

RESEARCH

Open Access



Exploring the unique association between high-density lipoprotein cholesterol and vitamin D deficiency in adults aged 20–59: findings based on the NHANES database

Biting Zhao^{2†} and Shuang Yang^{1*†}

Abstract

Background Serum lipids are highly heritable and play an important role in cardiovascular and metabolic health. However, the relationship between high-density lipoprotein cholesterol (HDL-C) and serum 25-hydroxyvitamin D [25(OH)D] levels is unclear. This study aims to explore the association between serum 25(OH)D levels and HDL-C in adults aged 20–59.

Methods This cross-sectional study was based on data from the National Health and Nutrition Examination Survey (NHANES). Multivariable logistic regression was used to assess the relationship between HDL-C and serum 25(OH)D, with further analysis using smooth spline fitting and generalized additive models.

Results A total of 28,084 adults were included in the study. After adjusting for multiple variables, we found a significant positive correlation between HDL-C and serum 25(OH)D levels ($\beta=8.3$, 95% CI: 7.24–9.35, $p<0.001$). Stratified subgroup analysis by gender showed that females consistently exhibited a positive correlation ($\beta=10.12$, 95% CI: 9.07–11.18, $p<0.001$), while males demonstrated an inverted U-shaped relationship between HDL-C and serum 25(OH)D.

Conclusion In the population aged 20–59, HDL-C levels are significantly associated with serum 25(OH)D levels. Clinically, simultaneous monitoring of HDL-C and vitamin D is recommended to better assess and manage cardiovascular health. Increasing vitamin D intake should be considered, especially for males with low HDL-C levels, to prevent related health issues.

Keywords High-density Lipoprotein Cholesterol, 25(OH)D, Adult Health, NHANES, Gender differences

[†]Biting Zhao and Shuang Yang contributed equally to this work.

*Correspondence:

Shuang Yang
1156724820@qq.com

¹Department of Upper Limb, The People's Hospital of Dali Prefecture, Dali 671000, Yunnan, P.R. China

²Department of Endocrinology, Dali First People's Hospital, Dali 671000, Yunnan, P.R. China



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

Background

In recent years, high-density lipoprotein cholesterol (HDL-C) and vitamin D have gained widespread attention for their roles in cardiovascular and metabolic health. HDL-C, known as “good” cholesterol, transports excess cholesterol from peripheral tissues to the liver for metabolism and has anti-inflammatory and antioxidant properties crucial for cardiovascular protection. Typically, HDL-C levels are inversely associated with the risk of cardiovascular diseases, with low levels considered a significant risk factor for atherosclerosis and other cardiovascular conditions [1].

Vitamin D, a fat-soluble vitamin, is synthesized in the skin upon exposure to ultraviolet light and is also obtainable through diet. Its 25-hydroxyvitamin D [25(OH)D] form is particularly crucial for bone health, facilitating calcium absorption and influencing bone metabolism significantly [2–4]. Deficiency in vitamin D has been linked to a spectrum of health issues, including osteoporosis, cardiovascular diseases, and compromised immune function [3]. Studies suggest that insufficient vitamin D levels may lead to insulin resistance, heightened inflammation, and impaired immune responses, all contributing to an elevated risk of chronic diseases [1, 5–8].

Despite some research exploring the correlation between HDL-C and vitamin D, studies specifically investigating the relationship between these two biomarkers remain limited. One notable study examined the association between 25(OH)D levels and various lipid components across a large sample, highlighting a statistically significant link between vitamin D deficiency and an atherogenic lipid profile [9]. Additional meta-analyses have provided insights into the effects of vitamin D supplementation on lipid profiles, revealing reductions in triglycerides (TG) alongside changes in HDL-C and LDL-C levels. However, discrepancies exist among findings, particularly evident in studies involving patients with conditions like polycystic ovary syndrome (PCOS), where vitamin D supplementation did not consistently improve HDL-C and TG levels [10].

The distinct roles of HDL-C and vitamin D in health are well-established, yet their interplay remains insufficiently explored, especially within the adult population aged 20 to 59 years. Some evidence suggests that vitamin D may elevate HDL-C levels by inhibiting cholesterol ester transfer protein (CETP) activity, while high HDL-C levels might enhance vitamin D metabolism through anti-inflammatory and antioxidant mechanisms [11, 12]. However, these mechanisms require broader validation, given the varied outcomes reported across different studies.

Understanding the relationship between HDL-C and vitamin D could yield novel insights into their collective impact on public health, particularly in preventing

cardiovascular diseases and promoting bone health. Additionally, gender differences may play a significant role in this relationship. Differences in hormone levels, metabolic characteristics, and lifestyle between men and women may influence the interplay between HDL-C and vitamin D. Therefore, this study specifically focuses on how gender moderates the relationship between HDL-C and 25(OH)D. This study utilizes data from the National Health and Nutrition Examination Survey (NHANES) from 2003 to 2018 to explore the association between serum HDL-C levels and 25(OH)D. By addressing these gaps, the study aims to contribute valuable knowledge that could inform strategies for enhancing cardiovascular and bone health outcomes.

Methods

Data source and study participants

The data for this study were derived from the National Health and Nutrition Examination Survey (NHANES) for the years 2003 to 2018. After excluding individuals with missing HDL or 25(OH)D data, those outside the 20 to 59 age range, and those with a diagnosis of cancer, a total of 28,084 participants were included in the analysis (Fig. 1).

Study variables

In NHANES 2003–2018, HDL-C was measured using the direct immunoassay method, and 25(OH)D levels were measured using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Control variables included age, gender, race (categorized as Latino/Latina, Caucasian (excluding those of Hispanic origin), African American (excluding those of Hispanic origin), or various additional racial backgrounds), Metric for assessing body composition based on height-to-weight ratio (BMI), Smoking habits (classified as positive if an individual has inhaled smoke from a minimum of one hundred cigarettes over their lifespan), Alcohol intake (4 or 5 cups or more per day), Presence of health issues like diabetes and high blood pressure (as diagnosed by healthcare professionals), total calcium, serum phosphate, ALT, AST, uric acid, creatinine, and urea nitrogen, as well as physical activity. Participants were grouped based on quartiles of HDL-C levels (Q1 being the lowest and Q4 the highest) to study the relationship between different HDL-C levels and serum 25(OH)D. Subgroup analyses based on gender were also conducted to explore potential gender differences in the relationship between HDL-C and 25(OH)D. All analyses were performed using R software and EmpowerStats, with a significance level set at 0.05. Detailed explanations of the computation methods for these variables are provided on the NHANES website (<https://www.cdc.gov/nchs/nhanes/>).

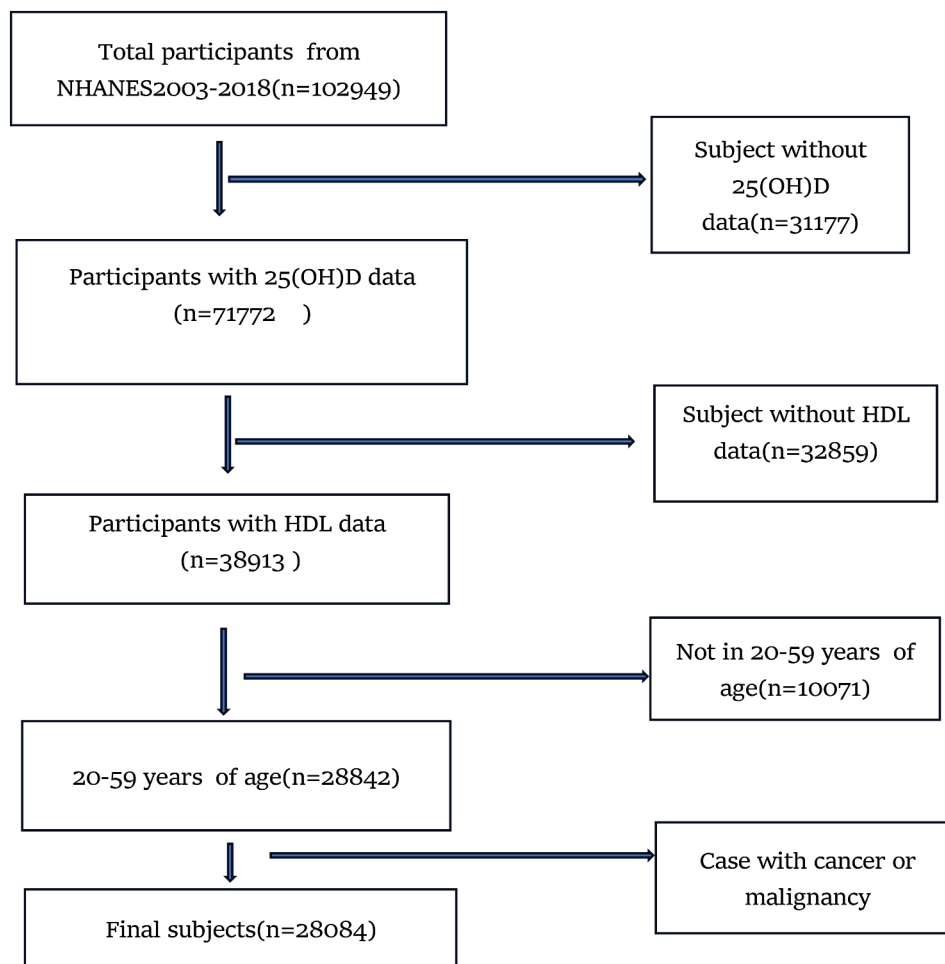


Fig. 1 Flow chart of the screening process for the selection of eligible participants in NHANES 2003–2018

Statistical analysis

Missing data were handled using multiple imputation by chained equations (MICE) to generate 5 complete datasets, analyzed separately and combined using Rubin's rules. To address dataset variability, weighted methods and variance estimation techniques were used. The relationship between HDL-C and serum 25(OH)D levels was analyzed using weighted multivariable logistic regression to adjust for multiple covariates, minimizing confounding effects. Weighted chi-square tests were used for categorical variables, while weighted linear regression models were used for continuous variables. Stratified multivariable regression analysis explored subgroup differences, and smoothing spline fitting and generalized additive models (GAMs) addressed non-linearity. Analyses were performed using R software and EmpowerStats, with significance set at 0.05.

Results

Demographic characteristics

Table 1 shows that with increasing HDL-C levels, participants tended to be younger, more physically active, more educated, and more likely to be female and Non-Hispanic White. Higher HDL-C levels were also associated with lower BMI, ALT, serum uric acid, urea nitrogen, creatinine levels, and lower prevalence of diabetes and hypertension, indicating better overall health profiles ($P < 0.001$ for all comparisons).

Overall relationship and gender-specific analysis

Table 2 shows that in the fully adjusted model (Model 3), there is a significant positive correlation between high-density lipoprotein cholesterol (HDL-C) levels and serum 25-hydroxyvitamin D [25(OH)D] levels, with a β coefficient of 8.30 (95% CI: 7.24–9.35, $P < 0.0001$). When analyzing by HDL-C quartiles, the highest quartile (Q4) had serum 25(OH)D levels that were 9.74 mmol/L higher than the lowest quartile (Q1) (95% CI: 8.50–10.98, $P < 0.0001$). Gender-specific analysis revealed a strong

Table 1 Weighted characteristics of the study population based on different cut-off values of high-density lipoprotein cholesterol

Cholesterol (mmol/L)	Q1	Q2	Q3	Q4	P-value
	0.26 - 1.135	1.14 - 1.36	1.37 - 1.655	1.66 - 5.07	
N	6431	6989	7312	7352	
Age(years)	37.67 ± 11.77	36.57 ± 12.01	36.30 ± 12.14	36.23 ± 12.02	<0.001
Sex, n (%)					<0.001
Male	4232 (65.81%)	3666 (52.45%)	3091 (42.27%)	2292 (31.18%)	
Female	2199 (34.19%)	3323 (47.55%)	4221 (57.73%)	5060 (68.82%)	
Race/ethnicity (%)					
Non-Hispanic White	59.56	58.27	59.62	63.76	
Non-Hispanic Black	12.59	12.33	10.58	7.03	
Mexican American	12.55	12.61	10.74	7.04	
Other race/ethnicity	18.89	17.62	17.57	15.35	
Education level (%)					
Less than high school	18.67	13.62	11.79	9.24	
High school	24.49	23.01	23.43	19.46	
More than high school	56.92	62.47	64.51	71.34	
Moderate activities (%)					
Yes	66.14	67.83	75.09	75.36	
No	33.95	33.17	24.91	24.40	
Body mass index (kg/m ²)	30.93 ± 8.15	28.35 ± 2.84	27.45 ± 5.52	26.43 ± 6.28	<0.001
ALT(U/L, mean ± SD)	28.99 ± 32.26	23.65 ± 19.39	21.15 ± 15.65	19.77 ± 17.43	<0.001
ASL(U/L, mean ± SD)	26.10 ± 19.23	24.04 ± 13.90	23.52 ± 14.48	24.49 ± 20.34	<0.001
Blood urea nitrogen(mg/dL, mean ± SD)	4.49 ± 1.75	4.40 ± 1.59	4.35 ± 1.67	4.22 ± 1.70	<0.001
Creatinine(mg/dL, mean ± SD)	80.28 ± 32.58	73.08 ± 27.38	72.54 ± 21.14	67.41 ± 14.26	<0.001
Serum uric acid(umol/L, mean ± SD)	344.01 ± 84.54	316.65 ± 81.46	295.97 ± 78.56	277.90 ± 78.34	<0.001
Total calcium(mg/dL, mean ± SD)	9.30 ± 0.35	9.36 ± 0.64	9.38 ± 0.53	9.36 ± 0.34	<0.001
Serum phosphorus(mg/dL, mean ± SD)	3.91 ± 0.60	3.70 ± 0.83	3.77 ± 0.75	3.85 ± 0.74	<0.001
25(OH)D(umol/L, mean ± SD)	60.27 ± 23.66	64.09 ± 25.32	65.63 ± 25.78	69.25 ± 28.24	<0.001
Smoked at least 100 cigarettes in life (%)					<0.001
Yes	1091 (3.88%)	2390 (8.51%)	1740 (6.20%)	1035 (3.69%)	
No	3020 (10.75%)	7049 (25.09%)	5589 (19.90%)	6170 (21.97%)	
Had at least 12 alcohol drinks/lifetime (%)					0.165
Yes	2721 (74.88%)	2473 (72.86%)	2523 (72.79%)	2607 (73.46%)	
No	911 (25.07%)	921 (27.14%)	943 (27.21%)	940 (26.49%)	
Diabetes (%)					<0.001
Yes	532 (8.86%)	444 (6.80%)	388 (5.75%)	292 (4.26%)	
No	5384 (89.63%)	6017 (92.13%)	6302 (93.32%)	6524 (95.09%)	
Hypertension (%)					<0.001
Yes	1493 (26.51%)	1383 (23.09%)	1365 (21.83%)	1324 (20.73%)	
No	4120 (73.17%)	4596 (76.73%)	4875 (77.96%)	5053 (79.11%)	

Mean ± SD for continuous variables: the *P* value was calculated by the weighted linear regression model

(%) for categorical variables: the *P* value was calculated by the weighted chi-square test

positive correlation in females ($\beta=9.69$, 95% CI: 8.66–10.72, $P<0.0001$) and a significant positive correlation in males ($\beta=4.62$, 95% CI: 3.42–5.82, $P<0.0001$).

Threshold effect analysis

Figure 2 shows a positive correlation between HDL-C and 25(OH)D levels, which remains significant after adjusting for multiple covariates.

Figure 3 indicates a nonlinear trend in this relationship. Table 3 provides a threshold effect analysis, identifying an inflection point at 2.07 mmol/L for the general

population. Below this point, there is a significant positive correlation between HDL-C and 25(OH)D ($\beta=10.07$, 95% CI: 8.49–11.65, $P<0.0001$), while above this point, the correlation is not significant ($\beta=-0.80$, 95% CI: -5.32–3.72, $P=0.7294$).

The association between high-density lipoprotein cholesterol (HDL-C) and serum 25-hydroxyvitamin D (25(OH)D). Adjustments were made for Adjusted for age, gender, race, education level, BMI, having smoked at least 100 cigarettes in lifetime, alcohol consumption, Moderate activities, diabetes status, hypertensionstatus, total

Table 2 The relationship between high-density lipoprotein cholesterol and 25(OH)D levels

	Model 1 β (95% CI) P value	Model 2 β (95% CI) P value	Model 3 β (95% CI) P value
HDL cholesterol	7.56 (6.82, 8.30) < 0.0001	8.16 (7.39, 8.92) < 0.0001	8.30 (7.24, 9.35) < 0.0001
Quintiles of direct HDL cholesterol			
0.26–1.135	Reference	Reference	Reference
1.14–1.36	3.82 (2.94, 4.70) < 0.0001	4.09 (3.21, 4.97) < 0.0001	3.28 (2.10, 4.45) < 0.0001
1.37–1.655	5.36 (4.49, 6.22) < 0.0001	5.85 (4.97, 6.73) < 0.0001	4.93 (3.73, 6.13) < 0.0001
1.66–5.07	8.98 (8.12, 9.85) < 0.0001	9.72 (8.83, 10.61) < 0.0001	9.74 (8.50, 10.98) < 0.0001
P for trend	< 0.001	< 0.001	< 0.001
Stratified by gender			
Male	5.63 (4.47, 6.78) < 0.0001	5.59 (4.44, 6.75) < 0.0001	4.62 (3.42, 5.82) < 0.0001
Female	10.12 (9.11, 11.14) < 0.0001	10.14 (9.12, 11.15) < 0.0001	9.69 (8.66, 10.72) < 0.0001

Model 1: Unadjusted for covariates. Model 2: Adjusted for age, gender, and race. Model 3: Adjusted for age, gender, race, education level, BMI, having smoked at least 100 cigarettes in lifetime, alcohol consumption, Moderate activities, diabetes status, hypertension status, total calcium, serum phosphorus, ALT, AST, uric acid, creatinine, and blood urea nitrogen. In the subgroup analysis stratified by gender, the model did not adjust separately for gender.

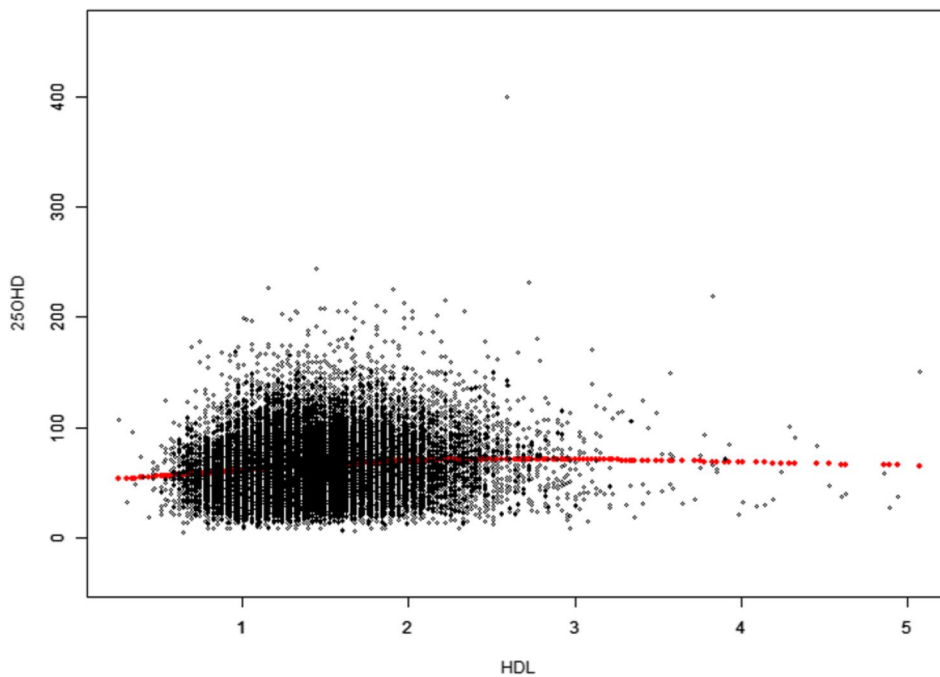


Fig. 2 The association between high-density lipoprotein cholesterol (HDL-C) and serum 25-hydroxyvitamin D (25(OH)D). Each black point represents a sample. Age, gender, race, education level, BMI, having smoked at least 100 cigarettes in a lifetime, alcohol consumption, moderate activities, diabetes status, hypertension status, total calcium, serum phosphorus, ALT, AST, uric acid, creatinine, and blood urea nitrogen were adjusted

calcium, serum phosphorus, ALT, AST, uric acid, creatinine, and blood urea nitrogen. In the subgroup analysis stratified by gender, the model did not adjust separately for gender.

Gender-specific threshold effect

Figure 4 illustrates the gender-specific relationships between HDL-C and serum 25(OH)D levels. In females, there is a consistent positive correlation across the entire range of HDL-C levels, with an inflection point at 1.84 mmol/L ($\beta=13.40$ below the point, $\beta = 3.66$ above it,

$P<0.001$) (Table 4). For males, the relationship is non-linear, showing an inverted U-shaped curve with an inflection point at 1.66 mmol/L ($\beta=10.70$ below the point, $\beta = -4.28$ above it, $P<0.001$) Table 5. These results indicate significant gender differences in the association between HDL-C and 25(OH)D levels.

Discussion

The results of this study demonstrate a significant positive correlation between HDL-C levels and serum 25(OH)D levels after adjusting for multiple confounding

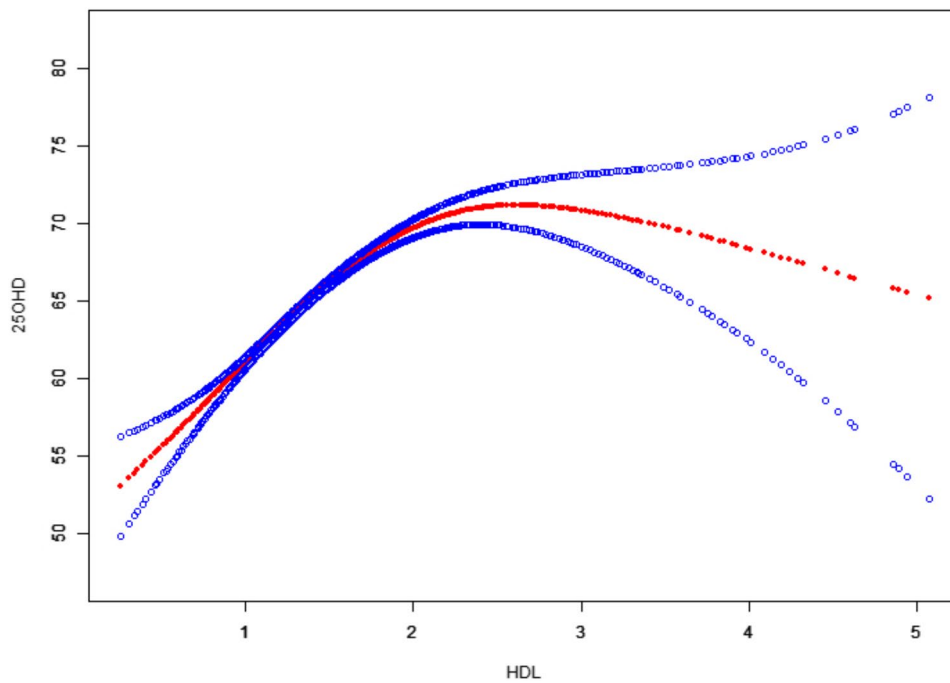


Fig. 3 The association between high-density lipoprotein cholesterol and serum 25-hydroxyvitamin D. The solid red line represents the smooth curve fit between variables. The blue bands represent the 95% confidence interval from the fit. Age, gender, race, education level, BMI, having smoked at least 100 cigarettes in a lifetime, alcohol consumption, moderate activities, diabetes status, hypertension status, total calcium, serum phosphorus, ALT, AST, uric acid, creatinine, and blood urea nitrogen were adjusted

Table 3 Analysis of the threshold effect of high-density lipoprotein cholesterol on serum 25(OH)D based on a two-piece Linear Regression Mode

25(OH)D	Adjusted β (95% CI) P value
Fitting by the standard linear model	8.15 (6.87, 9.44) <0.0001
Fitting by the two-piecewise linear model	
Inflection point	2.07
Direct HDL cholesterol < 2.07(mmol/L)	10.07 (8.49, 11.65) <0.0001
Direct HDL cholesterol > 2.07(mmol/L)	-0.80 (-5.32, 3.72) 0.7294
Log likelihood ratio	<0.001

variables. This finding is consistent with previous studies that have also reported a positive correlation between vitamin D and lipid levels. The data suggest that serum 25(OH)D, particularly in its active form 1,25-dihydroxyvitamin D3 [1,25-(OH)2D3], may play a role in modulating the secretion and mRNA expression of apolipoprotein AI. This protein serves as the primary apolipoprotein component of HDL-C. Consequently, these vitamin D-mediated effects could influence both the quantitative levels and functional aspects of HDL-C within the body [9, 13, 14]. HDL-C can reduce oxidative stress by neutralizing free radicals, thereby protecting vitamin D from oxidative degradation and promoting its stability and function. Additionally, HDL-C's anti-inflammatory effects can improve cellular environments, facilitating more effective vitamin D receptor activity and signaling pathways. However, this study further discovered a moderating effect of gender on this relationship,

showing a positive correlation in women ($\beta=9.69$, CI: 8.66, 10.72, $p<0.0001$), while in men, the relationship between HDL-C and 25(OH)D followed an inverted U-shaped curve .

In men, the relationship between HDL-C and 25(OH)D forms an inverted U-shaped curve, possibly reflecting that within a certain range of HDL-C levels, the protective effects of vitamin D are maximized, and outside this range, these effects may diminish or reverse. This inverted U-shaped relationship can be explained from several aspects:

- **Biological Mechanisms:** HDL-C and vitamin D are involved in critical metabolic pathways, with HDL-C enhancing vitamin D metabolic activity through its anti-inflammatory and antioxidant properties. Excessively high levels of HDL-C may activate negative feedback regulation, inhibiting

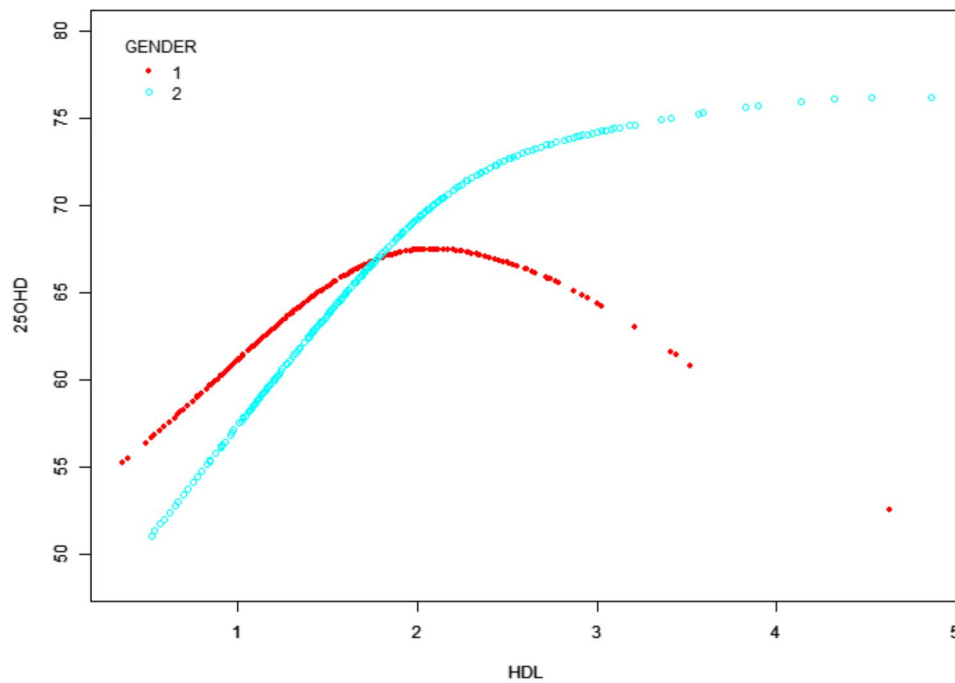


Fig. 4 The association between high-density lipoprotein cholesterol and serum 25-hydroxyvitamin D stratified by gender. Age, race, education level, BMI, having smoked at least 100 cigarettes in a lifetime, alcohol consumption, moderate activities, diabetes status, hypertension status, total calcium, serum phosphorus, ALT, AST, uric acid, creatinine, and blood urea nitrogen were adjusted

Table 4 Stratified by gender

25(OH)D	Adjusted β (95% CI) P value
Female	
Fitting by the standard linear model	10.12 (9.07, 11.18) <0.0001
Fitting by the two-piecewise linear model	
Inflection point	1.84
Direct HDL cholesterol < 1.84(mmol/L)	13.40 (11.82, 14.98) <0.0001
Direct HDL cholesterol > 1.84(mmol/L)	3.66 (1.12, 6.21) <0.0001
Log likelihood ratio	<0.001

Table 5 Stratified by gender

25(OH)D	Adjusted β (95% CI) P value
Male	
Fitting by the standard linear model	5.63 (4.53, 6.73) <0.0001
Fitting by the two-piecewise linear model	
Inflection point	1.66
Direct HDL cholesterol < 1.66(mmol/L)	10.70 (9.06, 12.34) <0.0001
Direct HDL cholesterol > 1.66(mmol/L)	-4.28 (-6.90, -1.67) 0.0013
Log likelihood ratio	<0.001

The association between high-density lipoprotein cholesterol (HDL-C) and serum 25-hydroxyvitamin D (25(OH)D) is stratified by gender. Adjustments were made for age, race, education level, BMI, having smoked at least 100 cigarettes in lifetime, alcohol consumption, Moderate activities,diabetes status, hypertensionstatus, total calcium, serum phosphorus, ALT, AST, uric acid, creatinine, and blood urea nitrogen.

the synthesis of vitamin D [15]. In men, androgens regulate key enzymes in lipid metabolism, such as hepatic lipase, impacting the levels of HDL-C and vitamin D. Appropriate levels of androgens promote a steady state of HDL-C, thereby supporting efficient transport and metabolism of vitamin D. However, excessively high androgen levels reduce

HDL-C, decreasing the bioavailability of vitamin D and leading to potential deficiencies. This dynamic regulation could explain the inverted U-shaped relationship observed between HDL-C and vitamin D in men [16].

- Nutritional and Lifestyle Factors: Dietary habits, physical activity, and other lifestyle choices can

differently impact HDL-C levels. High levels of HDL-C might be associated with a healthy lifestyle, whereas excessively high levels could reflect certain pathological states such as familial hypercholesterolemia, negatively influencing vitamin D metabolism [17].

- **Statistical and Methodological Explanations:** The inverted U-shaped curve identified in statistical models might also be influenced by unadjusted confounding factors that subsequently affect vitamin D levels [17, 18].
- **In women, the relationship between HDL-C and 25(OH)D shows a consistent positive correlation,** which may be related to the unique hormonal environment and metabolic characteristics of females. Estrogen, a key female hormone, plays a pivotal role in cardiovascular protection by modulating lipid metabolism. Estrogen not only boosts the amount of cardioprotective lipid-protein complexes but also diminishes the quantity of potentially harmful fat-carrying particles in the bloodstream [17, 19]. Moreover, estrogen enhances the functionality of vitamin D receptors, thereby augmenting both the bioavailability and efficacy of vitamin D, and consequently influencing its metabolic pathways [11, 20]. Additionally, women may prefer a diet high in fiber and low in fat, which is associated with higher HDL-C levels and improved vitamin D status. The level of physical activity, which is generally linked to better lipid profiles and vitamin D levels, may differ significantly between genders, further influencing these biomarkers. On the genetic level, gender-specific genetic differences may also affect lipid and vitamin D metabolism. For instance, specific genetic variants that influence lipoprotein metabolism may exhibit different phenotypes in women, further exacerbating biochemical differences between genders. Genetic variations directly related to estrogen levels and receptor activity may alter vitamin D metabolic pathways, affecting its activity and functionality in the body. The combined effects of these factors highlight the biological complexity of women in the relationship between HDL-C and vitamin D.
- **Public Health Implications:** The results of this study have important public health implications. Given the critical roles of both HDL-C and vitamin D in cardiovascular health, it is recommended to monitor these two indicators concurrently in clinical practice to more comprehensively assess and manage patients' cardiovascular risk. Additionally, our findings suggest that for individuals, particularly men, with lower HDL-C levels, improving their health status by increasing vitamin D intake should

be considered. This advice is particularly important in preventing osteoporosis and other diseases related to vitamin D deficiency.

- **Study Limitations:** This study has several limitations. As a cross-sectional study, we can only provide associative evidence between HDL-C and 25(OH)D, not causal relationships. Despite adjusting for various confounding factors, there might still be other unadjusted confounding factors affecting the results. Moreover, due to limitations in sample size and representativeness, the generalizability of the study results may be affected. Future research could use longitudinal designs and larger sample sizes to further verify and expand our findings.

Conclusion

This study demonstrates a significant positive correlation between HDL-C levels and serum 25(OH)D levels, with notable gender-specific differences. In females, the relationship is consistently positive, while in males, it follows an inverted U-shaped curve. These findings highlight the importance of considering gender when evaluating the relationship between HDL-C and vitamin D levels. The clinical and public health implications are significant. Concurrent monitoring of HDL-C and vitamin D levels is recommended to provide a more comprehensive assessment of cardiovascular risk. For individuals, particularly males with lower HDL-C levels, increasing vitamin D intake should be considered to improve overall health and prevent deficiencies related to cardiovascular and skeletal health.

Abbreviations

HDL	High density lipoproteins
HDL-C	High-density lipoprotein cholesterol
NHANES	National Health and Nutrition Examination Survey
25(OH)D	25-Hydroxyvitamin D

Acknowledgements

We would like to express our gratitude to all individuals involved in this study. Despite the absence of external funding, the completion of this research would not have been possible without the contributions and efforts of each author. We also extend our appreciation to our colleagues for their technical and academic support.

Authors' contributions

Biting Zhao was responsible for the concept and design of the study, data analysis and interpretation, and drafting the manuscript. He also played a critical role in revising the manuscript critically for important intellectual content and has given final approval of the version to be published. Shuang Yang contributed to the acquisition of data, conducted the experimental work, and assisted in data analysis. She was also involved in preparing figures and tables, and reviewing the manuscript drafts, ensuring the accuracy and integrity of the work. Both authors read and approved the final manuscript.

Author's Information

Shuang Yang, Master's degree, is the corresponding author of this study. They were primarily responsible for data analysis and initial manuscript drafting. They also contributed to the study's design and participated in result discussions.

Biting Zhao, Master's degree, was involved in data collection and preliminary analysis. They were responsible for the literature review and drafting the initial manuscript.

Funding

This study did not receive any specific grants from public, commercial, or not-for-profit sectors.

Availability of data and materials

Data are available from the NHANES (NHANES—National Health and Nutrition Examination Survey Homepage (cdc.gov)) in 2003–2018.

Declarations

Ethics approval and consent to participate

The survey data was obtained from the public NHANES database, where each participant had provided written informed consent. The study received ethical approval from the Ethics Review Committee at the National Center for Health Statistics (NCHS), allowing the use of the data for research purposes.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 25 May 2024 / Accepted: 5 September 2024

Published online: 18 September 2024

References

1. Surdu AM, Pinzariu O, Ciobanu DM et al. Vitamin D and its role in the lipid metabolism and the development of atherosclerosis. *Biomedicines* 2021;9(2):172.
2. Hsu S, Hoofnagle AN, Gupta DK, et al. Race, Ancestry, and vitamin D metabolism: the multi-ethnic study of atherosclerosis. *J Clin Endocrinol Metab*. 2020;105(12):e4337–4350.
3. Sirbe C, Rednic S, Grama A et al. An update on the effects of vitamin D on the Immune System and Autoimmune diseases. *Int J Mol Sci* 2022;23(17):9784.
4. Garland CF, Gorham ED, Mohr SB, et al. Vitamin D and prevention of breast cancer: pooled analysis. *J Steroid Biochem Mol Biol*. 2007;103(3–5):708–11.
5. Renke G, Starling-Soares B, Baesso T et al. Effects of vitamin D on cardiovascular risk and oxidative stress. *Nutrients* 2023;15(3):769.
6. Gil A, Plaza-Diaz J, Mesa MD, Vitamin D. Classic and Novel actions. *Ann Nutr Metab*. 2018;72(2):87–95.
7. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. *Chem Biol*. 2014;21(3):319–29.
8. Bennett AL, Lavie CJ. Vitamin D metabolism and the implications for atherosclerosis. *Adv Exp Med Biol*. 2017;996:185–92.
9. Lupton JR, Faridi KF, Martin SS, et al. Deficient serum 25-hydroxyvitamin D is associated with an atherogenic lipid profile: the very large database of lipids (VLDL-3) study. *J Clin Lipidol*. 2016;10(1):72–e8171.
10. Miao CY, Fang XJ, Chen Y, et al. Effect of vitamin D supplementation on polycystic ovary syndrome: a meta-analysis. *Exp Ther Med*. 2020;19(4):2641–9.
11. Maghbooli Z, Khorrami-Nezhad L, Adabi E, et al. Negative correlation of high-density lipoprotein-cholesterol and bone mineral density in postmenopausal Iranian women with vitamin D deficiency. *Menopause*. 2018;25(4):458–64.
12. Alkhatabeh MJ, Amara NA, Abdul-Razzak KK. Association of 25-hydroxyvitamin D with HDL-cholesterol and other cardiovascular risk biomarkers in subjects with non-cardiac chest pain. *Lipids Health Dis*. 2019;18(1):27.
13. Manousopoulou A, Al-Daghri NM, Garbis SD, et al. Vitamin D and cardiovascular risk among adults with obesity: a systematic review and meta-analysis. *Eur J Clin Invest*. 2015;45(10):1113–26.
14. Mirhosseini N, Rainsbury J, Kimball SM, Vitamin D, Supplementation. Serum 25(OH)D concentrations and Cardiovascular Disease Risk factors: a systematic review and Meta-analysis. *Front Cardiovasc Med*. 2018;5:87.
15. Huang X, Yang Y, Jiang Y, et al. Association between vitamin D deficiency and lipid profiles in overweight and obese adults: a systematic review and meta-analysis. *BMC Public Health*. 2023;23(1):1653.
16. Lu Z, Jiao Y, Li J. Higher genetically predicted triglycerides, LDL, and HDL increase the vitamin D Deficiency: a mendelian randomization study. *Front Nutr*. 2022;9:862942.
17. Sarmiento-Rubiano LA, Angarita Ruidiaz JA, Suarez Davila HF et al. Relationship between Serum Vitamin D Levels and HDL cholesterol in Postmenopausal women from Colombian caribbean. *J Nutr Metab*, 2018,2018: 9638317.
18. Wang Y, Si S, Liu J, et al. The associations of serum lipids with vitamin D status. *PLoS ONE*. 2016;11(10):e0165157.
19. Jeenduang N, Sangkaew B. The association between serum 25-hydroxyvitamin D concentrations and serum lipids in the Southern Thai population. *Arch Med Sci*. 2022;18(1):11–7.
20. LaCroix AZ, Kotchen J, Anderson G, et al. Calcium plus vitamin D supplementation and mortality in postmenopausal women: the women's Health Initiative calcium-vitamin D randomized controlled trial. *J Gerontol Biol Sci Med Sci*. 2009;64(5):559–67.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.