13] Vitamin B6 is an essential vitamin for the human body, playing a key role in carbohydrate and fat metabolism [14,15] while also exhibiting antioxidant properties [16,17]. Research indicates that dietary vitamin B6 intake is often insufficient in obese children and adolescents [18,19]. Studies in adults have shown that vitamin B6 supplementation can help reduce the waist-to-hip ratio, and vitamin B6 status (measured by pyridoxal-5′-phosphate, PLP levels) is positively associated with muscle mass [20,21]. However, the relationship between vitamin B6 status and central obesity in children and adolescents, as well as its potential impact on the association between tobacco exposure and central obesity, requires further investigation.

Consequently, the objective of this research is to investigate the correlation between vitamin B6 levels, as indicated by PLP, and central obesity among children and adolescents, and further analyze the impact of vitamin B6 on the association between tobacco exposure and central obesity.

Methods

Data Source and Participants

This study utilized a cross-sectional design, analyzing data from the National Health and Nutrition Examination Survey (NHANES) collected between 2005 and 2010. The NHANES database is a large-scale, ongoing program conducted by the National Center for Health Statistics (NCHS), a division of the Centers for Disease Control and Prevention (CDC) in the United States. It is designed to assess the health and nutritional status of adults and children across the U.S. population. NHANES employs a complex, multistage probability sampling design to ensure its findings are nationally representative. Data collection involves in-person interviews, physical examinations, and laboratory testing, covering a wide range of health topics, including chronic disease prevalence, nutritional status, and environmental exposures. NHANES data are widely used in public health research and policy-making to monitor trends, inform guidelines, and address emerging health concerns. This study utilized publicly available data from the NHANES database, which is anonymized and accessible for research purposes. The requirement of ethical approval for this was waived by the Institutional Review Board of the First Affiliated Hospital of Xiamen University, School of Medicine, Xiamen University, because the data was accessed from NHANES (a publicly available database). The need for written informed consent was waived by the Institutional Review Board of the First Affiliated Hospital of Xiamen University, School of Medicine, Xiamen University due to retrospective nature of the study. All methods were performed in accordance with the relevant guidelines and regulations. Clinical trial number: not applicable.

Inclusion criteria: (1) aged 6-17 years, and (2) availability of waist circumference measurements. Exclusion criteria were applied to participants with (1) missing serum PLP measurements, and (2)

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missing serum cotinine measurements. These inclusion and exclusion criteria ensured the selection of a representative sample for the analysis.

Data Collection

The variables included in this study were categorized into demographic characteristics, lifestyle factors, biochemical measurements, birth and anthropometric characteristics, and dietary intake. Demographic characteristics comprised age, categorized into ≤ 12 years and > 12 years based on differences in developmental stages and behavioral responses,gender (male and female), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, and others), poverty-to-income ratio (PIR: ≤ 1.3, 1.3-3.5, and > 3.5), and the educational level of the household reference person (less than high school and high school or above). Lifestyle factors included physical activity and screen time. Physical activity was categorized as "yes" or "no." For participants under 12 years, any activity recorded in PAQ706 (values 1-7) was classified as "yes." For participants aged 12 years or older, those who answered "yes" to either vigorous activity (PAQ605 or PAQ650) or to at least two items of moderate-intensity activity (PAQ620, PAQ635, or PAQ665) were categorized as physically active. Screen time was classified based on the total daily time spent watching television or videos (PAD590), using a computer (PAD600), or sedentary time (PAD680) as < 6 hours or ≥ 6 hours, a cutoff commonly used in studies examining the association between sedentary behavior and obesity in adolescents. Biochemical measurements included cotinine levels, categorized as ≤ 0.05 ng/mL and > 0.05 ng/mL based on the widely accepted threshold for distinguishing tobacco exposure from non-exposure. PLP levels were divided into ≥ 53.74 nmol/L and < 53.74 nmol/L according to the median value in the study population, consistent with common practice in nutritional epidemiology. Serum folate levels were categorized as > 48.33 nmol/L and ≤ 48.33 nmol/L using the median split, which allows for comparison of metabolic health outcomes across different folate status groups. Birth and anthropometric characteristics included birth weight, categorized as < 5.5 pounds, 5.5-9.0 pounds, ≥ 9.0 pounds, and unknown [22]. Due to a high proportion of missing data, the categories were expanded to include the "unknown" group. Dietary intake variables included total energy intake, carbohydrate intake, protein intake, fat intake, and vitamin B6 intake. Total energy intake was calculated from both dietary and supplementary sources. Carbohydrate, protein, and fat intake were expressed as percentages of energy using the following formulas: carbohydrate intake = (carbohydrate × 4 / total energy) × 100%; protein intake = (protein × 4 / total energy) × 100%; fat intake = (fat × 9 / total energy) × 100%.

Definition and Measurement of Tobacco Exposure and PLP

Tobacco exposure was assessed using serum cotinine levels, a biomarker for nicotine exposure. Participants were categorized into two groups based on cotinine levels: ≤ 0.05 ng/mL and > 0.05 ng/mL [23]. PLP, measured as LBXPLP in the dataset, is the active form of vitamin B6 and a crucial biological catalyst. Participants were divided into two groups based on the median PLP level (nmol/L).

Outcomes

The outcome variable of this investigation was central obesity, which was characterized by a waist circumference that met or exceeded the 90th percentile relative to age and gender [24].

Statistical Analysis

Weighted variables were utilized to account for the complex sampling design of NHANES. The masked variance unit pseudo-stratum was defined as SDMVSTRA, and the masked variance unit pseudo-primary sampling units were defined as SDMVPSU. The mobile examination center (MEC) exam weight (WTMEC2YR) was applied to ensure the data's representativeness. Confidence intervals (CIs) were calculated to evaluate the reliability of estimates. Continuous variables were summarized

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as means and standard errors [Mean (SE)], and comparisons between groups were conducted using independent sample t-tests. Categorical variables were presented as counts and percentages (N, %), and group comparisons were assessed using chi-square tests. For ordinal data, rank-sum tests were applied. Missing data were addressed using the multiple imputation by chained equations (MICE) method based on random forest algorithms, implemented via the miceforest package in Python. Sensitivity analyses were performed to compare results before and after multiple imputations to ensure robustness (Supplementary Table S1).

Weighted univariate logistic regression models were used to identify significant variables, which were subsequently included as covariates in the final analysis. The covariates included age, gender, race, PIR, educational level of the household reference person, physical activity, and birth weight (Supplementary Table S2). Weighted univariate and multivariate logistic regression models were employed to explore the association between tobacco exposure and central obesity. Three models were constructed: the Crude Model, which did not adjust for any variables; Model 1, which adjusted for demographic factors (age, gender, race, PIR, and educational level of the household reference person); and Model 2, which further adjusted for age, gender, race, PIR, educational level of the household reference person, physical activity, and birth weight.

To examine the moderating effect of PLP on the relationship between tobacco exposure and central obesity, interaction terms were incorporated into the models. Specifically, the Crude Model* included PLP, cotinine, and their interaction term (PLP × cotinine). Model 3 adjusted for demographic variables (age, gender, race, PIR, and educational level of the household reference person) based on the Crude Model*. Model 4 was further adjusted for age, gender, race, PIR, educational level of household reference person, physical activity, and birth weight in addition to the variables in the Crude Model*. The interaction term (PLP × cotinine) was the primary focus of testing the moderating effect of PLP on the association between tobacco exposure and central obesity. Subsequently, an analysis was conducted based on PLP levels (PLP ≥ 53.74 nmol/L and PLP < 53.74 nmol/L) to quantify the effect of tobacco exposure on central obesity within each PLP subgroup. To further investigate the association between tobacco exposure and central obesity under different PLP stratifications (PLP ≥ 53.74 nmol/L and PLP < 53.74 nmol/L), subgroup analyses were conducted based on age, gender, and sedentary time.

The association between variables was evaluated using odds ratios (OR) and 95% confidence intervals (CI). All statistical tests were two-sided, with a significance level of $\alpha = 0.05$. Data cleaning and handling of missing values were performed using Python 3.9, while statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Figures and visualizations were created using R version 4.0.

Results

Study Selection Process and Characteristics of Included Participants

The study selection process is outlined in Figure 1. Initially, data from 7,343 children and adolescents aged 6-17 years from the 2005-2010 NHANES database were screened. A total of 439 participants were excluded due to missing measurements of waist circumference, leaving 6,904 participants for further analysis. Subsequently, 961 participants were excluded due to missing PLP measurements, and 78 participants were excluded due to missing serum cotinine measurements. After applying these exclusion criteria, the final sample consisted of 5,865 participants, which were included in the analysis.

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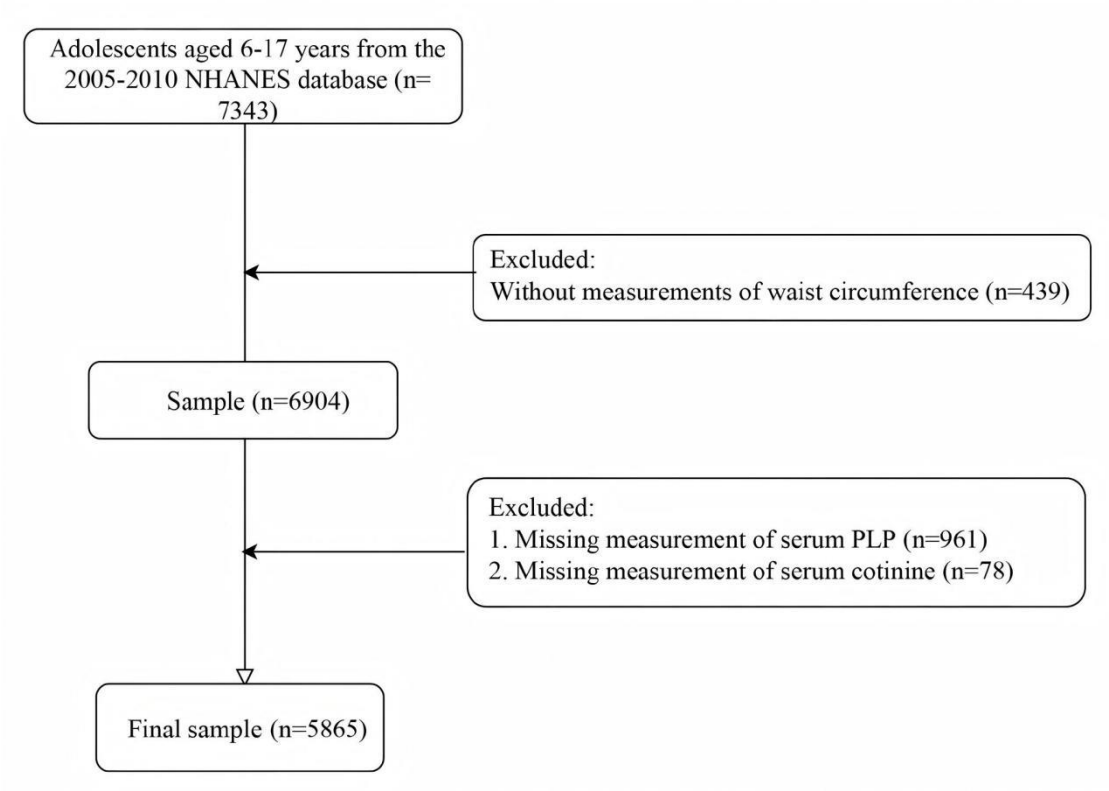

Figure 1. The study selection process.

Out of a total sample size of 5,865 participants, 1,272 were identified as having central obesity. The mean serum cotinine level was 6.33 ng/mL across the total sample. The mean level of PLP was 64.63 nmol/L overall. Regarding age, the mean age of the total sample was 11.85 years. Gender distribution revealed that 51.45% of the total sample was male. There were significant differences between the non-centrally obese participants and central obesity participants in age distribution, gender, race, PIR, educational level of household reference person, physical activity, birth weight, total energy, cotinine distribution, and PIR. Table 1 offers a detailed of various demographic and clinical characteristics of the study participants.

Table 1. Characteristics of the included participants.

Variables	Total (n=5865)	None-central obesity (n=4593)	Central obesity (n=1272)	Statistics	*P*
Cotinine, ng/mL, Mean (S.E)	6.33 (0.67)	6.53 (0.68)	5.50 (1.25)	t=0.87	0.390
Cotinine, n (%)				χ^2=11.08	<0.001
≤ 0.05 ng/mL	3020 (52.41)	2373 (53.80)	647 (46.61)		
> 0.05 ng/mL	2845 (47.59)	2220 (46.20)	625 (53.39)		
PLP, nmol/L, Mean (S.E)	64.63 (0.99)	65.62 (1.09)	60.48 (1.94)	t=2.40	0.021
PLP, n (%)				χ^2=8.17	0.004
≥ 53.74nmol/L	2760 (50.04)	2208 (51.39)	552 (44.44)		
< 53.74nmol/L	3105 (49.96)	2385 (48.61)	720 (55.56)		
Age, years, Mean (S.E)	11.85 (0.06)	11.86 (0.07)	11.80 (0.10)	t=0.52	0.606
Age, n (%)				χ^2=9.70	0.002
≤12	3280 (53.97)	2508 (52.95)	772 (58.21)		
>12	2585 (46.03)	2085 (47.05)	500 (41.79)		
Gender, n (%)				χ^2=4.45	0.035
Male	2997 (51.45)	2415 (52.32)	582 (47.86)		
Female	2868 (48.55)	2178 (47.68)	690 (52.14)		
Race, n (%)				χ^2=11.47	0.003
Non-Hispanic White	1702 (58.84)	1385 (59.98)	317 (54.10)		

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Non-Hispanic Black	1521 (13.94)	1233 (13.93)	288 (13.98)		
Others	2642 (27.22)	1975 (26.09)	667 (31.92)		
PIR, n (%)				χ^2=29.65	<0.001
≤1.3	2455 (29.67)	1865 (27.91)	590 (36.97)		
1.3-3.5	2168 (36.76)	1691 (36.40)	477 (38.28)		
>3.5	1242 (33.57)	1037 (35.69)	205 (24.74)		
Educational level of household reference person, n (%)				χ^2=38.49	<0.001
Less than high school	1846 (20.17)	1361 (18.50)	485 (27.10)		
High school or above	4019 (79.83)	3232 (81.50)	787 (72.90)		
Physical activity, n (%)				χ^2=7.16	0.007
No	656 (10.49)	493 (9.90)	163 (12.95)		
Yes	5209 (89.51)	4100 (90.10)	1109 (87.05)		
Screen time, n (%)				χ^2=0.69	0.405
≤ 6hours	4511 (71.88)	3539 (72.18)	972 (70.65)		
> 6hours	1354 (28.12)	1054 (27.82)	300 (29.35)		
Birth weight, n (%)				χ^2=11.47	0.009
< 5.5pounds	3654 (62.55)	2814 (61.98)	840 (64.93)		
5.5-9.0 pounds	569 (8.60)	467 (8.83)	102 (7.65)		
≥ 9.0 pounds	567 (10.12)	411 (9.59)	156 (12.33)		
Unknown	1075 (18.72)	901 (19.60)	174 (15.09)		
Total energy, kcal, Mean (S.E)	2091.98 (17.34)	2107.33 (20.26)	2028.21 (29.36)	t=2.23	0.030
Carbohydrate, %En, Mean (S.E)	53.83 (0.21)	53.82 (0.23)	53.89 (0.40)	t=-0.16	0.871
Protein, %En, Mean (S.E)	33.11 (0.15)	33.17 (0.17)	32.88 (0.30)	t=0.87	0.389
Fat, %En, Mean (S.E)	14.12 (0.08)	14.09 (0.08)	14.24 (0.19)	t=-0.87	0.387
Vitamin B6, mg, Mean (S.E)	2.01 (0.04)	2.03 (0.04)	1.93 (0.10)	t=0.90	0.373
Serum folate, n (%)				χ^2=2.79	0.095
> 48.33 nmol/L	2756 (50.17)	2179 (50.86)	577 (47.32)		
≤ 48.33 nmol/L	3109 (49.83)	2414 (49.14)	695 (52.68)		

Notes: PLP: pyridoxal-5′-phosphate; PIR: poverty-to-income ratio; T: t-test; χ^2: chi-square test; S.E: standard error.

Association Between of PLP and Tobacco Exposure with the Risk of Central Obesity in Children and Adolescents

The results suggested that both higher tobacco exposure (OR: 1.25, 95% CI: 1.03-1.53, *P*= 0.027) and lower PLP levels (OR: 1.28, 95% CI: 1.05-1.57, *P*= 0.016) were independently associated with an increased risk of central obesity in children and adolescents. Table 2 presents a detailed analysis of the relationship between PLP levels, tobacco exposure as measured by serum cotinine levels, and the risk of central obesity among the study participants.

Table 2. Association between of PLP and tobacco exposure with the risk of central obesity in children and adolescents.

Variables	Crude Model		Model 1		Model 2	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Cotinine, ng/mL						
≤ 0.05	Ref		Ref		Ref	
> 0.05	1.33 (1.11-1.60)	0.002	1.23 (1.01-1.50)	0.036	1.25 (1.03-1.53)	0.027
PLP, nmol/L						
≥53.74	Ref		Ref		Ref	
<53.74	1.32 (1.08-1.61)	0.007	1.29 (1.05-1.57)	0.014	1.28 (1.05-1.57)	0.016

Notes: PLP: pyridoxal-5′-phosphate; OR: odds ratio; CI: confidence interval; Ref: Reference; Crude Model: adjusted for none; Model 1: adjusted for age, Gender, Race, PIR, and educational level of household reference person; Model 2: adjusted for age, gender, race, PIR, educational level of household reference person, physical activity, and birth weight.

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The Impact of PLP on the Association Between Tobacco Exposure and the Risk of Central Obesity in Children and Adolescents

Table 3 shows the validation of the impact of PLP on the association between tobacco exposure and central obesity in children and adolescents. There was a significant interaction between cotinine and PLP levels, suggesting that their combined effects have a greater impact on the risk of central obesity than one factor alone (OR: 1.43, 95% CI: 1.03-1.98, *P* =0.033). Figure 2 illustrates that within the group of participants with PLP levels below 53.74 nmol/L, an increase in cotinine levels was associated with a rising trend in the risk of central obesity. This suggests that lower PLP levels may exacerbate the adverse effects of tobacco exposure on obesity outcomes. Conversely, in the group with PLP levels at or above 53.74 nmol/L, the risk of central obesity remained relatively stable despite increases in cotinine levels. This indicates that higher PLP levels may provide a protective effect, potentially mitigating the impact of tobacco exposure on the development of central obesity.

Table 3. Validation of the impact of PLP on the association between tobacco exposure and central obesity in children and adolescents.

Variables	Crude Model*		Model 3		Model 4	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Cotinine	1.09 (0.87-1.38)	0.447	1.00 (0.77-1.28)	0.982	1.02 (0.79-1.31)	0.888
PLP	1.09 (0.82-1.45)	0.537	1.05 (0.80-1.39)	0.703	1.05 (0.80-1.39)	0.695
Cotinine * PLP	1.39 (0.99-1.96)	0.057	1.44 (1.03-2.01)	0.032	1.43 (1.03-1.98)	0.033

Notes: PLP: pyridoxal-5′-phosphate; OR: odds ratio; CI: confidence interval; Ref: Reference; Crude Model*: The model included only cotinine, PLP, and their interaction term (Cotinine * PLP) (Cotinine and PLP were both binary variables); Model 3: Based on the Crude Model*, adjusted for age, gender, race, PIR, and educational level of the household reference person; Model 4: Based on the Crude Model*, adjusted for age, gender, race, PIR, educational level of the household reference person, physical activity, and birth weight.

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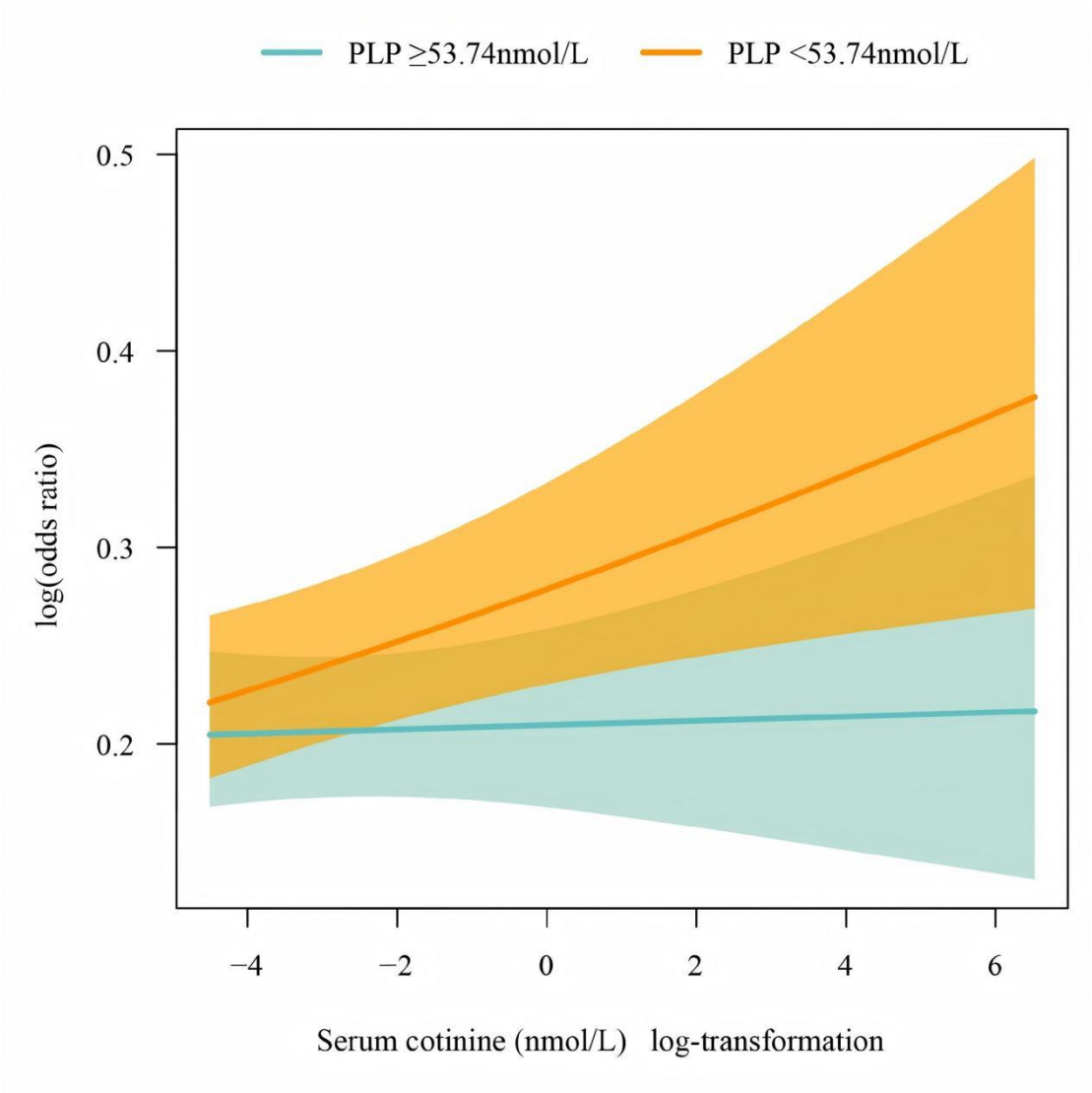

Figure 2. Interaction between PLP Levels and serum cotinine on the risk of central obesity.

Table 4 presents the association analysis of tobacco exposure and central obesity in the PLP group. Among children and adolescents with lower levels of PLP, exposure to cotinine was associated with an increased risk of central obesity (OR: 1.36, 95% CI: 1.05-1.76, *P* =0.022). Conversely, in children and adolescents with higher PLP levels, no significant relationship between cotinine exposure and the risk of central obesity was observed.

Table 4. Association analysis of tobacco exposure and central obesity stratified by PLP Levels.

Variables	Crude Model**		Model 5		Model 6	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
PLP≥53.74 nmol/L (n=2760)						
Cotinine ≤ 0.05	Ref		Ref		Ref	
Cotinine > 0.05	1.09 (0.87-1.38)	0.447	1.07 (0.82-1.39)	0.626	1.10 (0.85-1.43)	0.473
PLP<53.74 nmol/L (n=3105)						
Cotinine ≤ 0.05	Ref		Ref		Ref	
Cotinine > 0.05	1.52 (1.17-1.98)	0.002	1.36 (1.05-1.77)	0.023	1.36 (1.05-1.76)	0.022
Cotinine * PLP	1.39 (0.99-1.96)	0.057	1.44 (1.03-2.01)	0.032	1.43 (1.03-1.98)	0.033

Notes: PLP: pyridoxal-5′-phosphate; OR: odds ratio; CI: confidence interval; Ref: Reference; Crude Model**: adjusted for none; Model 5: adjusted for age, gender, race, PIR, and educational level of household reference

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person; Model 6 adjusted for age, gender, race, PIR, educational level of household reference person, physical activity, and birth weight.

Subgroup Analyses of the Impact of PLP on the Association Between Tobacco Exposure and the Risk of Central Obesity in Children and Adolescents

The validation of the impact of PLP on the association between tobacco exposure and the risk of central obesity in children and adolescents in subgroups is summarized in Table 5. In the age subgroup, the interaction between cotinine and PLP was significant for those aged 12 and under, with a cotinine exposure associated with a higher risk of central obesity in the lower PLP subgroup (OR: 1.59, 95% CI: 1.01-2.53, *P* =0.048). However, this interaction was not significant in the older age group. For the gender subgroup, the interaction between cotinine and PLP was significant for males showed a significant interaction effect, indicating that cotinine exposure was associated with central obesity in male children and adolescents with lower PLP levels (OR: 1.75, 95% CI: 1.14-2.69, *P* =0.012). In the screen time subgroup, individuals with screen time of 6 hours or less per day exhibited a significant interaction effect, suggesting that cotinine exposure was associated with an increased risk of central obesity in the lower PLP subgroup (OR 1.55, 95% CI: 1.07-2.23, *P* =0.020).

Table 5. Validation of the impact of PLP on the association between tobacco exposure and the risk of central obesity in children and adolescents in subgroups.

Subgroup & variable	Model			
	OR (95%CI)	*P*	OR (95%CI)	*P*
Subgroup I: Age	≤12 (n=3280)		>12 (n=2585)	
Cotinine	0.92 (0.65-1.29)	0.621	1.22 (0.76-1.97)	0.399
PLP	0.97 (0.70-1.36)	0.873	1.22 (0.81-1.84)	0.344
Cotinine * PLP	1.59 (1.01-2.53)	0.048	1.18 (0.72-1.93)	0.504
Subgroup II: Gender	Male (n=2997)		Female (n=2868)	
Cotinine	0.98 (0.64-1.50)	0.927	1.07 (0.68-1.67)	0.776
PLP	0.91 (0.66-1.25)	0.545	1.21 (0.85-1.73)	0.289
Cotinine * PLP	1.75 (1.14-2.69)	0.012	1.19 (0.75-1.88)	0.446
Subgroup III: Screen time	≤ 6hours (n=4511)		> 6hours (n=1354)	
Cotinine	0.90 (0.68-1.19)	0.442	1.50 (0.84-2.65)	0.163
PLP	0.99 (0.72-1.37)	0.961	1.26 (0.76-2.10)	0.360
Cotinine * PLP	1.55 (1.07-2.23)	0.020	1.10 (0.57-2.14)	0.767

Notes: PLP: pyridoxal-5′-phosphate; OR: odds ratio; CI: confidence interval; Ref: Reference; Subgroup I: adjusted for gender, race, PIR, educational level of household reference person, physical activity, and birth weight; Subgroup II: adjusted for gender, race, PIR, educational level of household reference person, physical activity, and birth weight. Subgroup III: adjusted for age, gender, race, PIR, educational level of household reference person, physical activity, and birth weight.

Table 6 shows the subgroup analyses of the impact of PLP on the association between tobacco exposure and the risk of central obesity in children and adolescents. Among children and adolescents with lower levels of PLP, cotinine was associated with an increased risk of central obesity, particularly in the subgroups consisting of individuals under the age of 12 (OR: 1.50, 95% CI: 1.02-2.21, *P* =0.039), males (OR: 1.63, 95% CI: 1.27-2.08, *P* <0.001), and those who spend six hours or less per day on screen time (OR: 1.35, 5% CI: 1.01-1.81, *P* =0.048).

Table 6. Subgroup analyses of the impact of PLP on the association between tobacco exposure and the risk of central obesity in children and adolescents.

Subgroup	PLP≥53.74 nmol/L		PLP<53.74 nmol/L	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age≤12	1.02 (0.71-1.48)	0.911	1.50 (1.02-2.21)	0.039
Gender =Male	1.03 (0.65-1.63)	0.903	1.63 (1.27-2.08)	<0.001

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Subgroup	PLP≥53.74 nmol/L		PLP<53.74 nmol/L	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age≤12	1.02 (0.71-1.48)	0.911	1.50 (1.02-2.21)	0.039
Sedentary time ≤ 6 hours	0.93 (0.70-1.24)	0.634	1.35 (1.01-1.81)	0.048

Notes: PLP: pyridoxal-5′-phosphate; OR: odds ratio; CI: confidence interval; Ref: Reference; Subgroup of age ≤12: adjusted for gender, race, PIR, educational level of household reference person, physical activity, and birth weight; Subgroup of gender =Male: adjusted for age, race, PIR, educational level of household reference person, physical activity, and birth weight; Subgroup of sedentary time ≤ 6hours: adjusted for age, gender, race, PIR, educational level of household reference person, physical activity, and birth weight.

Discussion

The research indicated that reduced levels of PLP and elevated concentrations of cotinine correlate with a heightened risk of central obesity among children and adolescents. Furthermore, an interaction between PLP and cotinine levels was observed. In children and adolescents with lower PLP levels, higher cotinine levels were linked to a risk of central obesity, indicating a potential exacerbating effect of tobacco exposure in the context of low PLP. Conversely, among those with higher PLP levels, the association between cotinine levels and central obesity was not significant, suggesting a possible mitigating or protective role of adequate PLP levels in counteracting the effects of tobacco exposure on central obesity. Subgroup analyses highlighted that this interaction was more pronounced in younger children, males, and those with limited screen time.

The study demonstrated a connection between increased cotinine levels and a greater risk of central obesity in young people. Results from the Ewha Birth and Growth study further indicated that elevated urinary cotinine levels, indicative of exposure to secondhand smoke, were correlated with a higher risk of metabolic syndrome, which encompasses abdominal obesity [25]. Similarly, in the NHANES conducted from 2007 to 2018 with 3,701 participants, it was observed that elevated cotinine levels (≥0.05 ng/mL) correlated with a heightened risk of developing metabolic syndrome [26]. Results from the Finnish Cardiovascular Risk Study (spanning 1980-2012 with 2,303 participants) and the Turkish Adult Risk Factor Study (from 1989-2010 with 632 participants) suggest that exposure to parental smoking during childhood is linked to a higher lifetime risk of being overweight/obese and having central obesity [8]. A cross-sectional study involving children aged 10 to 14 at the "Trilj" Elementary School in Trilj, Croatia, revealed that regular exposure to secondhand smoke was linked to increased BMI levels among the children [27]. Tobacco exposure is related to the increased levels of chronic inflammation throughout the body [28]. Central obesity is often accompanied by increased activity of inflammatory cytokines [29]. Tobacco exposure may increase the risk of central obesity by increasing the level of chronic inflammation throughout the body. In addition, oxidative stress plays an important role in obesity [30]. Tobacco exposure produces large amounts of free radicals, and induces oxidative stress [31].

The role of vitamins in the obesity has been reported. An analysis of NHANES data collected from 1999 to 2016, encompassing 7,718 adults exhibiting central obesity, revealed that the consumption of vitamin B12 and folate could offer protective benefits for those affected by central obesity [32]. A cross-sectional study conducted on 491 healthy adults (aged 18-64) at Hashemite University, Jordan, between January and May 2019, found that increased intake of vitamins B1, B2, and B6 may significantly reduce obesity [33]. A study using data from the 2013-2016 U.S. NHANES found an inverse relationship between obesity and the intake of vitamins A, B1, B2, B12, and D among 3,634 children and adolescents aged 6 to 19 [19]. A study involving 214 overweight/obese male adolescents and 321 normal-weight male adolescents suggested that higher vitamin B6 intake may have a protective effect against adolescent obesity [18]. This research indicated that reduced levels of PLP, the active form of vitamin B6, correlate with a higher risk of central obesity among children and adolescents. PLP is essential for regulating inflammation and mitigating oxidative stress [16]. Low PLP levels may lead to increased systemic inflammation and oxidative damage, both of which are associated with the development and progression of obesity [34]. Additionally, vitamin B6 is essential

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for energy metabolism, particularly in amino acid and lipid metabolism [35]. Deficiency in PLP can disrupt these metabolic pathways, potentially leading to fat accumulation and obesity. Vitamin B6 is involved in the synthesis of neurotransmitters and hormones, such as serotonin and norepinephrine, which regulate appetite and energy expenditure [36]. Low PLP levels may disrupt these pathways, potentially leading to overeating or reduced energy expenditure [37]. Our findings suggest that adequate PLP levels may be essential for preventing central obesity. Our study further revealed that PLP levels play a moderating role in the association between tobacco exposure and central obesity in children and adolescents. We hypothesize that this effect may also be mediated through the relationship between PLP levels, inflammation, and oxidative stress. The moderating role of PLP suggests that maintaining adequate PLP levels could be a potential strategy to mitigate the adverse effects of tobacco exposure on central obesity. Nutritional interventions focusing on vitamin B6 intake might help reduce obesity risk in exposed populations.

Subgroup analyses showed that the influence of PLP in mediating the association between tobacco exposure and central obesity was especially pronounced in younger children, males, and those with restricted screen time. Younger children, whose bodies and metabolic systems are still developing, may have a less mature immune system and greater vulnerability to oxidative stress and inflammation triggered by tobacco exposure [38]. PLP, with its anti-inflammatory and antioxidant properties, may play a more critical protective role in this age group. Sex differences may arise from variations in hormone levels and body composition, leading to differential responses to tobacco exposure [39], or from differing metabolic responses to dietary factors [40] Extended periods of screen time could elevate the risk of central obesity [41], which might affect how PLP moderates the link between tobacco exposure and central obesity in young people. Our findings underscore the necessity for tailored approaches to tackle the combined impact of tobacco exposure, lifestyle habits, and nutritional health in children and adolescents.

This study highlights the potential importance of environmental and nutritional factors in the prevention of central obesity among children and adolescents. The observed associations suggest that managing tobacco exposure at the family and community levels, alongside promoting healthy dietary practices and adequate nutritional intake, may be valuable in reducing the risk of central obesity. Specifically, strategies to minimize children's exposure to tobacco and to support adequate levels of PLP through dietary education and supplementation could play a role in addressing obesity-related health challenges. These findings also provide insights into the need for tailored obesity prevention strategies. Identifying individuals who may be at greater risk due to lower PLP levels or higher tobacco exposure could help guide more focused public health interventions. While the cross-sectional nature of this study limits causal inferences, the associations observed support the potential benefits of an integrated approach combining tobacco control, nutritional interventions, and lifestyle management.

This research boasts several significant strengths. Firstly, it pioneers the investigation of PLP's moderating influence on the link between tobacco exposure and central obesity risk among children and adolescents, offering crucial insights for developing obesity prevention strategies. Secondly, by leveraging data from the NHANES database, the study ensures generalizability and a substantial sample size, as it reflects a nationally representative sample of the United States population. Third, the use of serum cotinine levels to measure tobacco exposure offers a more objective and accurate assessment compared to self-reported measures. Nonetheless, several key limitations must be acknowledged. The cross-sectional nature of this study prevents the determination of causal relationships, and the role of PLP in the relationship between tobacco exposure and central obesity needs further substantiation through prospective cohort studies. Additionally, the findings are based on a U.S. population and may not be directly generalizable to children and adolescents from other regions or ethnic backgrounds, necessitating further research in diverse populations. Lastly, information collected through questionnaires is subject to recall bias, which may impact the accuracy of certain variables.

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Conclusions

Lower PLP levels and higher cotinine concentrations were associated with an increased risk of central obesity in children and adolescents, with a significant interaction suggesting that low PLP levels may amplify the impact of tobacco exposure on the risk of central obesity in children and adolescents. Our findings provide insights into the potential combined effects of nutritional and environmental factors on central obesity in children and adolescents.

List of Abbreviations

BMI: body mass index; NHANES: National Health and Nutrition Examination Survey; NCHS: National Center for Health Statistics; CDC: Centers for Disease Control and Prevention; MEC: mobile examination center

Ethics approval and consent to participate: The requirement of ethical approval for this was waived by the Institutional Review Board of Xinglin Hospital of Xiamen, The First Affiliated Hospital of Xiamen University, because the data was accessed from NHANES (a publicly available database). The need for written informed consent was waived by the Institutional Review Board of Xinglin Hospital of Xiamen, The First Affiliated Hospital of Xiamen University due to the retrospective nature of the study. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication: Not applicable.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available in the NHANES database, https://wwwn.cdc.gov/nchs/nhanes/.

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Authors' contributions: CLY and YXL contributed equally to this work and shared the co-first authorship. CLY contributed to the conceptualization and methodology of the study. YXL was responsible for data collection and analysis. MY assisted with the interpretation of the results and the drafting of the manuscript. YZW contributed to the revision and finalization of the manuscript. CJY and YSL, the co-corresponding authors, provided oversight and guidance throughout the research process and approved the final version of the manuscript for submission. All authors have read and agreed to the submitted version of the manuscript.

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