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Associations between lumbar bone mineral density, serum 25-hydroxyvitamin D and history of kidney stones in adults aged 30–69 years in the USA (NHANES 2011–2018)

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ABSTRACT

Objectives Most kidney stones contain calcium, which is closely associated with human bone health. Therefore, we aimed to determine the relationship between the history of kidney stones and human bone health. This study examined the associations between lumbar bone mineral density (BMD), serum 25-hydroxyvitamin D (25-OHD) and a history of kidney stones in individuals aged between 30 years and 69 years.

Design and data analysis A multivariate logistic regression model was used to estimate the relationship between lumbar BMD, serum 25-OHD levels and kidney stones in this cross-sectional study. All models incorporated survey sample weights and were adjusted for covariates.

Setting National Health and Nutrition Examination Survey (NHANES) 2011–2018. The exposure and outcomes of this study included the lumbar BMD and presence of kidney stones.

Participants All the 7500 participants for this cross-sectional survey were selected from the NHANES between 2011 and 2018.

Main outcome measures The main outcome of this study was the presence of kidney stones. The interviewers asked the questions on kidney stones while the respondents were at home, using a computer-assisted personal interview system.

Results Lumbar BMD was negatively correlated with a history of kidney stones in all three multivariate linear regression models; the negative association existed in all genders after adjusting for all confounding factors. In the multiple regression analysis, there was an interaction between serum 25-OHD and lumbar BMD ($p<0.05$) regarding the influence on kidney stones; the negative association between lumbar BMD and kidney stones was more obvious in the higher 25-OHD group (≥50 nmol/L).

Conclusion The study results suggest that maintaining a high lumbar BMD may reduce the incidence of kidney stone formation. Simultaneously, maintaining a high serum 25-OHD level may be more beneficial in preventing the occurrence or recurrence of stones while ensuring a high lumbar BMD.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Use of a large, nationally representative sample of the US population, increasing generalisability.
⇒ The content of calcium would affect bone mineral density (BMD), and serum 25-hydroxyvitamin D (25-OHD), in turn, was one of the important factors affecting calcium metabolism. Therefore, we introduced serum 25-OHD, which is closely associated with BMD, to explore whether serum 25-OHD levels affect the protective effect of BMD on kidney stones.
⇒ The nature of the cross-sectional study limits the conclusions to associations and cannot assess the causal association of lumbar spine BMD and serum 25-OHD with the history of nephrolithiasis.
⇒ In view of the limitations of National Health and Nutrition Examination Survey data, specificity for special groups such as adolescents, pregnant women or those over 70 years was poor.
⇒ Due to the lack of data on urinary calcium and the analysis of stone composition, our study has limitations on the related effects of different kinds of stones and urinary calcium excretion.

INTRODUCTION

Nephrolithiasis is a common disease that is influenced by multiple factors. After entering the 21st century, the incidence rate of kidney stones showed a significant upward trend, and the male-to-female ratio of 3:1 narrowed.[1 2] In a study of the National Health and Nutrition Examination Survey (NHANES) data from 2015 to 2018, the researchers found that the 12-month incidence of kidney stones was significantly higher than that stated in previous reports from the USA. The significantly higher incidence and prevalence of stones are concerning, which have an impact on disease treatment and the allocation of public medical resources.[3] Therefore, it is

necessary to screen those at high risk of kidney stone disease or recurrence.

Most kidney stones contain calcium,[4] which is closely related to human bone health. Therefore, we aimed to determine the relationship between a history of kidney stones and human bone health. As many patients with kidney stones have hypercalciuria, clinicians are concerned that their bone mineral density (BMD) may be reduced, which has inspired several recent studies.[5–8] Although many studies have found that the occurrence of kidney stones is associated with a decreased BMD, the results remain inconclusive.

More than 20 years have passed since the last relevant study on the NHANES data.[9] The main objective of this study was to measure the relationship between lumbar BMD and kidney stones among adults aged 30–69 years using data from the NHANES (2011–2018). We also introduced serum 25-hydroxyvitamin D (25-OHD), which is closely associated with BMD, to explore whether serum 25-OHD levels affect the protective effect of BMD on kidney stones.

METHODS

Data sources

The data used in this study were obtained from the NHANES, which is a research programme designed to assess the health and nutritional status of adults and children in the USA. This was a major project of the National Center for Health Statistics (NCHS). The NHANES is an extensive, consecutive, cross-sectional survey designed to be nationally representative. Researchers worldwide can access data from the NHANES, which is freely available via the internet.

The data used in this study have been deidentified and have been made publicly available (https://www.cdc.gov/nchs/nhanes/index.htm).

In our research, we summarised the data of the NHANES for four 2-year cycles from 2011 to 2018 (lumbar BMD data are missing from 2019 to present). From a total of 39 156 participants, we excluded 24 073 who were younger than 30 years or older than 69 years, 5983 with missing lumbar BMD, 1319 with missing data or refusal to answer the questionnaire about the history of kidney stones, and 281 participants without data on serum 25-OHD, serum calcium and other continuous variables. Finally, 7500 participants were analysed (figure 1).

Exposures

Lumbar BMD, an important index for measuring bone quality, reflects the degree of osteoporosis and predicts the risk of fracture. Measurement of lumbar BMD was performed by dual energy X-ray absorptiometry (DXA) scanning, and the software Apex V.3.2 was used in a Hologic discovery type a densitometer (Hologic, Bedford, Massachusetts, USA). The DXA examinations were performed by trained and certified radiologists.

Outcome

The main outcome of this study was the presence of kidney stones. The question used to investigate the presence of kidney stones was Have you ever had kidney stones? Participants can choose from four answers: 'yes', 'no', 'refused' or 'don't know'. The trained interviewers asked the questions on kidney stones while the respondents were at home, using a computer-assisted personal interview (CAPI) system. Even though many of NHANES interviewers had prior interviewing experience, they still have to complete a comprehensive training programme. The training included general interview techniques, role-playing exercises, and hands-on interviews with on-site respondents. The NCHS and contractor staff were responsible for the aforementioned training programme. Besides interview administration, the interviewers also participated in a series of cultural competency training sessions to help them recognise and respect cultural differences.

CAPI is a technique used for data collection using portable devices. In the last decade, CAPI has been widely used in social research because of its cost-effectiveness, ease of use and the immediate availability of data.[10–12] The usual working form of a CAPI system is that the questionnaire is managed and presented by a computer, and visitors can access and work according to the questions on the computer screen and input the answers given by the interviewees directly into the computer. If the interviewee is unwilling to answer through the interviewer, the interviewee can also input the answer directly into the computer to protect the interviewee's privacy. When the interview ends, the interviewer directly transmits the questionnaire results to the organiser through the internet. The organiser can then analyse the results immediately after receiving them. The CAPI system was programmed with built-in consistency checks to reduce data entry errors. The CAPI also uses online help screens to assist interviewers in defining the key terms used in the questionnaire.[12]

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

Covariates

Among the covariates, we selected age, blood urea nitrogen, serum 25-OHD, serum calcium, serum creatinine, serum glucose, serum phosphorus, serum sodium, serum uric acid, alkaline phosphatase, total cholesterol, total protein, serum potassium, serum triglycerides and body mass index (BMI) as continuous variables; gender, race, physical activities (consist of high-intensity exercise, fitness or recreational activities, such as running or basketball, that cause large increases in respiration or heart rate, lasting at least 10 min), smoking behaviour and ratio of family income to poverty (calculated by dividing family (or individual) income by the poverty guidelines specific to the survey year; if the income reported by the

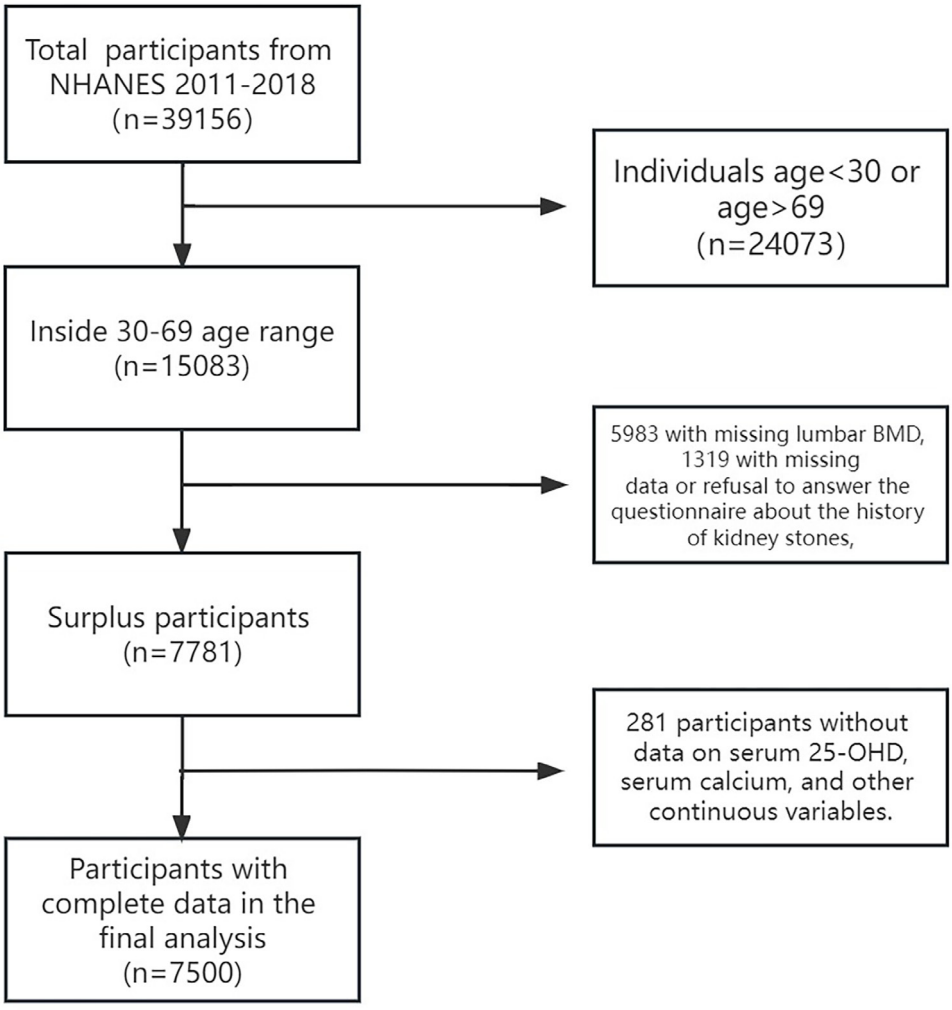

Figure 1 Flowchart of sample selection from the NHANES 2011–2018. BMD, bone mineral density; NHANES, National Health and Nutrition Examination Survey; 25-OHD, 25-hydroxyvitamin D.

respondent was <$20 000 or ≥$20 000, the value was not calculated; if the family income was reported as a more detailed category, the midpoint of the range was used to compute the ratio; values at or above 5.00 were coded as 5.00 or more because of disclosure concerns; values were not computed if income data were missing) were considered categorical variables. All data were collected from the National Health and NHANES website.

Statistical methods

The weight of the sample analysis package in this study was edited and considered using NCHS V.3.4 (http://www.R-project.org) and EmpowerStats software (http://www.empowerstats.com/). The CI was set at 95%. The association between lumbar BMD, serum 25-OHD levels, and a history of renal calculi was evaluated using multivariable logistic regression models. We constructed three models: model 1, no covariates were adjusted; model 2, only adjusted for age, sex, race and BMI; and model 3, all the covariates listed in table 1 were adjusted. We also performed the subgroup analyses stratified according to sex, lumbar BMD status, and serum 25-OHD status.

RESULTS

Table 1 presents the demographic and laboratory data of the participants. Women had a significantly higher lumbar BMD. Participants with higher lumbar BMD had a higher serum creatinine level, BMI, education level, level of physical activity, and ratio of family income to poverty, as well as lower alkaline phosphatase, total cholesterol, serum triglyceride, smoking rate, and stone incidence rate than participants with lower lumbar BMD.

Association between lumbar BMD and kidney stones

We found that lumbar BMD was negatively associated with a history of kidney stone formation in all three models (table 2). The trend in the different lumbar BMD quartile arrays remained significant ($p<0.05$). This negative association existed in both men and women after adjusting for all confounding factors (OR=0.281, 95% CI 0.131 to 0.601; OR=0.299, 95% CI 0.129 to 0.693) in the subgroup analysis stratified by sex and race, as well as in non-Hispanic whites. In addition, a weighted generalised additive model and smooth curve fitting was used to solve the non-linear relationship and confirm the results

Table 1 Weighted characteristics of the study sample : the cohort of adults aged 30–69 (n=7500)

	Lumbar BMD Q1 (g/cm²) (n=1873)	Lumbar BMD Q2 (g/cm²) (n=1869)	Lumbar BMD Q3 (g/cm²) (n=1882)	Lumbar BMD Q4 (g/cm²) (n=1876)	P value
Age (years)	46.4±8.7	44.5±8.6	44.0±8.7	44.2±8.6	<0.05
Gender					<0.05
Men/women	55.6/44.4	49.8/50.2	48.9/51.1	50.7/49.3	
Race					<0.05
Mexican American	11.2	11.5	9.0	4.9	
Other Hispanic	8.0	6.7	5.6	4.9	
Non-Hispanic white	64.6	62.6	66.5	64.5	
Non-Hispanic black	5.9	8.4	10.8	17.7	
Other race, including multiracial	10.3	10.8	8.1	8.0	
Blood urea nitrogen(mmol/L)	4.7±1.6	4.7±1.5	4.6±1.5	4.7±1.7	0.19
Serum calcium (mmol/L)	2.3±0.1	2.3±0.1	2.3±0.1	2.3±0.1	0.92
Serum creatinine (μmol/L)	74.9±19.6	75.8±23.6	75.9±28.8	78.7±32.0	<0.05
Serum glucose (mmol/L)	5.5±1.6	5.5±2.0	5.5±1.9	5.6±2.3	0.15
Serum phosphorus (mmol/L)	1.2±0.2	1.2±0.2	1.2±0.2	1.2±0.2	<0.05
Serum sodium (mmol/L)	139.2±2.3	139.3±2.3	139.1±2.3	139.1±2.2	0.19
Serum 25-hydroxyvitamin D (nmol/L)	67.3±26.6	67.5±25.8	70.1±27.6	68.2±26.4	<0.05
Alkaline phosphatase (U/L)	73.3±27.0	69.1±22.3	65.4±20.1	64.2±23.1	<0.05
Total cholesterol (mmol/L)	5.3±1.1	5.2±1.1	5.1±1.0	5.0±1.0	<0.05
Total protein (g/L)	71.0±4.5	70.9±4.3	71.1±4.5	71.1±4.1	0.61
Serum uric acid (μmol/L)	319.8±78.3	321.5±83.5	314.4±82.6	321.2±83.6	<0.05
Serum potassium (mmol/L)	4.0±0.3	4.0±0.3	3.9±0.3	4.0±0.3	<0.05
BMI (kg/m^2)	29.3±6.1	29.7±6.6	29.2±6.7	30.3±7.3	<0.05
Serum triglycerides (mmol/L)	1.9±1.4	1.9±1.9	1.8±1.3	1.7±1.4	<0.05
Education level					<0.05
Less than 9th grade	6.9	4.3	3.1	2.0	
9–11th grade (includes 12th grade with no diploma)	11.2	9.3	7.8	7.9	
High school graduate/General Educational Development or equivalent	21.5	22.1	19.0	19.5	
Some college or associates degree	30.5	30.6	32.0	32.0	
College graduate or above	29.9	33.7	38.1	38.6	
Vigorous recreational activities					<0.05
Yes	22.7	28.8	31.6	33.3	
No	77.3	71.2	68.4	66.7	
Smoked at least 100 cigarettes in life					<0.05
Yes	47.6	42.6	42.1	42.8	
No	52.4	57.4	57.9	57.2	
Stones					<0.05
Yes	13.7	9.2	9.4	8.6	
No	86.3	90.8	90.6	91.4	
Ratio of family income to poverty					<0.05
<1.99	35.8	33.7	28.9	28.9	
1.99–3.49	21.0	22.8	21.0	21.6	
>3.49	43.2	43.5	50.1	49.5	

Continued

Table 1 Continued

	Lumbar BMD Q1 (g/cm²) (n=1873)	Lumbar BMD Q2 (g/cm²) (n=1869)	Lumbar BMD Q3 (g/cm²) (n=1882)	Lumbar BMD Q4 (g/cm²) (n=1876)	P value

Notes: Mean±SD for continuous variables: p value was calculated by weighted linear regression model; % for categorical variables: p value was calculated by weighted χ^2 test.
BMI, body mass index; BUN, blood urea nitrogen.

(figure 2). This is one of the modules of the EmpowerStats software for statistical applications. This module examines non-linear relationships between outcome variables and risk factors (exposure) using generalised additive models. It is helpful to determine the relationship between non-straightness and whether there is a threshold effect. The outcome variable in this study was dichotomous; therefore, the smooth curve fitting of EmpowerStats software was performed using the gam() function in the mgcv package of R, with the curve fitting term defined by the s() function. The model automatically determined the degree of freedom according to the minimum GCV method.[13] After the aforementioned analytical tests, the negative linear relationship between BMD and stone formation remained unchanged.

Interaction between serum 25-OHD and lumbar BMD

According to Holick,[14] the Endocrine Society defines vitamin D deficiency as a 25-OHD level of <20 ng/mL (50 nmol/L). Therefore, we divided the serum 25-OHD level into two groups with a tangent point of 50 nmol/L and conducted an interaction analysis. We found an interaction between serum 25-OHD and lumbar BMD ($p<0.05$) that influenced kidney stones in model 3 (table 3). Furthermore, we performed a stratified analysis of the aforementioned two 25-OHD groups in the multiple regression analysis between lumbar BMD and kidney stones (table 2). The results showed that the negative correlation between lumbar BMD and kidney stones

Table 2 Association between lumbar BMD (g/cm²) and kidney stones

	Model 1, OR (95% CI)	Model 2, OR (95% CI)	Model 3, OR (95% CI)
Lumbar BMD (g/cm²)	0.324 (0.193 to 0.543)	0.374 (0.219 to 0.641)	0.321 (0.184 to 0.560)
Quintiles of lumbar BMD			
Lowest quintile	Reference	Reference	Reference
Q2	0.695 (0.562 to 0.860)	0.725 (0.585 to 0.900)	0.699 (0.562 to 0.869)
Q3	0.685 (0.554 to 0.848)	0.733 (0.590 to 0.911)	0.697 (0.559 to 0.870)
Q4	0.669 (0.540 to 0.829)	0.716 (0.573 to 0.896)	0.681 (0.542 to 0.855)
P for trend	<0.001	0.004	0.001
Stratified by 25-OHD			
<50	0.512 (0.209 to 1.253)	0.721 (0.277 to 1.873)	0.534 (0.199 to 1.438)
≥50	0.263 (0.139 to 0.497)	0.277 (0.144 to 0.534)	0.249 (0.126 to 0.489)
Total	0.328 (0.195 to 0.550)	0.249 (0.126 to 0.489)	0.249 (0.126 to 0.489)
Stratified by gender			
Men	0.363 (0.180 to 0.733)	0.360 (0.173 to 0.749)	0.281 (0.131 to 0.601)
Women	0.284 (0.133 to 0.606)	0.291 (0.129 to 0.658)	0.299 (0.129 to 0.693)
Stratified by race			
Mexican American	0.678 (0.139 to 3.300)	0.799 (0.161 to 3.970)	0.341 (0.059 to 1.954)
Other Hispanic	1.069 (0.231 to 4.960)	0.979 (0.204 to 4.692)	0.635 (0.117 to 3.448)
Non-Hispanic white	0.223 (0.098 to 0.504)	0.220 (0.098 to 0.494)	0.214 (0.093 to 0.495)
Non-Hispanic black	0.537 (0.162 to 1.778)	0.615 (0.184 to 2.059)	0.612 (0.170 to 2.203)
Other race, including multiracial	0.285 (0.063 to 1.283)	0.222 (0.048 to 1.035)	0.175 (0.034 to 0.910)

Model 1 adjusted for none.
Model 2 adjusted for gender, age, race and BMI.
Model 3 adjusted for gender, age, race, BMI, education level, BUN, serum calcium, serum creatinine, serum glucose, serum phosphorus, serum sodium, physical activities, smoking behaviour, poverty to income ratio, alkaline phosphatase, total cholesterol, total protein, serum uric acid, serum potassium and serum triglycerides.
BMD, bone mineral density; BMI, body mass index; BUN, blood urea nitrogen; 25-OHD, 25-hydroxyvitamin D.

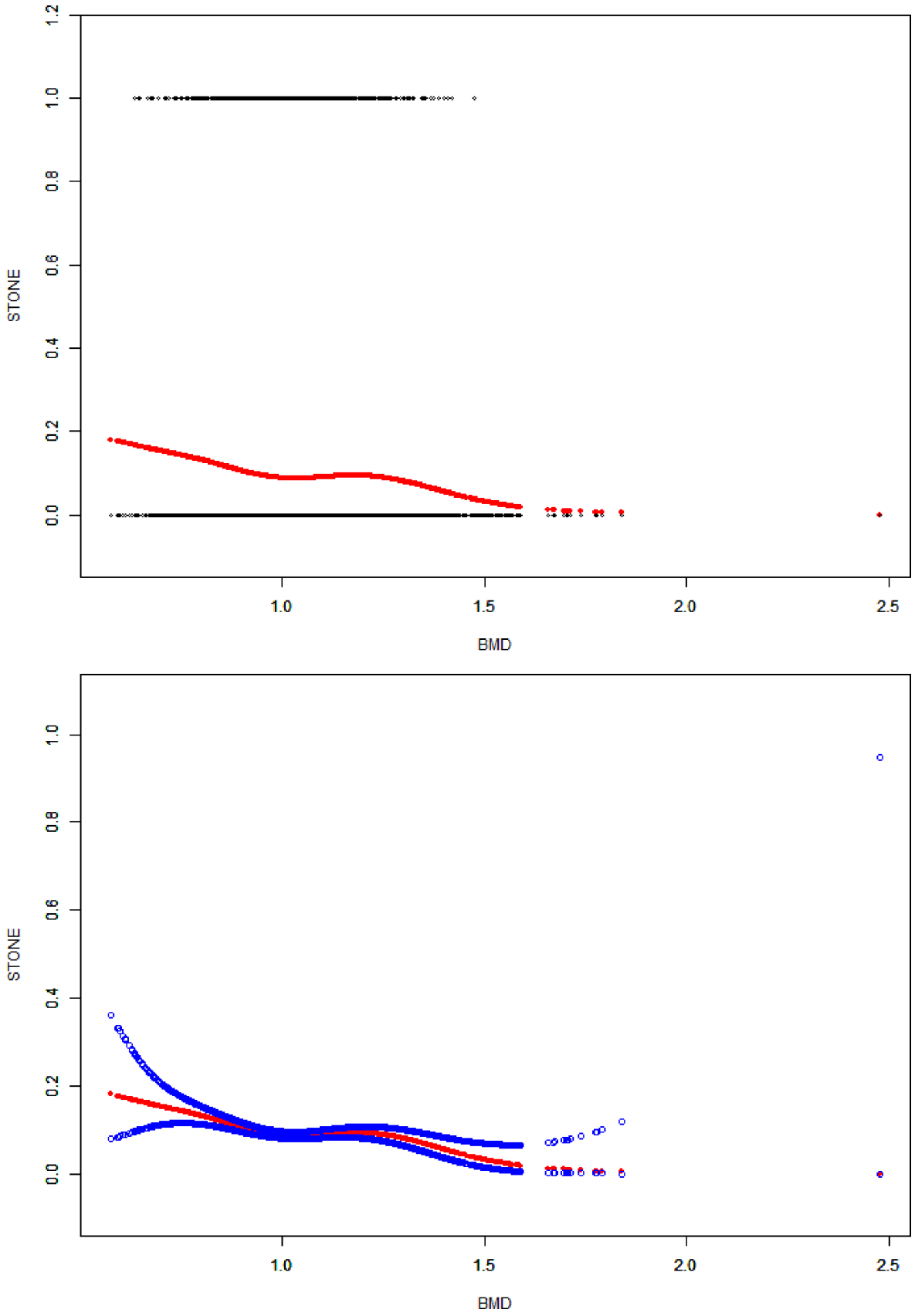

Figure 2 Association between lumbar BMD and history of kidney stones. Each black point represents a sample. The solid red line represents the smooth curve fit between variables. Blue bands represent the 95% CI from the fit. Gender, age, race, body mass index, education level, blood urea nitrogen, serum calcium, serum creatinine, serum glucose, serum phosphorus, serum sodium, physical activities, smoking behaviour, poverty to income ratio, alkaline phosphatase, total cholesterol, total protein, serum uric acid, serum potassium, and serum triglycerides were adjusted. BMD, bone mineral density.

Table 3 Interaction between serum 25-OHD (nmol/L) and lumbar BMD (g/cm²)

	Model 1, OR (95% CI)	Model 2, OR (95% CI)	Model 3, OR (95% CI)
Serum 25-OHD (nmol/L)			
<50	0.512 (0.209 to 1.253)	0.718 (0.278 to 1.854)	0.670 (0.254 to 1.767)
≥50	0.263 (0.139 to 0.497)	0.278 (0.145 to 0.534)	0.282 (0.144 to 0.551)
P interaction	0.23	0.11	0.03

Model 1 adjusted for none.
Model 2 adjusted for gender, age, race and BMI.
Model 3 adjusted for gender, age, race, BMI, education level, BUN, serum calcium, serum creatinine, serum glucose, serum phosphorus, serum sodium, physical activities, smoking behaviour, poverty to income ratio, alkaline phosphatase, total cholesterol, total protein, serum uric acid, serum potassium, serum triglycerides.
BMD, bone mineral density; BMI, body mass index; BUN, blood urea nitrogen; 25-OHD, 25-hydroxyvitamin D.

is more obvious (OR=0.249, 95% CI 0.126 to 0.489) in the higher 25-OHD group (≥50 nmol/L).

DISCUSSION

The overall purpose of this study was to explore the relationship between lumbar BMD, serum 25-OHD levels and a history of kidney stones in a nationally representative sample of people of the US population aged 30–69 years. Our results suggest that a low lumbar BMD is correlated with a history of renal calculus both in men and women, and particularly in non-Hispanic white subjects. Although there were some non-linear correlations, the trend was consistent with that of a previous multivariable linear regression analysis. The negative correlation between lumbar BMD and kidney stones is more obvious in the higher serum 25-OHD group (≥50 nmol/L). This finding suggests that maintaining a high lumbar BMD may reduce the incidence of kidney stone formation. Simultaneously, while ensuring a high lumbar BMD, maintaining a high serum 25-OHD level may be more beneficial for preventing the occurrence or recurrence of stones.

In recent years, an increasing number of clinical investigators have noted an association between BMD and history of kidney stones in patients. Consistent with the results of the present study, several studies have also verified, from all aspects, that there is an inverse association between history of kidney stones and BMD.[5 15–18] In a 2016 consensus statement, experts recommended that the BMD of patients with hypercalciuric stones or a predisposition to this condition should be measured by DXA.[19] This non-invasive examination is convenient and efficient; however, the mechanisms underlying this effect remain unclear. Stones are common in patients with high calcium levels in the urine.[20] Hypercalciuria occurs because of a net loss of calcium from the body; therefore, patients usually excrete more calcium than they absorb. Some researchers have speculated that this extra urinary calcium is derived from bone.[21 22] In another group, researchers found that sequence variants in the *CLDN14* gene may be associated with kidney stones and BMD.[23] A study published in 2022 also demonstrated that for adults, the risk of developing kidney stones and osteoporosis increases mutually.[24] We have attached the table of this large cohort studies to the supplementary materials as a comparative table for this study (online supplemental material 1).

Vitamin D plays an important biological role in humans, and vitamin D deficiency is associated with diseases caused by anaemia and oxidative stress.[25] Although it has been shown that vitamin D may be responsible for stone formation in selected patients with certain genetic or clinical features,[26 27] serum 25-OHD content did not differ between patients with and without stones, according to a previous cross-sectional study.[28 29] An interventional study in 2019 found that regular doses of vitamin D supplementation in patients with vitamin D deficiency may not increase the risk of hypercalciuria.[30] Several studies have also confirmed that increasing the intake of vitamin D can increase BMD and improve bone quality, with significant beneficial effects on the risk of fractures.[31–33] Therefore, for patients with kidney stones or those with a tendency to develop stones, it is reasonable to assume that daily vitamin D supplementation might reduce the risk of stone recurrence or occurrence through the interaction between serum 25-OHD and lumbar BMD. Studies by Larsson *et al* and Reid *et al* suggested an insignificant causal relationship between chronically elevated serum 25-OHD concentrations and higher BMD in the general healthy population. Forty nanomoles per litre is a sufficient concentration of serum 25-OHD.[34 35] There are also some studies that suggest that vitamin D supplementation at lower amounts is safer in the normal population. The current findings do not support the beneficial effects of high-dose vitamin D supplements on bone health, which may even confer a substantial reduction in BMD, risk of falls, fractures or a small increase in myocardial infarction.[36] Excluding people with normal renal function, in kidney transplant recipients, a recent study showed that supplementation with inactive vitamin D did not modify the urinary calcium nor the BMD, Z-score or T-score at lumbar bodies and the femoral neck in kidney transplant recipients.[37] According to the current available evidence, the benefits of vitamin D supplementation in humans are more biased towards a 'U-shaped' association. Therefore,

although daily vitamin D supplementation may be beneficial in patients with kidney stones, treatment measures should be adjusted at any time based on changes in the condition to facilitate a positive balance between risks and benefits.

To make the current findings highly generalisable, the NHANES database aims to provide nationally representative estimates. However, this method has certain limitations. First, the character of this cross-sectional study limits the conclusions to associations and cannot assess the causal association of lumbar spine BMD and serum 25-OHD with a history of nephrolithiasis. Second, due to patients with kidney stones being concentrated in the middle-aged and older age groups and because pregnant women were excluded from DXA examination, individuals aged 30–69 years with a non-pregnant status from the NHANES database were selected for the study. Therefore, the specificity for certain groups, such as adolescents, pregnant women, or those >70 years of age, was poor. Third, as we only assessed BMD at the lumbar spine without introducing BMD at other sites, the present study may have been less clinically representative. Finally, owing to the lack of data on urinary calcium and analysis of stone composition, our study has limitations regarding the related effects of different types of stones and urinary calcium excretion.

CONCLUSION

Our results suggest that low lumbar BMD is associated with a history of renal calculus, both in men and women and particularly in non-Hispanic white subjects. This finding suggests that maintaining a high lumbar BMD may reduce the incidence of kidney stone formation. At the same time, the negative correlation between lumbar BMD and kidney stones is more obvious in the higher 25-OHD group (≥50 nmol/L), which means that maintaining a high serum 25-OHD level may be more beneficial to prevent the occurrence or recurrence of kidney stones while ensuring a high lumbar BMD.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants, but the National Health and Nutrition Examination Survey (NHANES) is a publicly available database and all records have been identified. This study was approved by the ethics review board of the National Center for Health Statistics and written informed consents were obtained from each participant. We searched the official website of NHANES and referenced articles from other NHANES databases but could not find any ID.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. It is publicly available for people to collect data from the official website for users and researchers worldwide. (www.cdc.gov/nchs/ nhanes/). Data are available upon reasonable request.

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REFERENCES

1 Cicerello E, Mangano MS, Cova G, *et al*. Changing in gender prevalence of nephrolithiasis. Urologia 2021;88:90–3.
2 Cicerello E, Ciaccia M, Cova GD, *et al*. The new patterns of nephrolithiasis: what has been changing in the last millennium? periodical the new patterns of nephrolithiasis: what has been changing in the last millennium. 2021;93:195–9.
3 Hill AJ, Basourakos SP, Lewicki P, *et al*. Incidence of kidney stones in the United States: the continuous National health and nutrition examination survey. J Urol 2022;207:851–6.
4 Hoffman A, Braun MM, Khayat M. Kidney disease: kidney stones. *FP Essent* 2021;509:33–8.
5 Ganesan C, Thomas I-Chun, Romero R, *et al*. Osteoporosis, fractures, and bone mineral density screening in veterans with kidney stone disease. J Bone Miner Res 2021;36:872–8.
6 Nicoli F, Dito G, Guabello G, *et al*. Hypercalciuria in postmenopausal women with reduced bone mineral density is associated with different mineral metabolic profiles: effects of treatment with thiazides and anti-Resorptives. *Front Med* 2021;8.
7 Penido MGMG, Tavares MdeS. Beyond kidney stones: why pediatricians should worry about hypercalciuria. World J Clin Pediatr 2021;10:137–50.
8 Ryan LE, Ing SW. Idiopathic hypercalciuria: can we prevent stones and protect bones? Cleve Clin J Med 2018;85:47–54.
9 Lauderdale DS, Thisted RA, Wen M, *et al*. Bone mineral density and fracture among prevalent kidney stone cases in the third National health and nutrition examination survey. J Bone Miner Res 2001;16:1893–8.
10 Brahme R, Godbole S, Gangakhedkar R, *et al*. Use of computer-assisted personal interviewing and information management system in a survey among HIV high-risk groups in India: strengths, weaknesses, opportunities, and threats analysis. Indian J Community Med 2018;43:107–12.
11 Shin S, Park E, Sun DH, *et al*. Development and evaluation of a web-based computer-assisted personal interview system (CAPIS) for open-ended dietary assessments among Koreans. Clin Nutr Res 2014;3:115–25.
12 Kissinger L, Lorenzana R, Mittl B, *et al*. Development of a computer-assisted personal interview software system for collection of tribal fish consumption data. Risk Anal 2010;30:1833–41.
13 Perperoglou A, Sauerbrei W, Abrahamowicz M, *et al*. A review of spline function procedures in R. BMC Med Res Methodol 2019;19:46.
14 Holick MF. The vitamin D deficiency pandemic: approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord 2017;18:153–65.
15 Assimos DG. Re: Vascular calcification and bone mineral density in recurrent kidney stone Formers. *J Urol* 2015;194:S0022-5347(15)04170-1.

16 Arrabal-Polo MÁ, Sierra Girón-Prieto M, Orgaz-Molina J. Calcium renal lithiasis and bone mineral density. Importance of bone metabolism in urinary lithiasis. *Actas Urológicas Españolas* 2013;37:362–7.
17 Prochaska M, Taylor E, Vaidya A, *et al*. Low bone density and Bisphosphonate use and the risk of kidney stones. *Clin J Am Soc Nephrol* 2017;12:1284–90.
18 Wong P, Milat F, Fuller PJ, *et al*. Urolithiasis is prevalent and associated with reduced bone mineral density in B-Thalassaemia major. *Intern Med J* 2017;47:1064–7.
19 Gambaro G, Croppi E, Coe F, *et al*. Metabolic diagnosis and medical prevention of calcium nephrolithiasis and its systemic manifestations: a consensus statement. *J Nephrol* 2016;29:715–34.
20 Krieger NS, Chen L, Becker J, *et al*. Increased Osteoclast and decreased Osteoblast activity causes reduced bone mineral density and quality in genetic Hypercalciuric stone-forming rats. *JBMR Plus* 2020;4:e10350.
21 Pietschmann F, Breslau NA, Pak CYC. Reduced vertebral bone density in hypercalciuric nephrolithiasis. J Bone Miner Res 1992;7:1383–8.
22 Silva AMM da, Reis LM dos, Pereira RC, *et al*. Bone involvement in idiopathic Hypercalciuria. *CN* 2002;57:183–91.
23 Thorleifsson G, Holm H, Edvardsson V, *et al*. Sequence variants in the CLDN14 gene associate with kidney stones and bone mineral density. *Nat Genet* 2009;41:926–30.
24 Kim SY, Chung J, Park DS, *et al*. The reciprocal relationship between osteoporosis and renal stones. J Clin Med 2022;11:6614.
25 Zhang C, Wang J, Xie X, *et al*. Low serum vitamin D concentration is correlated with anemia, microinflammation, and oxidative stress in patients with peritoneal dialysis. *J Transl Med* 2021;19:411.
26 Letavernier E, Daudon M. Vitamin D, hypercalciuria and kidney stones. Nutrients 2018;10:366.
27 Hesswani C, Noureldin YA, Elkoushy MA, *et al*. Combined vitamin D and calcium supplementation in vitamin D inadequate patients with urolithiasis: impact on hypercalciuria and de novo stone formation. Can Urol Assoc J 2015;9:403–8.
28 Nguyen S, Baggerly L, French C, *et al*. 25-Hydroxyvitamin D in the range of 20 to 100 ng/mL and incidence of kidney stones. Am J Public Health 2014;104:1783–7.
29 Tang J, McFann KK, Chonchol MB. Association between serum 25-hydroxyvitamin D and nephrolithiasis: the National health and nutrition examination survey III, 1988-94. Nephrol Dial Transplant 2012;27:4385–9.
30 Ganji MR, Shafii Z, Hakemi MS. Vitamin D supplementation and risk of hypercalciuria in stone formers. *Iran J Kidney Dis* 2019;13:27–31.
31 Zhang Q, Shi L, Peng N, *et al*. Serum concentrations of 25-Hydroxyvitamin D and its association with bone mineral density and serum parathyroid hormone levels during winter in urban males from Guiyang, Southwest China. *Br J Nutr* 2016;115:960–6.
32 Bischoff-Ferrari HA. Optimal serum 25-Hydroxyvitamin D levels for multiple health outcomes. *Adv Exp Med Biol* 2014;810:500–25.
33 Marić I, Kizivat T, Smolić M, *et al*. LIFESTYLE risk factors and bone mass in recurrent stone-forming patients: a cross-sectional study in 144 subjects. *Acta Clin Croat* 2019;58:439–45.
34 Larsson SC, Melhus H, Michaëlsson K. Circulating serum 25-Hydroxyvitamin D levels and bone mineral density: Mendelian randomization study. *J Bone Miner Res* 2018;33:840–4.
35 Reid IR, Bolland MJ, Grey A. Effects of vitamin D supplements on bone mineral density: a systematic review and meta-analysis. *Lancet* 2014;383:146–55.
36 Burt LA, Billington EO, Rose MS, *et al*. Effect of high-dose vitamin D supplementation on volumetric bone density and bone strength: A randomized clinical trial. *JAMA* 2019;322:736–45.
37 Battaglia Y, Bellasi A, Bortoluzzi A, *et al*. Bone mineral density changes in long-term kidney transplant recipients: A real-life cohort study of native vitamin D supplementation. *Nutrients* 2022;14:323.