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Vitamin D Status and Cardiometabolic Risk Factors in the US Adolescent Population

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Abstract

OBJECTIVE—Evidence on the association of vitamin D with cardiovascular risk factors in youth is very limited. We examined whether low serum vitamin D levels [25(OH)D] are associated with cardiovascular risk factors in US adolescents aged 12–19 years.

METHODS—Cross-sectional analysis of 3,577 fasting, nonpregnant adolescents without diagnosed diabetes who participated in the 2001–2004 National Health and Nutrition Examination Survey (NHANES). Risk factors for cardiovascular disease measured using standard methods and defined according to age-modified Adult Treatment Panel-III definitions.

RESULTS—Mean 25(OH)D in US adolescents was 24.8 ng/mL; lowest in black (15.5 ng/mL), intermediate in Mexican American (21.5 ng/mL), and highest in white (28.0 ng/mL) adolescents ($p < 0.001$, for each pair-wise comparison). Low 25(OH)D levels were strongly associated with overweight status and abdominal obesity ($p_{\text{trend}} < 0.001$, for both). Following adjustment for age, sex, race/ethnicity, body mass index, socioeconomic status, and physical activity, 25(OH)D levels were inversely associated with systolic blood pressure ($p = 0.02$) and plasma glucose concentrations ($p = 0.01$). The adjusted odds ratio (95% CI) for those in the lowest (< 15 ng/mL) compared to the highest quartile (> 26 ng/mL) of 25(OH)D for hypertension was 2.36 (1.33, 4.19); for fasting hyperglycemia 2.54 (1.01, 6.40); for low HDL-cholesterol 1.54 (0.99, 2.39); for hypertriglyceridemia 1.00 (0.49, 2.04); and for metabolic syndrome 3.88 (1.57, 9.58).

CONCLUSIONS—Low serum vitamin D in US adolescents is strongly associated with an increased prevalence of hypertension, hyperglycemia, and metabolic syndrome, independent of adiposity. Whether the low concentrations of vitamin D among adolescents predicts future adverse health events remains to be determined.

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Keywords

cardiovascular; children; dietary supplements

At the end of the 19th century, there was an epidemic of vitamin D-deficient rickets in US children that resulted in growth retardation, muscle weakness, skeletal deformities, and tetany.¹ With the fortification of milk and other foods with vitamin D and the encouragement of moderate sunlight exposure, rickets was almost completely eradicated by the middle of the 20th century.² While rickets in children and osteomalacia in adults may represent the extreme consequences of severe vitamin D deficiency, lesser degrees of deficiency or insufficiency may have important health effects. Indeed, increased parathyroid hormone levels during childhood and adolescence, secondary to vitamin D deficiency or insufficiency results in calcium resorption from the skeleton, which may lower peak bone mass and increase the risk of developing osteoporosis during adulthood.^{3–5}

Although a great deal of attention has been justifiably placed on understanding the consequences of vitamin D deficiency or insufficiency on bone health, a growing body of evidence from several lines of scientific inquiry indicates hypovitaminosis D may influence the development of cardiovascular disease.⁶ Low 25-hydroxyvitamin D [25(OH)D] levels, an indicator of vitamin D status incorporating both cutaneous production from sunlight exposure and dietary intake,⁷ have been observed in cerebrovascular,^{8,9} heart failure,¹⁰ and coronary heart disease patients.^{8,11} Furthermore, low vitamin D has been linked with higher rates of metabolic syndrome,¹² hypertension,¹³ diabetes,¹⁴ myocardial infarction,¹⁵ peripheral arterial disease,¹⁶ and cardiovascular disease.¹⁷

While cardiovascular disease events occur most frequently during or after the fifth decade of life, pathological evidence suggests precursors of cardiovascular disease originate in childhood.^{18,19} Longitudinal studies have shown risk factor levels in young adulthood track into and predict the occurrence of cardiovascular disease in adulthood.^{20,21} A significant association between vitamin D and cardiovascular risk factors in youth would suggest that the successful repletion of vitamin D has the potential to improve the cardiovascular risk profile during childhood and adolescence, and lower the risk of developing cardiovascular disease in adulthood. Compared to adults, however, very little is known about the association between vitamin D and risk factors for cardiovascular disease in youth. The present study sought to examine the association of serum vitamin D levels with select cardiovascular disease risk factors and the prevalence of metabolic syndrome among a nationally representative population-based sample of US adolescents aged 12–19 years.

METHODS

Study population

The present study was based on data from the 2001–2004 National Health and Nutrition Examination Survey (NHANES) conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. Since 1999, NHANES has been a continuous series of cross-sectional surveys which employ a complex, multistage, stratified

probability sampling design to select participants representative of the civilian, noninstitutionalized US population. Data collection occurs during a home interview and a health examination conducted within a mobile examination center. The Institutional Review Board at the Centers for Disease Control and Prevention annually reviews the overall design of NHANES. Written informed consent is obtained for all subjects 18 years of age or from the parent or guardian of those <18 years. Written assent is also obtained from participants <18 years.

A total of 4,666 adolescents aged 12–19 years completed a health examination as part of NHANES 2001–2004. For our purposes, we excluded girls who were pregnant ($n = 105$), those who had fasted for less than 6 hours or greater than 24 hours prior to the health examination and blood draw ($n = 796$), those who did not have a valid 25(OH)D measurement ($n = 228$), and those with diagnosed diabetes (based upon a physician diagnosed history or use of medication; $n = 9$). The remaining 3,528 adolescents formed the sample population for the current analysis.

Data collection

Information regarding age, race/ethnicity, family income, and physical activity was obtained by a family member who was most knowledgeable about the child (usually a mother or father) or self-report. Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Mexican American, or “other,” including those who identified as multiracial or of other Hispanic origin. Socioeconomic status was estimated with the poverty-to-income ratio, which divides family (defined as 2 or more related people who live together) income by the poverty threshold. Poverty thresholds are updated annually and are adjusted for inflation. In 2002, for example, the average poverty threshold was \$19,307 for a family of 4 and \$22,831 for a family of 5. A poverty-to-income ratio less than 1 indicates that the family is below the poverty threshold (range, 0–5). Information on physical activity was obtained during the household interview for subjects 12–15 years of age and during the health examination interview for those 16–19 years. The frequency and duration of walking/bicycling for transportation, home or yard work, and moderate to vigorous intensity leisure-time physical activities during the past month was requested. Responses to these questions were incorporated into a single summary variable expressed in metabolic equivalent-minutes/day (MET-min/day) using intensity values recommended by the National Center for Health Statistics.²² Use of dietary supplements containing vitamin D during the previous month was ascertained.

A certified technician measured blood pressure a maximum of 4 times in seated subjects after a 5 minute rest with a mercury-gravity sphygmomanometer. Child, adult, and large arm cuff sizes were available. The average of all available measurements was used for analysis. Body weight to the nearest 0.1 kilogram and standing height to the nearest 0.1 centimeter were measured once using a Toledo electronic scale and Seca stadiometer. Body mass index was calculated as weight in kilograms divided by the square of height in meters. Waist circumference was measured to the nearest 0.1 centimeter using a steel measuring tape placed level with the iliac crest at the end of a normal expiration.

Laboratory measures

During the health examination blood samples were obtained by venipuncture and immediately centrifuged, aliquoted, and frozen to -20°C . The frozen serum and plasma samples were then shipped on dry ice to central laboratories and stored at -70°C until analysis. Serum 25(OH)D [25(OH)D₂ + 25(OH)D₃] levels were measured by radioimmunoassay (Diasorin Inc., Stillwater, MN). Total (intra-assay and inter-assay) coefficients of variation ranged from 6.3–13.2%, the limit of detection was 3 ng/mL, and the reference range was 10–55 ng/mL. We categorized 25(OH)D into quartiles using cutting points based upon the weighted population distribution of vitamin D in the current study sample.

Plasma glucose was measured using standard hexokinase enzymatic assays. Glycosylated hemoglobin (HbA_{1c}) was determined with boronate affinity high performance liquid chromatography (Primus Corporation, Kansas City, MO) and standardized to the reference method used in the Diabetes Complications and Control Trial.²³ Lipid measurements were performed at the Johns Hopkins University Lipoprotein Analytical Laboratory. HDL-cholesterol was measured on a Hitachi model 704 analyzer (Roche Diagnostics, Indianapolis, IN) after precipitation of the other lipoproteins with a heparin-manganese chloride mixture. Triglyceride levels were determined by using a series of enzymatic reactions producing glycerol and then hydrogen peroxide.

Definitions

For this analysis, the majority of cardiovascular risk factors were defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III) definition modified for age.^{24,25} These risk factors were defined as follows: waist circumference 90th percentile for age and sex;^{26,27} HDL cholesterol 40 mg/dL; triglycerides 110 mg/dL; systolic or diastolic blood pressure 90th percentile for age, sex, and height,²⁸ or use of blood pressure medications; and fasting glucose 100 mg/dL.²⁹ Thresholds for the oldest age group were applied to subjects older than the highest age category for the blood pressure (17 years) criteria. The presence of the metabolic syndrome phenotype was defined as 3 of these 5 characteristics. A body mass index 95th percentile for age and sex was used to define “obese” on the basis of growth charts published by the Centers for Disease Control and Prevention in 2000.³⁰

Statistical analysis

All analyses were weighted to the US population to provide nationally representative estimates. SAS-callable SUDAAN statistical software, version 9.0 (Research Triangle Institute, Research Triangle Park, NC) was used to account for the complex sampling design and weighting of the NHANES sample. Participant characteristics were described using means and proportions and their 95% confidence intervals. Mean 25(OH)D concentrations according to sub-groups were compared by independent sample t-tests. We calculated multivariable-adjusted mean metabolic cardiovascular risk factor levels according to quartiles of serum 25(OH)D and examined these associations with a test for linear trend. Multivariable logistic regression models were used to estimate odds ratios and 95% confidence intervals for cardiovascular risk factors according to quartiles of 25(OH)D.

Models for body mass index and waist circumference were adjusted for age, sex, race/ethnicity, poverty-to-income ratio, and physical activity. Subsequent risk factor models adjusted additionally for body mass index. Tests for a linear trend were determined by entering the continuous 25(OH)D variable into the model as an ordinal term. A similar pattern of results was obtained by entering either the median of the quartile categories of 25(OH)D as a continuous variable or the quartile categories as an ordinal variable to the multivariable logistic regression models. Statistical significance was defined at the $p < 0.05$ level using two-sided tests.

RESULTS

The sociodemographic and clinical characteristics of the US adolescent population included in the current study are presented in Table 1. During 2001–2004, the prevalence of obesity was 17.6%, abdominal obesity 16.4%, high blood pressure 6.4%, elevated fasting glucose 2.5%, low HDL-cholesterol 20.7%, and elevated triglycerides 21.9%. The prevalence of metabolic syndrome was 5.9%. Only 3.3% of adolescents reported using supplements which contained vitamin D during the previous month, with an average (95% CI) dose of 509.4 (427.0, 591.8) IU/day.

Table 2 displays the mean 25(OH)D level according to demographic and clinical characteristics of the cohort. Mean 25(OH)D levels were highest in white, intermediate in Mexican Americans, and lowest in black adolescents ($p < 0.001$, for each pair-wise comparison). Mean 25(OH)D levels were higher among adolescents who reported the use of vitamin D supplements and lower in those defined as obese or abdominally obese. Vitamin D levels were also lower in adolescents with high blood pressure, low HDL cholesterol, and those with metabolic syndrome. Although not statistically significant, there was a trend toward a lower mean 25(OH)D level in girls and those with elevated fasting glucose. No differences were observed in vitamin D status by age or level of triglycerides.

Table 3 shows the adjusted mean cardiovascular disease risk factor levels according to quartiles of serum 25(OH)D. After adjusting for age, sex, race/ethnicity, poverty-to-income ratio, and physical activity, significant trends for a lower body mass index and waist circumference were observed in adolescents with higher vitamin D levels. Mean systolic blood pressure and fasting glucose were also lower in those with higher levels of vitamin D, even after additional adjustment for adiposity. No association was observed between vitamin D and diastolic blood pressure, HbA_{1c}, HDL-cholesterol, or triglyceride concentrations.

The multivariable-adjusted association between 25(OH)D and obesity, abdominal obesity, high blood pressure, elevated fasting glucose, low HDL-cholesterol, elevated triglycerides, and metabolic syndrome are shown in Table 4. Adjusted odds ratios for obesity, abdominal obesity, high blood pressure, and metabolic syndrome increased significantly with decreasing quartile of vitamin D. Compared to adolescents with the highest serum 25(OH)D levels, the adjusted odds ratio for elevated fasting glucose was 2.54 (95% CI: 1.01, 6.40) for those in the lowest 25(OH)D quartile. The associations between low vitamin D status and high blood pressure, elevated fasting glucose, and metabolic syndrome were independent of the potential confounding effects of age, sex, race/ethnicity, poverty-to-income ratio,

physical activity, and body mass index. A similar pattern of association between vitamin D, high blood pressure, and elevated fasting glucose was observed when models were adjusted for abdominal adiposity as reflected by waist circumference as opposed to body mass index (data not shown). No association was observed between 25(OH)D and low HDL-cholesterol or increased triglyceride concentration.

DISCUSSION

In this nationally representative population-based sample of US adolescents, low serum concentrations of vitamin D were significantly associated with obesity status, abdominal obesity, high blood pressure, fasting hyperglycemia, and metabolic syndrome. These results are consistent with the limited data in adult populations showing vitamin D levels are associated with major cardiometabolic risk factors. Associations with high blood pressure, fasting hyperglycemia, and metabolic syndrome were independent of several potential confounding factors, including adiposity, physical activity, and race/ethnicity. To the best of our knowledge, this is the first nationally representative study to examine the prevalence of cardiovascular risk factors according to different concentrations of vitamin D in youth.

Our results are consistent with previous studies which have suggested that low vitamin D levels in adulthood may influence the risk of developing hypertension,^{13,31} diabetes,¹⁴ and metabolic syndrome.^{32,33} Hypovitaminosis D has also been strongly associated with a higher frequency of myocardial infarction,¹⁵ cardiovascular disease,¹⁷ and related mortality.³⁴ Few other studies have examined the relations between vitamin D and cardiovascular disease risk factors in youth. For example, in a small study of 127 overweight children and adolescents attending an endocrine clinic, Alemzadeh et al³⁵ showed vitamin D levels were positively associated with insulin sensitivity and inversely correlated with HbA_{1c} levels, suggesting a possible role for vitamin D in the pathogenesis of diabetes and cardiovascular disease originating in childhood. Future studies are necessary to determine the long-term consequences of vitamin D deficiency, including whether low vitamin D levels during childhood significantly predict the occurrence of type 2 diabetes and cardiovascular disease in adulthood.

The associations of vitamin D with high blood pressure, elevated fasting glucose, and metabolic syndrome were independent of overall obesity and abdominal adiposity. These findings are in agreement with the results of previous studies suggesting these associations cannot be completely accounted for by the low vitamin D levels of those with excess adiposity.^{12,33,36,37} Although increased parathyroid hormone levels secondary to vitamin D deficiency may increase intracellular calcium in adipocytes leading to increased lipogenesis and weight gain,³⁸ the inverse association observed between serum vitamin D levels and adiposity is likely to be at least partly due to the sequestering of vitamin D within adipose tissue.^{39,40} In a small randomized, placebo-controlled trial of vitamin D supplementation up to 40,000 IU per week for 12 months, no change in body weight or other indicators of adiposity in adults aged 21–70 years was observed.⁴¹ Decreased skin exposure to UV-light as a result of clothing preferences and reduced outdoor activities may also contribute to the low vitamin D levels of adolescents with higher amounts of adiposity.

In the current study we observed an independent cross-sectional association between vitamin D, systolic blood pressure, and hypertension. Some,^{13,31} but not all,⁴² prospective observational studies of middle-aged men and women support an association between low vitamin D levels or dietary intake and incident hypertension. In addition, two small, short-term intervention studies, one which assigned patients with mild hypertension to receive UVB for 6 weeks⁴³ and the other 800 IU/day of oral vitamin D for 8 weeks,⁴⁴ resulted in significant reductions in blood pressure. There is increasing evidence that vitamin D may be a negative endocrine regulator of the renin-angiotensin system. The activated metabolite of 25(OH)D, 1,25-dihydroxyvitamin D [1, 25(OH)₂D], has been shown to inhibit renin gene expression.⁴⁵ Furthermore, vitamin D receptor null mice exhibit increased renin levels, systemic hypertension, and ultimately develop cardiac hypertrophy.⁴⁶ In addition, the 1 α -hydroxylase enzyme that converts 25(OH)D to 1,25(OH)₂D is expressed in a variety of tissues, including human endothelial cells and vascular smooth muscle cells,^{47,48} which suggests another mechanism by which vitamin D may influence the systemic control of blood pressure.

In the current study, a doubling of the odds ratio for elevated fasting glucose was observed among adolescents in the first quartile of serum vitamin D compared with the fourth quartile, independent of adiposity. While the exact mechanisms linking vitamin D insufficiency with hyperglycemia and subsequent diabetes risk are not completely understood, there is accumulating evidence that vitamin D may directly influence pancreatic beta cell secretory function through their nuclear vitamin D receptors as well as influence insulin sensitivity through insulin receptor expression regulation of intracellular calcium.⁴⁹ In animal models, the administration of high doses of 1,25(OH)₂D has been shown to prevent the development of type 1 diabetes, primarily through immune regulation.⁵⁰ Indirect mechanisms may include effects on inflammatory pathways and increased parathyroid hormone concentrations, secondary to vitamin D deficiency, which have been shown to be inversely associated with insulin sensitivity in healthy adults.^{51,52} The effects of vitamin D on insulin sensitivity may also explain, at least in part, the independent association with metabolic syndrome observed in the current study.⁵³

This study had a number of strengths, including its nationally representative population-based sample of US adolescents, standardized data collection protocols, and rigorous quality control procedures. However, the cross-sectional nature of this study limits a causal inference among low vitamin D status and cardiometabolic risk factors. Future studies with a long-term longitudinal design are warranted to identify the temporal sequence among these variables. Additional limitations include the lack of information regarding residential geographic location, the season during which blood samples were obtained, and the measurement of parathyroid hormone levels. However, even if the results of the current study are due to secondary hyperparathyroidism, the appropriate treatment would include the repletion of vitamin D, which justifies our focus on vitamin D levels.

In conclusion, we found low vitamin D levels in US adolescents were strongly associated with several important risk factors for cardiovascular disease, including high blood pressure, fasting hyperglycemia, and metabolic syndrome, independent of adiposity and several other potential confounding factors. Additional research is necessary to determine whether low

vitamin D status during childhood and adolescence may impact the subsequent development of cardiovascular disease during adulthood. Evidence from randomized clinical trials is required before vitamin D supplementation can be recommended in the primary prevention of metabolic cardiovascular risk factors in youth.

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Glossary

25(OH)D	25-hydroxyvitamin D
NHANES	National Health and Nutrition Examination Survey
NCEP ATP III	National Cholesterol Education Program Adult Treatment III
1,25(OH)₂D	1,25-dihydroxyvitamin D

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Table 1

Characteristics of US adolescents aged 12–19 years, NHANES, 2001–2004

Characteristic	Mean or Percent (95% CI)
Unweighted <i>n</i>	3,528
Age, years	15.4 (15.3, 15.6)
Sex, %	
Boys	51.5 (49.5, 53.5)
Girls	48.5 (46.5, 50.5)
Race/ethnicity, %	
White	64.7 (59.3, 70.1)
Black	13.5 (10.5, 16.5)
Mexican American	11.0 (7.9, 14.1)
Poverty-to-income ratio	2.56 (2.43, 2.69)
Physical activity, MET-min/day	486.9 (458.5, 515.2)
Supplemental vitamin D user, %	3.3 (2.7, 3.9)
Anthropometrics	
Body mass index 95 th percentile, %	17.6 (15.5, 19.7)
Waist circumference 90 th percentile, %	16.4 (14.5, 18.5)
Blood pressure	
Systolic blood pressure, mmHg	108.5 (107.8, 109.2)
Diastolic blood pressure, mmHg	61.5 (60.8, 62.3)
High blood pressure, % [*]	6.4 (5.3, 7.5)
Diabetes-related measures	
Fasting glucose, mg/dL	86.1 (85.5, 86.6)
HbA _{1c} (mean percent)	5.2 (5.1, 5.2)
Fasting glucose 100 mg/dL, %	2.5 (1.9, 3.1)
Lipids	
HDL cholesterol 40 mg/dL, %	20.7 (18.4, 23.4)
Triglycerides 110 mg/dL, %	21.9 (19.4, 24.7)
Metabolic syndrome, % [†]	5.9 (4.8, 7.0)

NHANES denotes National Health and Nutrition Examination Survey; CI, confidence interval.

^{*} Defined as systolic or diastolic blood pressure 90th percentile for age, sex, and height,²⁸ or medication use.[†] Defined according to the method of Cook et al^{24,25}

Table 2

Mean 25-hydroxyvitamin D [25(OH)D] levels among US adolescents aged 12–19 years and according to sub-groups, NHANES, 2001–2004

	Unweighted <i>n</i>	Mean 25(OH)D level (95% CI), ng/mL	<i>P</i> value
Overall	3,528	24.8 (23.8, 25.9)	--
Age, years			
12–15	1,786	24.7 (23.9, 25.6)	0.730
16–19	1,742	24.9 (23.5, 26.3)	
Sex			
Boys	1,811	25.2 (24.3, 26.1)	0.082
Girls	1,717	24.4 (23.5, 25.3)	
Race/ethnicity			
Non-Hispanic white	1,054	28.0 (27.0, 29.0)	< 0.001, for each pair-wise comparison
Non-Hispanic black	1,117	15.5 (14.6, 16.4)	
Mexican American	1,119	21.5 (20.6, 22.4)	
Vitamin D supplement user			
Yes	91	29.6 (26.6, 32.7)	0.001
No	3,437	24.7 (23.6, 25.7)	
Body mass index 95 th percentile*			
Yes	650	21.4 (20.3, 22.5)	< 0.001
No	2,834	25.6 (24.5, 26.8)	
Waist circumference 90 th percentile*			
Yes	573	22.1 (20.9, 23.3)	< 0.001
No	2,893	25.5 (24.3, 26.6)	
High blood pressure [†]			
Yes	213	22.7 (21.1, 24.3)	0.003
No	3,217	25.0 (24.2, 25.8)	
Fasting glucose 100 mg/dL			
Yes	109	22.8 (20.3, 25.3)	0.063
No	3,400	24.9 (24.1, 25.7)	
HDL cholesterol 40 mg/dL			
Yes	649	22.6 (21.7, 23.5)	< 0.001
No	2,867	25.4 (24.6, 26.2)	
Triglycerides 110 mg/dL			
Yes	653	23.8 (22.4, 25.2)	0.114
No	2,855	25.0 (24.2, 25.8)	
Metabolic syndrome [‡]			
Yes	192	20.8 (19.3, 22.3)	< 0.001
No	3,336	25.1 (24.0, 26.1)	

NHANES denotes National Health and Nutrition Examination Survey; CI, confidence interval.

* According to age and sex.^{26,27}

[†] Defined as systolic or diastolic blood pressure ≥ 90th percentile for age, sex, and height,²⁸ or use of blood pressure medications.

[‡] Defined according to the method of Cook et al^{24,25}

Table 3

Adjusted mean (95% confidence interval) cardiovascular disease risk factors according to quartiles of 25-hydroxyvitamin D [25(OH)D] among US adolescents aged 12–19 years, NHANES, 2001–2004

	Quartile of serum 25(OH)D, ng/mL				<i>P</i> _{trend}
	I (< 15.0)	II (15.0–21.0)	III (21.1–26.0)	IV (> 26.0)	
Body mass index, kg/m ² *	26.0 (25.2, 26.8)	24.3 (23.7, 24.9)	23.5 (23.1, 24.0)	22.1 (21.7, 22.5)	< 0.001
Waist circumference, cm *	87.5 (85.3, 89.7)	83.9 (82.5, 85.3)	81.3 (80.1, 82.5)	77.8 (76.6, 79.0)	< 0.001
Blood pressure, mmHg					
Systolic [†]	109.7 (108.4, 111.0)	108.5 (107.5, 109.5)	108.1 (107.0, 109.2)	108.1 (107.3, 108.9)	0.020
Diastolic [†]	61.7 (60.3, 63.1)	62.1 (60.8, 63.4)	61.2 (60.2, 62.2)	61.2 (60.0, 62.4)	0.082
Diabetes measures					
Fasting glucose, mg/dL [†]	88.3 (86.9, 89.7)	86.2 (85.3, 87.1)	85.3 (84.7, 85.9)	85.6 (85.0, 86.2)	0.010
HbA _{1c} (%) [†]	5.17 (5.09, 5.25)	5.18 (5.14, 5.22)	5.14 (5.10, 5.18)	5.16 (5.14, 5.18)	0.673
Lipids, mg/dL					
HDL-cholesterol [†]	52.0 (49.9, 53.1)	51.4 (49.9, 54.1)	51.3 (50.1, 52.5)	53.7 (52.3, 55.1)	0.112
Triglycerides [†]	95.7 (78.1, 113.3)	84.8 (78.5, 91.1)	88.1 (81.3, 94.9)	83.4 (79.2, 87.6)	0.695

NHANES denotes National Health and Nutrition Examination Survey.

* Adjusted for age (years), sex, race/ethnicity (non-Hispanic white, non-Hispanic Black, Mexican American, other), poverty-to-income ratio (continuous), and physical activity (MET-min/day).

[†] Adjusted for variables listed above in addition to body mass index (kg/m²).

Age-, sex-, and race/ethnicity-adjusted prevalence, adjusted odds ratios (OR), and 95% confidence intervals (CI) of select cardiovascular disease risk factors according to serum 25-hydroxyvitamin D [25(OH)D] level among US adolescents 12–19 years, NHANES, 2001–2004

Table 4

	Quantile of Serum 25(OH)D, ng/mL				<i>P</i> _{trend}
	I (<15.0)	II (15.0–21.0)	III (21.1–26.0)	IV (>26.0)	
Body mass index 95 th percentile*					
Prevalence, %	30.7 (25.8, 36.1)	22.6 (19.6, 25.9)	16.5 (13.9, 19.4)	10.4 (7.9, 13.6)	< 0.001
Adjusted OR (95% CI) [†]	5.24 (3.47, 7.91)	2.99 (1.98, 4.53)	2.02 (1.34, 3.06)	1.00 (referent)	< 0.001
Waist circumference 90 th percentile*					
Prevalence, %	26.9 (22.1, 32.4)	20.8 (18.1, 23.8)	16.1 (13.7, 18.8)	9.7 (7.7, 12.1)	< 0.001
Adjusted OR (95% CI) [†]	7.21 (4.36, 11.94)	3.64 (2.14, 6.20)	2.19 (1.25, 3.83)	1.00 (referent)	< 0.001
High blood pressure [‡]					
Prevalence, %	11.2 (7.6, 16.2)	6.7 (5.1, 8.7)	4.4 (3.1, 6.3)	3.7 (2.6, 5.3)	0.013
Adjusted OR (95% CI) [§]	2.36 (1.33, 4.19)	1.26 (0.65, 2.44)	1.04 (0.55, 1.97)	1.00 (referent)	0.046
Fasting glucose 100 mg/dL					
Prevalence, %	6.4 (3.8, 10.7)	2.9 (2.0, 4.4)	3.0 (1.9, 4.8)	1.3 (0.7, 2.3)	0.144
Adjusted OR (95% CI) [§]	2.54 (1.01, 6.40)	1.18 (0.50, 2.79)	0.85 (0.39, 1.88)	1.00 (referent)	0.101
HDL cholesterol 40 mg/dL					
Prevalence, %	29.9 (25.8, 34.3)	20.9 (17.9, 24.4)	18.8 (15.7, 22.3)	12.5 (10.2, 15.2)	< 0.001
Adjusted OR (95% CI) [§]	1.54 (0.99, 2.39)	1.33 (0.89, 1.99)	1.10 (0.72, 1.70)	1.00 (referent)	0.084
Triglycerides 110 mg/dL					
Prevalence, %	23.0 (18.1, 28.8)	20.7 (17.4, 24.5)	17.6 (15.1, 20.4)	17.0 (14.6, 19.7)	0.119
Adjusted OR (95% CI) [§]	1.00 (0.49, 2.04)	1.03 (0.59, 1.80)	0.91 (0.66, 1.26)	1.00 (referent)	0.371
Metabolic syndrome					
Prevalence, %	14.6 (10.4, 20.1)	6.9 (5.2, 9.2)	5.2 (3.6, 7.5)	2.2 (1.5, 3.2)	< 0.001
Adjusted OR (95% CI) [§]	3.88 (1.57, 9.58)	2.35 (1.09, 5.07)	2.05 (0.89, 4.70)	1.00 (referent)	0.003

NHANES denotes National Health and Nutrition Examination Survey.

* According to age and sex.^{26,27}

[†] Adjusted for age, sex, race/ethnicity, poverty-to-income ratio, and physical activity.

[‡] Defined as systolic or diastolic blood pressure 90th percentile for age, sex, and height,²⁸ or medication use.

[§] Adjusted for age, sex, race/ethnicity, poverty-to-income ratio, physical activity, and body mass index.

^{||} Defined according to the method of Cook et al^{24,25}