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Association between relative fat mass and kidney stones in American adults

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Our study aimed to investigate the association between RFM and kidney stones, focusing specifically on the mediating role of high-density lipoprotein cholesterol (HDL-C). We performed a cross-sectional analysis using data from the National Health and Nutrition Examination Survey (NHANES) covering the years 2007 to 2018. Our analytical approach included multivariate logistic regression modeling, subgroup analysis, generalized additive modeling (GAM), smoothed curve fitting, and receiver operating characteristic (ROC) curve, as well as mediation analysis to assess the association between RFM and kidney stones. Finally, we categorized RFM into normal and elevated groups to conduct a sensitivity analysis. This study involved 29,712 participants, with a kidney stone prevalence of 9.88%. We discovered a positive association between RFM and kidney stones (OR = 1.41 per SD increment, 95% CI: 1.24, 1.60). Subgroup analysis revealed a consistent positive association across all subgroups, with a notably higher likelihood of developing kidney stones in young adulthood (P for interaction < 0.05). The smooth curve fitting shows that RFM is nonlinearly and positively correlated with the prevalence of kidney stones. Additionally, HDL-C was found to be negatively associated with kidney stones. Importantly, HDL-C demonstrated a significant mediating effect, with a mediation ratio of 13.52%. ROC analysis indicated that RFM (AUC = 0.616) provided better diagnostic accuracy than traditional measures such as BMI (AUC = 0.565) and WC (AUC = 0.599). Furthermore, the sensitivity analysis further supports the robustness of our findings. RFM is nonlinearly and positively correlated with the prevalence of kidney stones, with HDL cholesterol playing a significant mediating role in this relationship. However, further studies are needed to confirm these associations and explore potential mechanisms.

Keywords Kidney stones, Relative fat mass, NHANES, Cross-sectional study, High-density lipoprotein cholesterol

Abbreviations

RFM	Relative fat mass
NHANES	National Health and Nutrition Examination Survey
GAM	Generalized additive model
PIR	Income to poverty ratio
BMI	Body mass index
WC	Waist circumference
WHTR	Waist-to-height ratio
WHR	Waist-to-hip ratio
AVI	Abdominal volume index
ABSI	A body shape index
BRI	Body roundness index
HDL-C	High-density lipoprotein cholesterol
MEC	Mobile Examination Center
SD	Standard deviation
KSD	Kidney stone disease
ROC	Receiver operating characteristic
AUC	Area under the curve

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Kidney stones are a major public health problem affecting millions of people worldwide. The prevalence of kidney stones is increasing in many countries, driven by factors such as dietary habits, lifestyle changes, and rising obesity rates[1,2]. A recent cross-sectional study reported a higher prevalence of kidney stones in men than in women in the U.S. adult population. However, over the past decade, the prevalence has remained stable in men but has increased in women[3]. Factors such as metabolic obesity, diabetes mellitus, an aging population, changing dietary habits, and inadequate fluid intake have all contributed to the increased prevalence of kidney stones[4]. This rising trend has also been documented over forty years in Japan. In 2005, there were 134.0 estimated cases of upper urinary tract stones per 100,000 individuals. (192.0 for males and 79.3 for females), compared with 54.2 per 100,000 people in 1965[5]. Renal stones' high incidence and recurrence rate seriously affect the lives of patients and cause significant social and economic losses. Therefore, there is a pressing requirement to explore the risk factors of renal stones to reduce the social and economic burden and improve the postoperative prognosis.

Specifically, metabolic obesity is a significant risk factor connected to the incidence of kidney stones[6]. However, Relative Fat Mass (RFM), as a novel obesity indicator calculated from waist circumference and height measurements, not only provides a direct estimation of body fat content but is also particularly suitable for clinical and epidemiological studies[7]. RFM provides a more nuanced understanding of adiposity and body fat distribution in patients with lean body mass, offering greater insight than traditional indicators such as Body Mass Index (BMI)[8,9]. Additionally, it is a more accurate predictor of diabetes than BMI, demonstrating enhanced predictive accuracy[7]. Recently, several studies have utilized RFM as an indicator of obesity. RFM was demonstrated to be a more accurate predictor of severe liver disease and mortality than body mass index in a short study that validated its use to measure the percentage of adiposity in men and women with Down syndrome[10,11]. Moreover, RFM can be used as an indicator to rule out metabolic syndrome[9]. In recent years, the social value of RFM in effectively identifying the risk of obesity-related health problems in individuals has been recognized, thereby contributing to a better understanding of public health dynamics in different populations[12]. Obesity can seriously affect all aspects of human health, including an increased risk of cardiovascular disease, diabetes, and metabolic syndrome[13,14]. Dyslipidemia is a prevalent and significant risk factor for cardiovascular disease in obese people. Low levels of HDL-C, or high-density lipoprotein cholesterol, and elevated levels of lipoproteins rich in triglycerides are the hallmarks of obesity-associated dyslipidemia[15].

Therefore, in this study, we investigated any possible relationship between RFM and the prevalence of renal calculi in U.S. adults using information from the 2007–2018 NHANES. We examined whether levels of HDL-C mediated the association between RFM and kidney stone prevalence. Our results might offer strong proof of the involvement of lipid metabolism in the kidney stone population and offer a valuable reference for healthcare professionals in their daily work.

Materials and methods

Data availability

Study participants were recruited from the NHANES database, which utilizes a complex, multi-stage, stratified, and clustered probability design to ensure a representative sample of the U.S. population. Conducted regularly on a 2-year cycle since 1999, the NHANES database aims to gather detailed information about the health, nutrition, and sociological aspects of Americans. Each individual participating in this study is involved in a specific cycle and is assigned a unique identification number. Data on demographics, lifestyle, and health status are obtained through questionnaires, medical examinations, and laboratory tests. The study received approval from the National Center for Health Statistics Ethics Review Board, and all participants provided signed informed consent forms.

Characteristics of the population

This study analyzed data from NHANSE participants from the 2007–2008, 2009–2010, 2011–2012, 2013–2014, 2015–2016, and 2017–2018 cycles who reported previous kidney stones. Initially, 59,842 participants were considered; however, after excluding cases with missing data on kidney stones, relative fat mass, HDL-C, and individuals under 20 years of age, the final sample included 29,712 participants. (Fig. 1)

Study variables

In this study, the main outcome measure was the occurrence of kidney stones. Data were collected through the Health Status Questionnaire (HSQ) in NHANES, which relied on participants' self-reported kidney health problems (KIQ026) obtained during personal interviews. The questionnaire specifically asked, "Have you ever had a kidney stone?" with options for responses being either 'yes' or 'no'. An affirmative response indicated a history of kidney stones. The reliability of these self-reported measures has been confirmed by previous studies[16,17].

Relative Fat Mass (RFM) was calculated using waist circumference (WC), height, and gender. In the formula, the female gender is assigned a value of 1 and the male gender a value of 0. Both height and WC were accurately measured by medical professionals at the Mobile Examination Center (MEC)[12]. We referenced previous literature related to RFM and conducted both quartile grouping and dichotomous grouping of RFM based on obesity status (normal group and elevated group). Obesity, as defined by RFM, was diagnosed using validated cutoff points: RFM ≥ 40% for females and RFM ≥ 30% for males[7,18].

$$RFM = 64 - \left(20 \times \frac{\text{height (cm)}}{\text{WC (cm)}}\right) + (12 \times \text{gender})$$

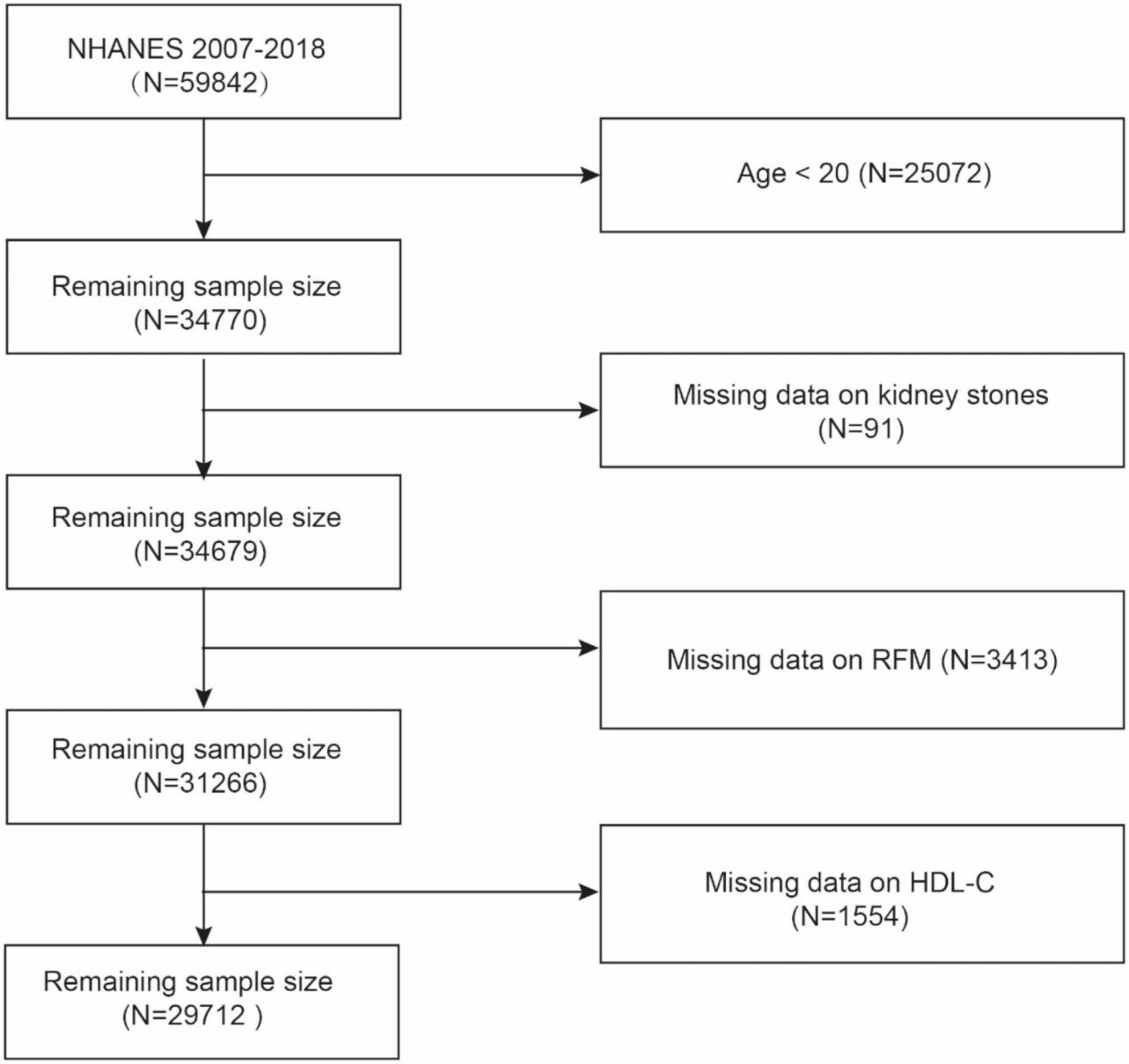

Fig. 1. Flow chart.

Covariates

The selection of covariates for this research incorporated various demographic, socioeconomic, anthropometric, lifestyle, and health-related dimensions. The chosen covariates were age, gender, race, educational attainment, marital status, the ratio of household income to the poverty threshold, body mass index (BMI), and levels of high-density lipoprotein cholesterol (HDL-C). Drinking status was categorized based on individuals who reported consuming at least 12 alcoholic beverages in the preceding year. Similarly, smoking status was categorized for those who reported smoking a minimum of 100 cigarettes throughout their lifetime. The diagnosis of diabetes mellitus was determined by any of the following: a confirmation from a physician or healthcare professional, a fasting blood glucose level of 126 mg/dl or above, an HbA1c percentage of 6.5% or above, or the utilization of diabetes medications, including insulin. Hypertension was identified through any of these methods: a physician's or healthcare professional's diagnosis, the use of antihypertensive drugs, or a minimum of 140 mmHg on average for the systolic and 90 mmHg for the diastolic levels. For clarity and methodological transparency, this study consulted previous literature for detailed variable descriptions[19]. Comprehensive data for all study variables are accessible on the NHANES website at www.cdc.gov/nchs/nhanes/.

Statistical analysis

All statistical analyses were conducted using the appropriate NHANES survey weights following CDC guidelines. We employed weighted linear regression and chi-square tests to assess differences among the quartile groups of

Relative Fat Mass (RFM). Continuous variables were expressed as weighted survey means and 95% confidence intervals, and categorical variables were expressed as weighted survey percentages and 95% confidence intervals.

To explore the association between Relative Fat Mass (RFM) and the prevalence of kidney stones, we utilized three logistic regression models and Spearman's correlation analysis: unadjusted, minimally adjusted, and fully adjusted for covariates. Model 1 was unadjusted. Model 2 included adjustments for age, race, and sex. Model 3 was further adjusted to incorporate body mass index (BMI), household income to poverty ratio (PIR), education, marital status, smoking status, alcohol consumption, diabetes, and hypertension, building on the adjustments made in Model 2. We conducted weighted multivariate logistic regression to elucidate the association between Relative Fat Mass (RFM) and kidney stones, treating RFM both as a continuous variable and in categorical form (quartiles). We also estimated trends by considering RFM quartiles as continuous variables. To further examine the nonlinear relationship between RFM and kidney stone prevalence, we utilized a generalized additive model (GAM) with smooth curve fitting. Subsequent subgroup analyses and interaction tests focused on potential confounders as detailed in the baseline table. Receiver operating characteristic (ROC) curves were used to evaluate the predictive power of anthropometric indices (RFM, WC, BMI) for kidney stones, and the area under the curve (AUC) values were compared. For the sensitivity analysis, we categorized RFM into normal and elevated groups.

Finally, we utilized weighted multivariate logistic regression analyses to examine the association between high-density lipoprotein cholesterol (HDL-C) and the prevalence of kidney stones. Additionally, to evaluate the possible mediating role of HDL-C on the association between kidney stones and RFM, mediation studies were carried out. The significance of the mediating effect was tested using 1000 bootstrap samples, and the proportion of the effect mediated by HDL-C was calculated using the formula: (indirect effect/total effect) × 100%. Statistical analyses for this study were conducted using EmpowerStats (Version 4.2) and R software (version 4.3.2). The significance threshold was set at $P < 0.05$.

Results

Basic characteristics of the study population

Participants' initial clinical features are shown, weighted by the Relative Fat Mass (RFM) quartile levels (Q1-Q4). A total of 29,712 participants were included in this study. The population-weighted mean age was 47.27 (95% CI: 46.83, 47.72) years, with 48.48% (95% CI: 47.90%, 49.07%) being male. The overall mean RFM was 35.40 (95% CI: 35.22, 35.58), with RFM levels in the Q1-Q4 quartiles reported as 24.78 (95% CI: 24.65, 24.91), 32.14 (95% CI: 32.08, 32.20), 39.11 (95% CI: 39.04, 39.18), and 46.98 (95% CI: 46.89, 47.08), respectively. The prevalence of kidney stones was 9.88% (95% CI: 9.40%, 10.38%) across all participants. The quartile levels of kidney stone prevalence were 7.51% (95% CI: 6.71%, 8.39%), 11.88% (95% CI: 10.86%, 12.99%), 9.13% (95% CI: 8.28%, 10.07%), and 11.18% (95% CI: 10.19%, 12.25%). (Table 1)

Association between RFM and kidney stones

Multiple logistic regression analysis revealed a positive association between RFM levels and the prevalence of kidney stones in both unadjusted and adjusted models (Table 2). In the fully adjusted model (Model 3), each standard deviation (SD) increase in RFM was associated with a 41% increase in the likelihood of developing kidney stones (OR = 1.41, 95% CI: 1.24, 1.60). Additionally, participants in the highest RFM quartile (Q4) were shown to be 97% more likely to develop kidney stones than those in the lowest quartile (Q1), when RFM was changed from a continuous to a categorical variable (OR = 1.97, 95% CI: 1.48, 2.63). Furthermore, when RFM was grouped into quartiles, the positive association between RFM levels and kidney stone prevalence not only persisted but also became more significant with increasing RFM (p for trend < 0.001). We further explored the nonlinear relationship between RFM levels and kidney stone prevalence using generalized additive modeling (GAM) with smooth curve fitting. The findings revealed a nonlinear positive correlation between the two (Fig. 2). The Spearman correlation analysis revealed a positive correlation between RFM and kidney stones (Spearman correlation coefficient = 0.56, $P < 0.01$). (Figure S1)

Subgroup analysis

To determine if the association between RFM levels and the prevalence of kidney stones was consistent across different populations, we conducted subgroup analyses. The results of these analyses indicated that the association between RFM and kidney stone prevalence was consistently positive across all subgroups. Notably, the strength of this association varied significantly by age (P for interaction < 0.05). In people aged 20–50 years, each 1 SD increase in RFM was associated with a 67% increase in the likelihood of developing kidney stones (OR = 1.67, 95% CI: 1.40, 1.98). In those > 50 years of age, the likelihood of developing kidney stones increased by 31% for every 1 SD increase in RFM (OR = 1.31, 95% CI: 1.10, 1.58). (Fig. 3)

Association between high-density lipoprotein cholesterol and kidney stones

Multiple logistic regression analysis showed that HDL-C levels were negatively associated with kidney stone incidence. In the fully adjusted model (model 3), each unit increase in HDL-C was associated with a 25% reduction in the likelihood of developing kidney stones (OR = 0.75, 95% CI: 0.67, 0.84). Compared with the lowest quartile, the highest quartile group (Q4) was 22% less likely to develop kidney stones (OR = 0.78, 95% CI: 0.68, 0.89). (Table 3)

Mediation analysis

We also employed mediation analysis to explore the role of HDL-C as a mediator in the relationship between RFM and kidney stone prevalence. The results indicated that HDL-C had a significant mediating effect, accounting for 13.52% of the association (Fig. 4).

Characteristic	Relative fat mass (%)				*P*-value
	Q1 (*N* = 7428)	Q2 (*N* = 7428)	Q3 (*N* = 7428)	Q4 (*N* = 7428)	
Age(years)	42.08 (41.52, 42.64)	48.07 (47.46, 48.69)	48.17 (47.58, 48.75)	51.28 (50.74, 51.82)	< 0.0001
Gender (%)					< 0.0001
Male	96.36 (95.72, 96.92)	72.72 (70.85, 74.52)	18.99 (17.54, 20.52)	0.05 (0.02, 0.12)	
Female	3.64 (3.08, 4.28)	27.28 (25.48, 29.15)	81.01 (79.48, 82.46)	99.95 (99.88, 99.98)	
Race (%)					< 0.0001
Mexican American	7.24 (6.08, 8.60)	9.37 (7.81, 11.20)	7.75 (6.42, 9.32)	10.73 (8.82, 12.99)	
Other Hispanic	5.57 (4.65, 6.66)	5.94 (4.97, 7.07)	5.97 (4.92, 7.23)	6.34 (5.35, 7.49)	
Non-Hispanic White	65.53 (62.72, 68.24)	69.42 (66.59, 72.11)	68.37 (65.35, 71.24)	63.10 (59.43, 66.62)	
Non-Hispanic Black	11.35 (10.03, 12.81)	7.95 (6.84, 9.22)	9.41 (8.12, 10.88)	14.20 (12.22, 16.45)	
Other Race	10.31 (9.05, 11.72)	7.33 (6.46, 8.30)	8.50 (7.37, 9.79)	5.64 (4.85, 6.53)	
Education level (%)					< 0.0001
< High school	14.89 (13.46, 16.43)	15.24 (13.82, 16.79)	13.89 (12.70, 15.18)	18.87 (17.46, 20.37)	
High school	22.42 (20.53, 24.44)	22.41 (20.91, 23.99)	21.88 (20.54, 23.29)	25.21 (23.93, 26.53)	
> High school	62.69 (60.05, 65.26)	62.34 (59.97, 64.66)	64.23 (62.09, 66.31)	55.92 (54.12, 57.70)	
Marital status (%)					< 0.0001
Never married	26.73 (25.13, 28.41)	16.66 (14.83, 18.66)	14.66 (13.38, 16.03)	14.03 (12.99, 15.13)	
Married/Living with partner	62.30 (60.45, 64.12)	69.56 (67.63, 71.42)	64.34 (62.64, 66.00)	58.71 (57.03, 60.37)	
Widowed/divorced/Separated	10.97 (10.07, 11.93)	13.79 (12.64, 15.02)	21.00 (19.74, 22.33)	27.27 (25.88, 28.69)	
PIR (%)					< 0.0001
<1.3	22.25 (20.63, 23.95)	18.86 (17.41, 20.41)	20.96 (19.51, 22.50)	28.67 (26.91, 30.51)	
1.3–3.5	32.43 (30.53, 34.40)	33.14 (31.47, 34.86)	34.39 (32.83, 35.98)	38.02 (36.47, 39.59)	
≥3.5	45.32 (42.78, 47.89)	47.99 (45.76, 50.24)	44.65 (42.42, 46.89)	33.31 (31.16, 35.52)	
BMI (kg/m^2)					< 0.0001
<25	51.07 (49.32, 52.83)	27.59 (25.81, 29.45)	34.82 (33.34, 36.33)	0.85 (0.65, 1.11)	
25–30	45.21 (43.50, 46.94)	26.74 (25.22, 28.33)	39.74 (38.32, 41.17)	18.98 (17.66, 20.37)	
≥30	3.72 (3.16, 4.37)	45.66 (43.93, 47.40)	25.44 (24.07, 26.86)	80.17 (78.77, 81.50)	
Smoke at least 100 cigarettes per year (%)					< 0.0001
Never	51.73 (49.84, 53.62)	51.33 (49.34, 53.31)	59.72 (57.97, 61.44)	60.82 (59.18, 62.44)	
Now	25.55 (23.84, 27.33)	18.72 (17.51, 19.98)	17.99 (16.63, 19.43)	15.88 (14.87, 16.94)	
Former	22.72 (21.43, 24.06)	29.95 (28.36, 31.60)	22.30 (20.86, 23.80)	23.30 (21.79, 24.88)	
At least 12 drinks per year(%)					< 0.0001
No	6.88 (6.07, 7.79)	8.47 (7.45, 9.62)	11.59 (10.55, 12.71)	16.97 (15.59, 18.45)	
Yes	93.12 (92.21, 93.93)	91.53 (90.38, 92.55)	88.41 (87.29, 89.45)	83.03 (81.55, 84.41)	
Hypertension (%)					< 0.0001
No	74.89 (73.50, 76.24)	60.03 (58.23, 61.81)	64.40 (62.97, 65.81)	48.70 (47.21, 50.18)	
Yes	25.11 (23.76, 26.50)	39.97 (38.19, 41.77)	35.60 (34.19, 37.03)	51.30 (49.82, 52.79)	
Diabetes (%)					< 0.0001
No	93.89 (93.05, 94.63)	85.23 (84.05, 86.33)	88.47 (87.50, 89.38)	77.40 (76.26, 78.49)	
Yes	6.11 (5.37, 6.95)	14.77 (13.67, 15.95)	11.53 (10.62, 12.50)	22.60 (21.51, 23.74)	
Kidney stones (%)					< 0.0001
No	92.49 (91.61, 93.29)	88.12 (87.01, 89.14)	90.87 (89.93, 91.72)	88.82 (87.75, 89.81)	
Yes	7.51 (6.71, 8.39)	11.88 (10.86, 12.99)	9.13 (8.28, 10.07)	11.18 (10.19, 12.25)	
HDL-C (mmol/L)	1.35 (1.34, 1.36)	1.32 (1.30, 1.34)	1.49 (1.47, 1.51)	1.36 (1.35, 1.37)	< 0.0001
RFM (%)	24.78 (24.65, 24.91)	32.14 (32.08, 32.20)	39.11 (39.04, 39.18)	46.98 (46.89, 47.08)	< 0.0001
Height (cm)	176.11 (175.82, 176.39)	172.10 (171.75, 172.44)	164.54 (164.20, 164.89)	160.60 (160.35, 160.86)	< 0.0001
Waist circumference (cm)	89.68 (89.30, 90.06)	100.23 (99.60, 100.86)	97.28 (96.58, 97.97)	111.83 (111.42, 112.25)	< 0.0001

Table 1. Baseline characteristics of the study population. *PIR* the ratio of income to poverty, *BMI* body mass index, *Q* quartile, *HDL-C* high-density lipoprotein-cholesterol; total cholesterol, *RFM* relative fat mass.

ROC analysis

This study used ROC curves to evaluate the discriminative ability of three anthropometric indices in patients with kidney stones. ROC curve analysis indicated that RFM had a significantly higher diagnostic ability for kidney stones than WC and BMI. The areas under the curve (AUC) for RFM, WC, and BMI were 0.616, 0.599,

Characteristic	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
RFM (Per SD increment)	1.10 (1.06, 1.14)	1.60 (1.49, 1.72)	1.41 (1.24, 1.60)
RFM (Quartile)			
Q1	Reference	Reference	Reference
Q2	1.72 (1.54, 1.93)	1.65 (1.47, 1.85)	1.42 (1.23, 1.63)
Q3	1.18 (1.04, 1.33)	1.93 (1.66, 2.25)	1.49 (1.22, 1.82)
Q4	1.46 (1.30, 1.64)	3.05 (2.54, 3.66)	1.97 (1.48, 2.63)
P for trend	< 0.001	< 0.001	< 0.001

Table 2. Association between RFM and kidney stones. Model 1: no covariates were adjusted. Model 2: age, gender, and race were adjusted. Model 3: age, gender, race, education level, marital status, PIR, BMI, smoking status, alcohol drinking status, diabetes status, and hypertension status were adjusted.

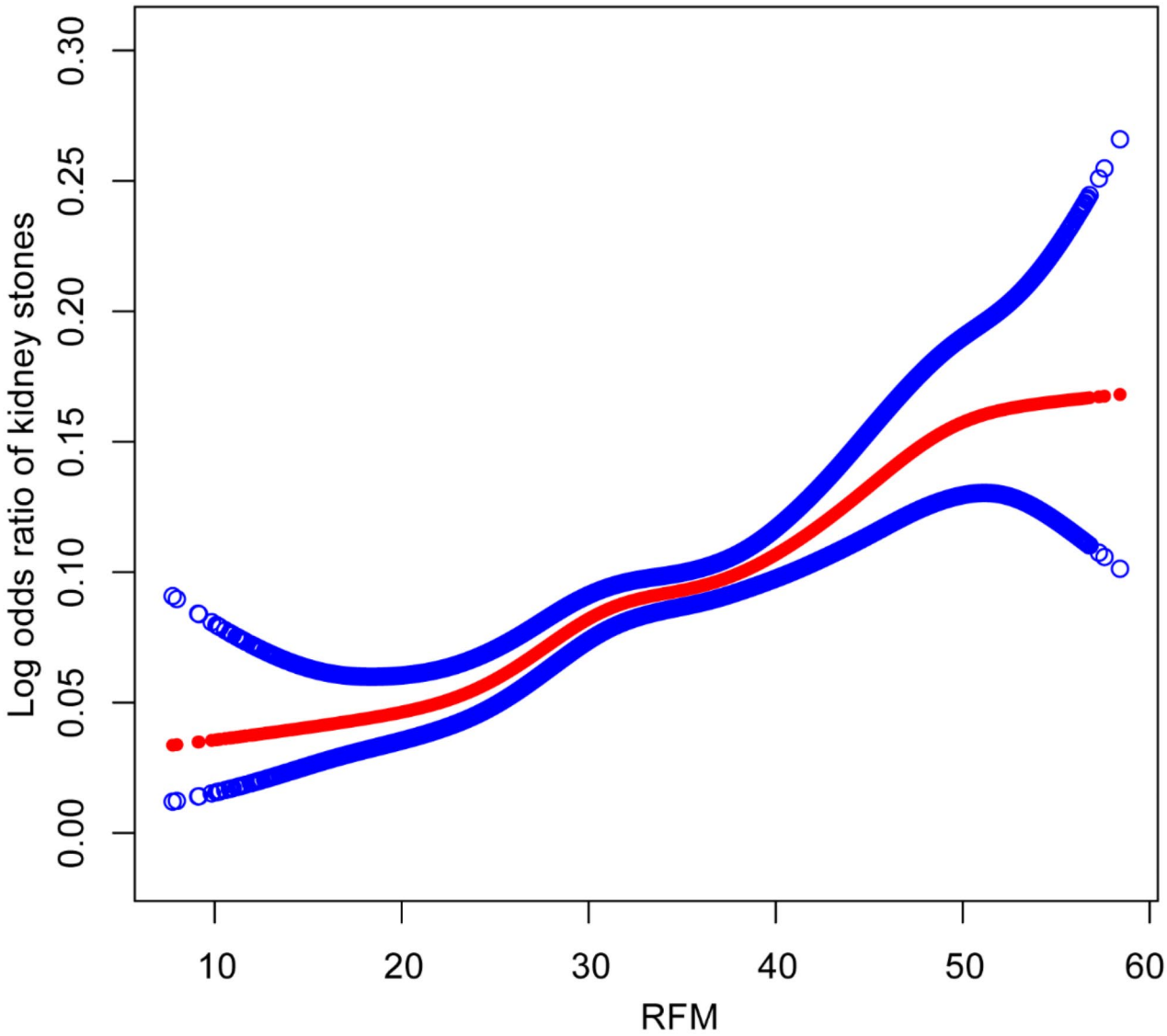

Fig. 2. Nonlinear association between RFM and renal stones. Age, gender, race, education level, Marital status, PIR, BMI, smoking status, alcohol drinking status, diabetes, and hypertension were adjusted.

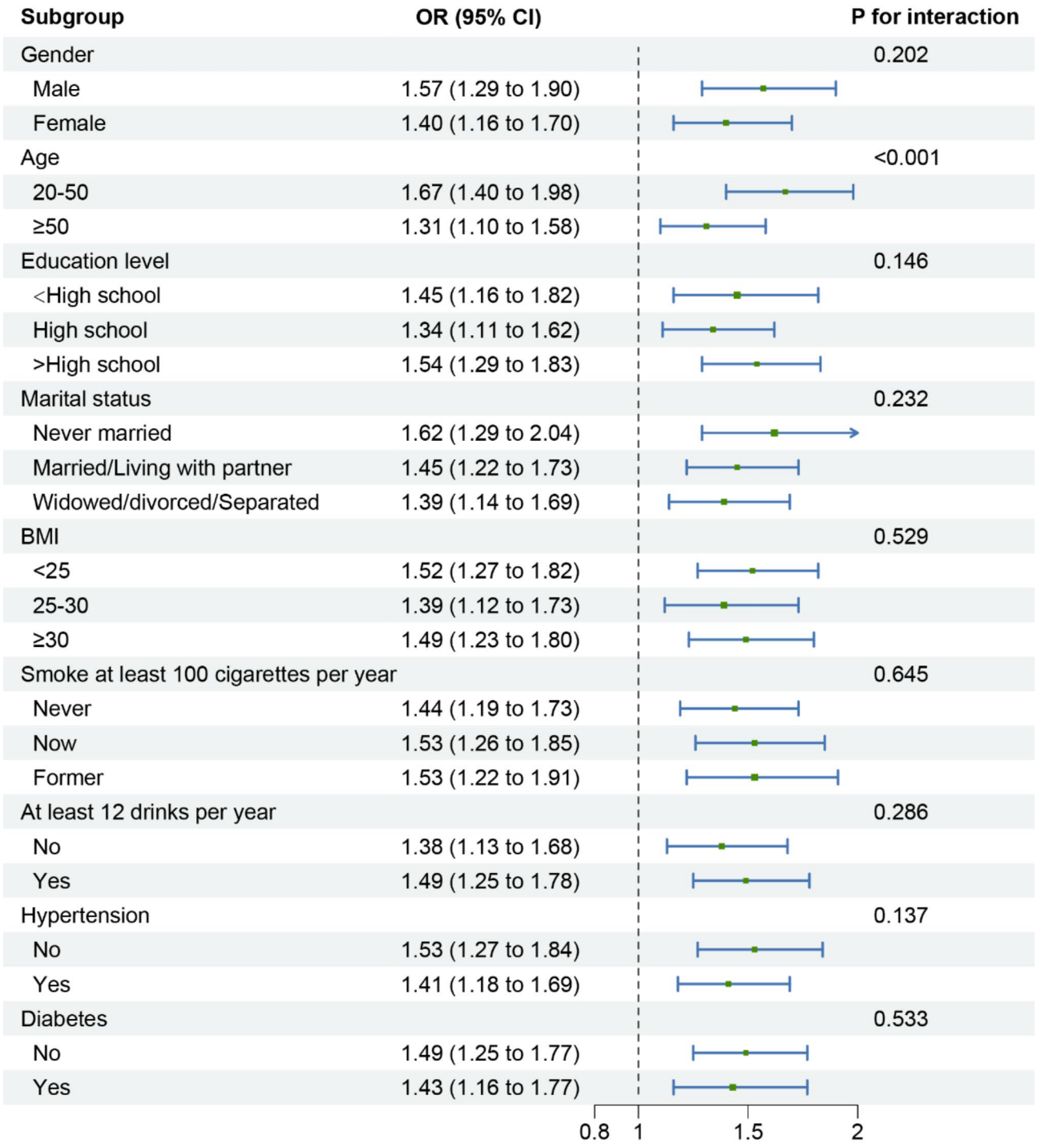

Fig. 3. Subgroup analysis of the association between RFM and the prevalence of kidney stones. Note 1: The above model adjusted for age, gender, race, education level, Marital status, PIR, BMI, smoking status, alcohol drinking status, diabetes, and hypertension. Note 2: In each case, the model is not adjusted for the stratification variable.

and 0.565, respectively. These findings suggest that RFM may offer greater diagnostic efficacy than traditional anthropometric indices (WC and BMI) in predicting the risk of kidney stones. (Fig. 5) (Table 4).

Sensitivity analysis

We categorized RFM into normal and elevated groups for multivariate logistic regression analysis, and the results demonstrated a positive correlation between RFM and kidney stones. In model 3, compared to the normal RFM

Characteristic	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
HDL-C (Continuous)	0.57 (0.51, 0.63)	0.58 (0.52, 0.65)	0.75 (0.67, 0.84)
HDL-C (Quartile)			
Q1	Reference	Reference	Reference
Q2	0.91 (0.82, 1.01)	0.94 (0.85, 1.05)	1.02 (0.92, 1.14)
Q3	0.71 (0.64, 0.79)	0.75 (0.67, 0.84)	0.89 (0.79, 1.00)
Q4	0.57 (0.51, 0.65)	0.60 (0.53, 0.67)	0.78 (0.68, 0.89)
P for trend	< 0.001	< 0.001	< 0.001

Table 3. Association between high-density lipoprotein cholesterol and kidney stones. Model 1: no covariates were adjusted. Model 2: age, gender, and race were adjusted. Model 3: age, gender, race, education level, marital status, PIR, BMI, smoking status, alcohol drinking status, diabetes status, and hypertension status were adjusted.

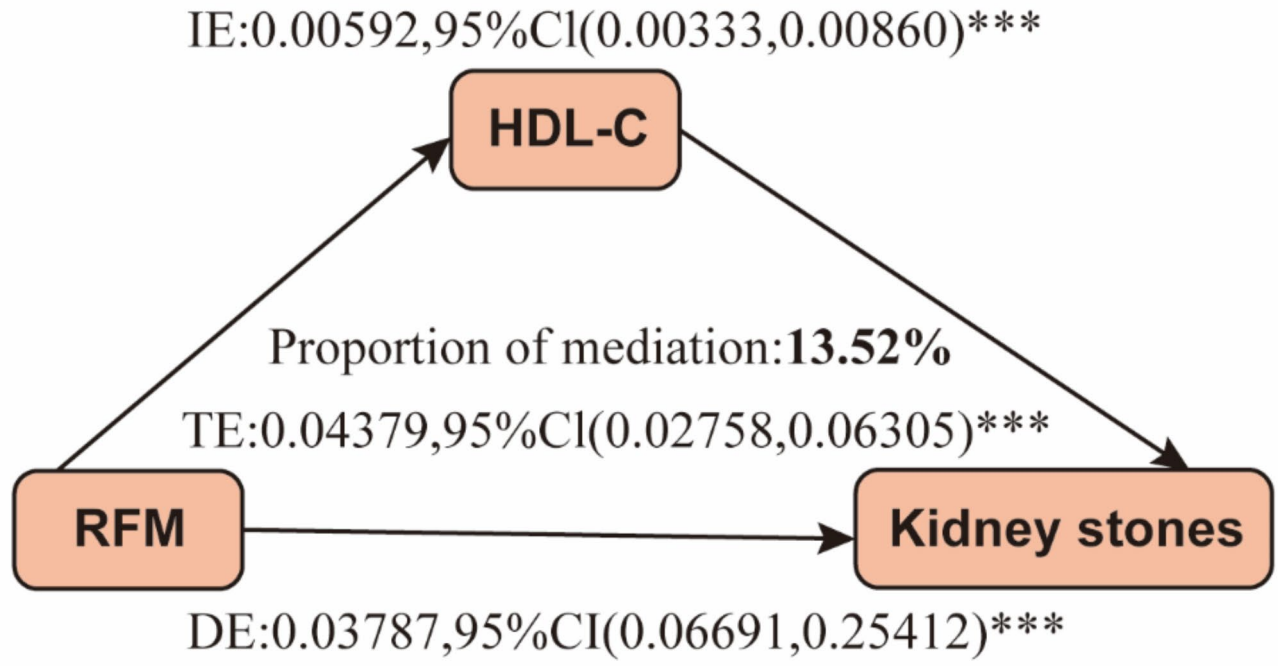

Fig. 4. Mediation analysis of high-density lipoprotein cholesterol between RFM and kidney stones. Age, gender, race, education level, marital status, PIR, BMI, smoking status, alcohol drinking status, diabetes status, and hypertension status were adjusted. *HDL-C* high-density lipoprotein cholesterol, *TE* Total effect, *IE* Indirect effect, *DE* Direct effect. $^{*}p < 0.05$, $^{***}p < 0.001$. $p < 0.05$ suggests significant differences.

group, each unit increase in the elevated RFM group was associated with a 20% increase in the likelihood of kidney stone occurrence (OR = 1.20, 95% CI: 1.04–1.37, $P = 0.0101$). (Table S1)

Discussion

We found that greater RFM levels were linked to a higher risk of kidney stones in this cross-sectional research of 29,712 adults. This correlation was consistent across several subgroups, such as those based on sex, body mass index, drinking and smoking behaviors, and the existence of diabetes or hypertension. Subsequently, we discovered that HDL-C was inversely related to the prevalence of kidney stones. Furthermore, the association between RFM and kidney stones was substantially mediated by HDL-C, suggesting a potential preventive mechanism. Based on these findings, we propose that targeting HDL-C levels may offer a new strategy for preventing kidney stones in obese patients. ROC analysis indicated that compared to traditional anthropometric indices (BMI, WC), RFM had higher diagnostic accuracy for kidney stones. Furthermore, sensitivity analysis confirmed the robustness of our results.

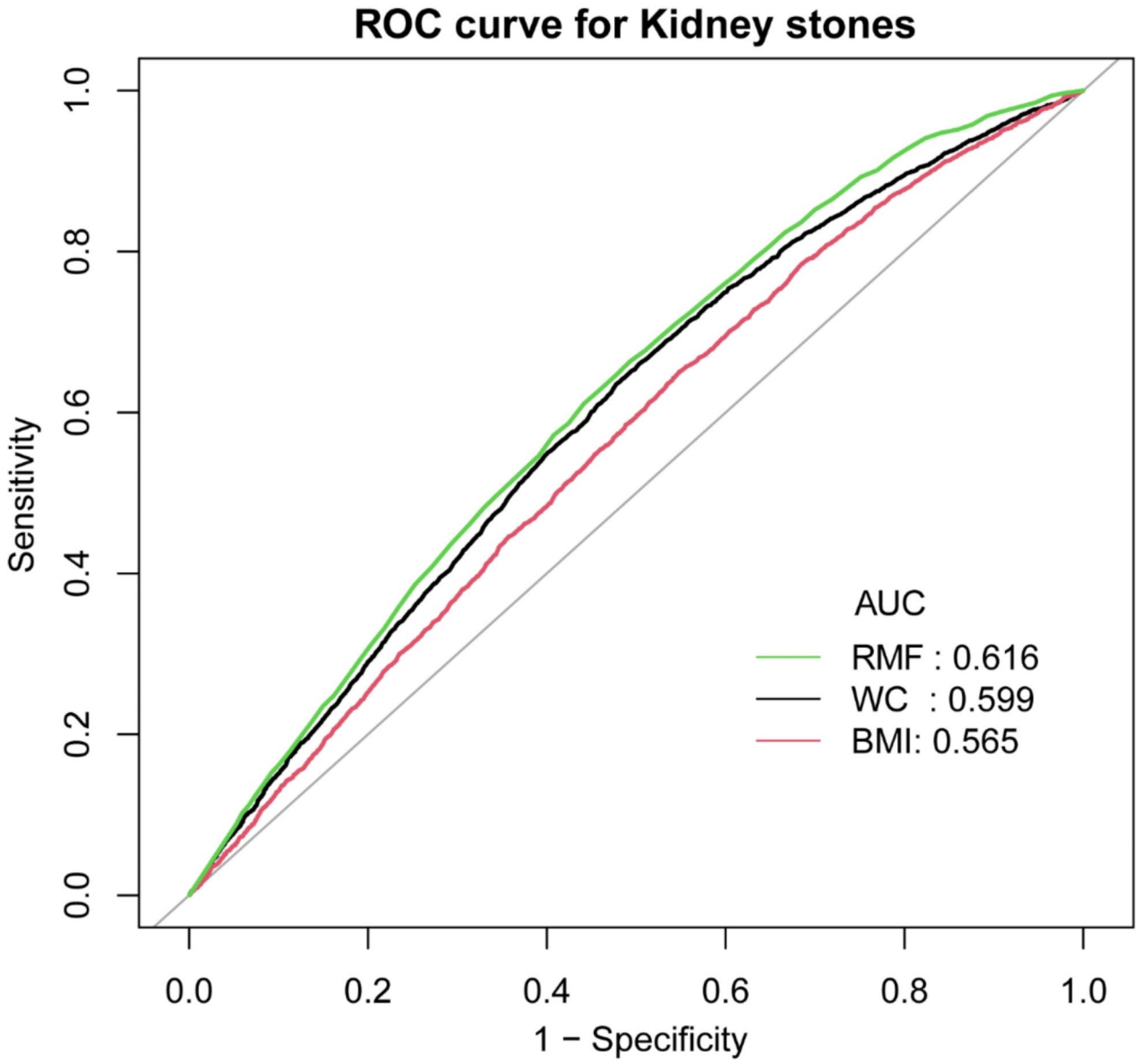

Fig. 5. ROC curves and the AUC values of the anthropometric indicators (RFM, BMI, WC) in diagnosing kidney stones.

Test	AUC[a]	95%CI[b] low	95%CI upp	Best threshold	Specificity	Sensitivity	*P* for different in AUC
WC	0.5992	0.5886	0.6098	98.450	0.5223	0.6353	Reference
BMI	0.5653	0.5546	0.5761	27.245	0.4513	0.6512	< 0.001
RFM	0.6162	0.6059	0.6265	48.500	0.507	0.6635	< 0.001

Table 4. Comparison of AUC values for RFM, WC, and BMI. [a]AUC: area under the curve. [b]95%CI: 95% confidence interval.

This is the first study that, as far as we know, evaluates the connection between RFM levels and kidney stones. Previous studies have examined the association between kidney stones and other indicators of obesity. According to Xudong Hu et al. there is a favorable relationship between kidney stone risk and waist circumference, BRI, BMI, and ABSI. Importantly, ABSI and BRI were found to predict the prevalence of kidney stones with significantly greater discriminatory power than both BMI and waist circumference[20]. Ye Z et al. demonstrated that the combination of overweight or obesity with an unhealthy metabolic profile significantly increased the risk of kidney stone disease (KSD) in the general U.S. population[21]. In addition, Yuan S. et al. proposed a causal

relationship between high body mass index (BMI) and increased risk of KSD, utilizing Mendelian randomization analysis to support their findings[22]. Similarly, Rahman IA et al. demonstrated an association between multiple metabolic disorders—specifically hypertension, diabetes, obesity, and dyslipidemia—and increased odds of developing KSD[23]. Visceral fat obesity and uric acid stones were found to be strongly correlated in a retrospective investigation by Kim et al. Furthermore, it was demonstrated that visceral fat obesity was more predictive of stone-type classification than either urine pH or BMI[24]. Michelle J et al. demonstrated that an obese BMI is associated with an increased risk of KSD. However, once BMI exceeds 30 kg/m^2, additional increases do not significantly escalate the risk of developing stone disease[25]. Interestingly, Ming-Ru Lee et al. found that BMI, abdominal volume index (AVI), waist circumference (WC), waist-to-hip ratio (WHR), waist-to-height ratio (WHTR), and body roundness index (BRI) were all associated with a higher prevalence and occurrence of kidney stones, mirroring the results observed in our study[26]. Additionally, compared to women, men younger than 50 years of age were more likely to develop kidney stones, a finding that aligns with our observations.

There are several possible mechanisms to explain the impact of obesity on kidney stone incidence. First, overweight individuals exhibit higher urinary excretion rates of calcium, oxalate, and uric acid, creating a state of urinary supersaturation that predisposes to stone accumulation in the kidneys[27]. In addition, overweight individuals often consume diets rich in protein, fat, and sodium, which can alter kidney metabolism and pH, subsequently increasing the likelihood of stone formation[28]. Several factors and mechanisms are involved in reducing HDL-C levels in obesity and recent studies have demonstrated that obesity profoundly alters HDL metabolism, leading to changes in HDL subclass distribution, composition, and function[15,29,30]. More specifically, intra-abdominal visceral fat deposition is a significant negative correlate of HDL-cholesterol. The specific subfractions of HDL that are altered in obese states include HDL2, apolipoprotein A-I, and pre-β1 subfractions. Decreased HDL levels in obesity are attributed to both an enhanced uptake of HDL2 by adipocytes and an increased catabolism of apolipoprotein A-I on HDL particles[29,30].

Strengths and limitations

There are various advantages to this study. The NHAHES database serves as the basis for this cross-sectional investigation and utilizes a complex, multistage probability sampling design that ensures a sample representative of the U.S. population in terms of gender, age, and race, allowing generalization to the entire U.S. population. We have also adjusted for confounders to ensure the reliability of our results. Additionally, we conducted subgroup and mediation analyses to gain deeper insights into the association between RFM and kidney stones.

In addition, this study has some limitations. First, the cross-sectional nature of our study precludes investigation of the causal relationship between RFM and kidney stone prevalence. Despite accounting for multiple covariates, we cannot exclude the effects of all potential confounders. Third, the diagnosis of kidney stones was based solely on self-reported data from the NHANES questionnaire. Although self-reported kidney stone diagnoses have been validated in large epidemiological studies, the possibility of recall bias persists. This reliance on self-reporting may lead to underreporting or misreporting of kidney stone prevalence, potentially affecting the accuracy of the study results. Additionally, the NHANES dataset lacks information on the composition of kidney stones, which is a key factor in understanding the mechanisms of stone formation. Different types of stones, such as calcium oxalate, uric acid, and struvite, have distinct metabolic causes and are influenced by different risk factors. Due to the absence of stone composition data, we were unable to investigate whether lipid metabolism (especially HDL cholesterol levels) is differentially associated with specific stone types. Furthermore, the dataset does not provide information on the number of kidney stone episodes or recurrences. Despite these limitations, this study provides new insights into the association between RFM and the prevalence of kidney stones, particularly highlighting the regulatory role of HDL-C. Future studies that include clinical validation of kidney stone diagnoses, stone composition data, and recurrence information will help to more comprehensively understand the metabolic factors contributing to kidney stone formation.

Conclusion

There is a significant non-linear positive correlation between RFM and kidney stones. Specifically, compared with traditional body measurements (BMI, WC), RFM exhibits higher accuracy in diagnosing kidney stones. HDL-C plays a crucial mediating role in the relationship between RFM and kidney stones.

Data availability

The survey data are publicly available on the internet for data users and researchers throughout the world (www.cdc.gov/nchs/nhanes/).

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Author contributions

HL and YZ designed the research. MJ, HH and YY collected, analyzed the data and drafted the manuscript. HJ revised the manuscript. All authors contributed to the article and approved the submitted version.

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Declarations

Competing interests

The authors declare no competing interests.

Ethical statement

The portions of this study involving human participants, human materials, or human data were conducted in accordance with the Declaration of Helsinki and were approved by the NCHS Ethics Review Board. The patients/participants provided their written informed consent to participate in this study.

Additional information

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