MSM

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2026; 32: e952525
DOI: 10.12659/MSM.952525

Received: 2025.12.22
Accepted: 2026.05.25
Available online: 2026.07.02
Published: 2026.XX.XX

Association of Estimated Glucose Disposal Rate With Prevalent Kidney Stones: A Large-Scale Cross-Sectional Study in China

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Data Interpretation D
Manuscript Preparation E
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Financial support: This study was funded by the National Natural Science Foundation of China (Grant No. 82002675) and the Yangzhou Science and Technology Program–Social Development Project (Grant No. YZ2024120)

Conflict of interest: None declared

Background: Insulin resistance is associated with kidney stone risk, and estimated glucose disposal rate (eGDR) is a validated surrogate marker of insulin resistance. This study examined the association between eGDR and kidney stone prevalence.

Material/Methods: Data were derived from a cross-sectional dataset collected at the Health Management Center, Affiliated Hospital of Yangzhou University (HMC-AHYU). Participants were stratified into 4 groups according to eGDR quartile. Logistic regression models were used to estimate the association between eGDR and kidney stone prevalence. Nonlinear relationships were explored via restricted cubic splines and threshold-effect analyses. Subgroup analyses were conducted to examine potential effect modification, and receiver operating characteristic curves were used to compare discriminative performances among metrics.

Results: Overall, 23 527 individuals from HMC-AHYU were included. When stratified by quartile, lower eGDR values were associated with increased odds of kidney stones. After multivariable adjustment, each 1-unit increase in eGDR was associated with a 16% reduction in the odds of kidney stones (odds ratio [OR] = 0.84, 95% confidence interval [CI]: 0.81-0.87). Compared with the lowest quartile (Q1), the highest quartile (Q4) exhibited 48% lower odds (OR = 0.52, 95% CI: 0.41-0.65), with a significant dose-response relationship observed across quartiles. Threshold-effect analyses identified eGDR inflection points at 9.02 and 10.87. eGDR demonstrated the strongest discriminative ability for kidney stones (area under the curve = 0.692, 95% CI: 0.679-0.705). Validation using 1000 bootstrap resamples confirmed model stability.

Conclusions: Lower eGDR levels were associated with increased kidney stone prevalence. eGDR may serve as a biomarker for high kidney stone risk.

Keywords: **Glucose • Insulin Resistance • Kidney Calculi**

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/952525

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Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Introduction

Kidney stone disease represents a growing global public health burden, with both prevalence and economic costs continuing to rise [1,2]. These upward trends are largely driven by evolving dietary patterns and lifestyle behaviors in modern societies. Increasing rates of adiposity, coupled with inadequate hydration, declining intake of plant-based foods, and rising consumption of sugar-sweetened beverages, collectively contribute to the growing disease burden [3,4]. Recurrence rates can reach 50% within 5 years [5]. Prompt identification of individuals with a high metabolic predisposition to kidney stones is critical for preventive intervention.

Insulin resistance (IR) is a metabolic disorder in which peripheral tissues, including skeletal muscle, adipose tissue, and the liver, exhibit reduced responsiveness to insulin, thus impairing glucose uptake and utilization [6]. A growing body of observational and mechanistic evidence indicates that impaired insulin signaling is a key contributing factor in kidney stone formation [7]. Although the hyperinsulinemic-euglycemic clamp remains the reference standard for assessing IR, its requirement for intravenous infusions, repeated blood sampling, and substantial expense limits its applicability in routine clinical practice and large-scale population studies [8]. Consequently, several surrogate indices have been developed to estimate IR, including the metabolic score for insulin resistance (METS-IR) [9], triglyceride-glucose (TyG) index [10], and estimated glucose disposal rate (eGDR) [11]. Among these, eGDR is readily calculated; it has demonstrated reliable associations with acute ischemic stroke outcomes [12] and cardiovascular disease risk [13,14]. Unlike indices based solely on biochemical markers, eGDR uniquely incorporates hypertension and waist circumference—2 factors that directly influence the urinary environment, including calcium excretion and urinary pH [15,16]. To date, the potential association between eGDR and kidney stone prevalence remains unexplored, and no empirical studies have addressed this gap in the literature.

This study used cross-sectional data from the Health Management Center, Affiliated Hospital of Yangzhou University (HMC-AHYU). The objective was to evaluate the association between eGDR and kidney stone prevalence, then provide a metabolically oriented framework for risk stratification in general health screening populations.

Material and Methods

Ethics Approval and Consent to Participate

This study was approved by the HMC-AHYU Ethics Committee (Approval No. 2025-YKL06-K05) and conducted in accordance with the Declaration of Helsinki and local regulations. Given the retrospective study design, the requirement for written informed consent was waived.

Study Population and Design

This study was based on data from adults who underwent comprehensive health checkups at HMC-AHYU between 2023 and 2024. The following data were collected by certified staff after a 12-hour fast: demographic characteristics, medical history, standard clinical laboratory measurements, and ultrasound findings (interpreted by intermediate-level sonologists).

After data review, only participants with sufficient information for the planned analyses were retained. Exclusion criteria for the HMC-AHYU cohort were as follows: (1) age less than 18 years (n = 7731); (2) absence of kidney stone ultrasound examination (n = 27 428); and (3) missing data regarding glycated hemoglobin A1c (HbA1c), waist circumference (WC), or hypertension status (n = 186 909). Given the large number of participants excluded under criterion 3, baseline characteristics were compared between the excluded and included populations to assess potential selection bias. Kidney stone prevalence was highly consistent between groups (**Table 1**). An additional 373 participants with incomplete data for secondary covariates were excluded from the primary analysis. These covariates comprised triglycerides (TG), fasting glucose, creatinine, uric acid, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), systolic blood pressure (SBP), diastolic blood pressure (DBP), height, body mass index (BMI), waist-to-height ratio (WHtR), and diabetes status. The final analytical cohort comprised 23 527 participants from HMC-AHYU (**Figure 1**). For sensitivity analyses, the 373 individuals with missing secondary covariate data were retained, yielding a total eligible cohort of 23 900 participants.

IR Indices

eGDR was calculated as follows: eGDR = 21.158 - (0.09 × WC [cm]) - (3.407 × hypertension [yes = 1, no = 0]) - (0.551 × HbA1c [%]) [12].

Additional IR indices were calculated using established formulas. The TyG index was calculated as ln (TG [mg/dL] × fasting glucose [mg/dL]/2) [17]. The triglyceride-glucose-body mass index (TyG-BMI) was calculated as TyG × BMI (kg/m^2) [18]. The triglyceride-glucose-waist circumference (TyG-WC) index was calculated as TyG × WC (cm) [18]. The triglyceride-glucose-waist-to-height ratio (TyG-WHtR) was calculated as TyG × WC (cm)/height (cm) [18]. The TG/HDL-C ratio was calculated as TG (mg/dL)/HDL-C (mg/dL) [19]. The METS-IR was calculated as ln (2 × fasting glucose [mg/dL] + TG [mg/dL]) × BMI (kg/m^2)/ln (HDL-C [mg/dL]) [20].

Table 1. Comparison of baseline characteristics between included and excluded cohorts.

Variables	Included cohort (n = 23 527)	Excluded cohort (n = 186 909)	SMD
Age (years)	52.45 ± 14.69	46.89 ± 14.74	0.378
Male, n (%)	17 239 (73.27%)	101 775 (54.45%)	0.400
Height, cm	170.06 ± 7.89	168.22 ± 9.71	0.208
Weight, kg	71.56 ± 12.15	69.07 ± 13.76	0.191
BMI, kg/m^2	24.64 ± 3.13	24.270± 3.84	0.104
SBP, mm Hg	128.49 ± 18.36	125.14 ± 18.90	0.180
DBP, mm Hg	79.87 ± 11.35	78.04 ± 11.86	0.158
Total cholesterol (mg/dL)	193.41 ± 38.07	190.47 ± 37.21	0.078
Creatinine (mg/dL)	0.88 ± 0.24	0.82 ± 0.24	0.268
Uric acid (mg/dL)	6.05 ± 1.46	5.14 ± 1.37	0.660
HDL-C (mg/dL)	49.24 ± 11.79	50.93 ± 12.50	0.139
LDL-C (mg/dL)	108.25 ± 29.39	106.11 ± 28.94	0.073
Fasting glucose (mg/dL)	102.50 ± 23.26	100.64 ± 24.91	0.077
TG (mg/dL)	167.38± 151.03	154.16± 148.26	0.088
Smoking status, n (%)	4326 (18.39%)	21 782 (11.65%)	0.189
Alcohol consumption, n (%)	5327 (22.64%)	21 678 (11.60%)	0.296
Prevalence of kidney stones, n (%)	1645 (6.99%)	10 892 (5.83%)	0.048

Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as frequency (percentage). Given the large sample size in this study, *P*-values may indicate statistical significance even when differences are clinically negligible. Therefore, SMDs were used to assess the magnitude of baseline imbalances between cohorts. An SMD < 0.10 was considered indicative of a negligible difference. Variables used to calculate eGDR, including WC, HbA1c, and hypertension status, were unavailable for the excluded cohort because missing data for these variables constituted part of the exclusion criteria. Consequently, these parameters could not be compared between cohorts and are not presented in this table. Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; eGDR, estimated glucose disposal rate; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; SMD, standardized mean difference; TG, triglycerides; WC, waist circumference.

Kidney Stones

In this study, kidney stones were diagnosed by ultrasonography using a 3.5-5 MHz convex abdominal probe (LOGIQ E9, GE, USA). To ensure objectivity, all examinations and image interpretations were performed by experienced sonographers (> 5 years of practice) who had been blinded to participants' laboratory data and clinical histories. Ultrasound findings were integrated with clinical information and subsequently reviewed by a second senior sonographer for quality control. Kidney stones were defined as echogenic foci measuring ≥ 2 mm with posterior acoustic shadowing located in the renal parenchyma or collecting system. The present study included all detected cases of kidney stones; isolated ureteral stones were excluded to maintain specific focus on renal metabolic associations. Due to the retrospective nature of the health checkup records, detailed information regarding stone composition and size distributions beyond the 2-mm threshold was unavailable.

Covariate Definitions

Covariates collected at HMC-AHYU were age, sex, smoking status, alcohol consumption, hypertension, and diabetes. Hypertension was defined as an SBP of at least 140 mm Hg, a DBP of at least 90 mm Hg, a self-reported physician diagnosis, or current use of antihypertensive medications. Diabetes mellitus was defined as a self-reported history of diabetes, current use of oral hypoglycemic agents or insulin, or laboratory criteria (eg, fasting glucose ≥ 7.0 mmol/L or HbA1c ≥ 6.5%).

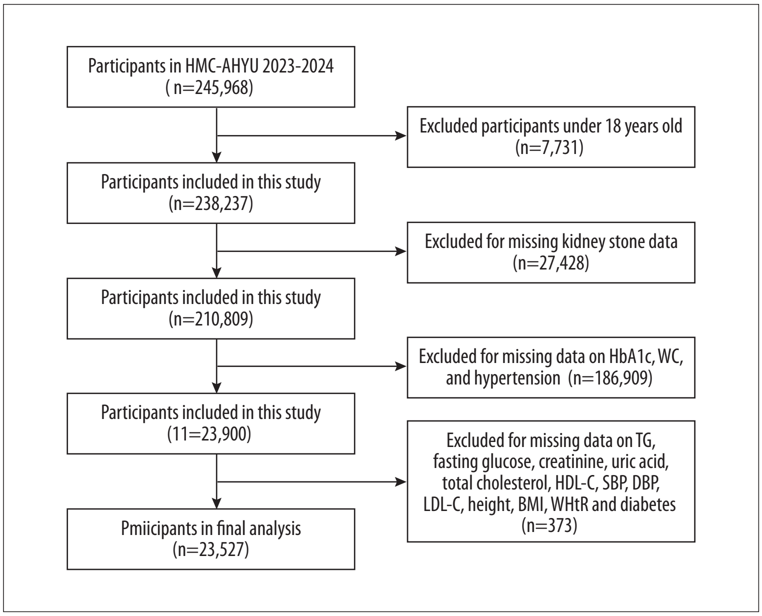

Figure 1. Flow diagram of participant selection. Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; eGDR, estimated glucose disposal rate; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HMC-AHYU, Health Management Center, Affiliated Hospital of Yangzhou University cohort; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TG, triglycerides; WC, waist circumference; WHtR, waist-to-height ratio.

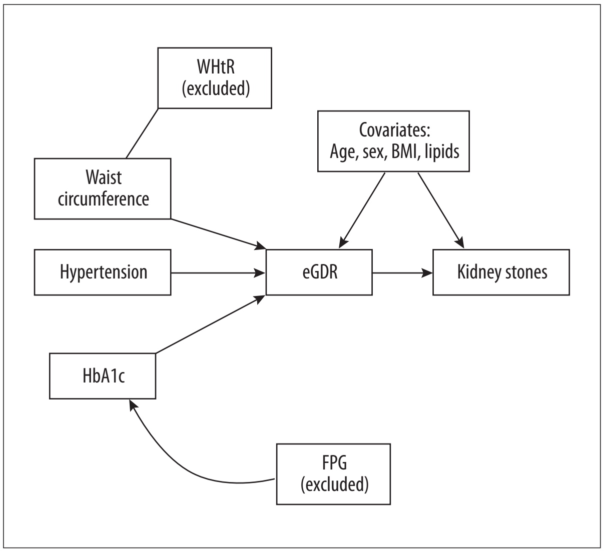

Figure 2. DAG for covariate selection. The DAG illustrates the theoretical causal framework used to identify potential confounding pathways between eGDR and kidney stone prevalence. eGDR was considered the primary exposure, and kidney stone prevalence was the outcome. To prevent overadjustment and multicollinearity, variables included in the eGDR calculation (WC, hypertension, and HbA1c) and their direct proxies (WHtR and FPG) were considered redundant and intentionally excluded from multivariable models. Age, sex, BMI, and lipid profiles were identified as independent confounders requiring adjustment. Abbreviations: BMI, body mass index; DAG, directed acyclic graph; eGDR, estimated glucose disposal rate; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin A1c; WC, waist circumference; WHtR, waist-to-height ratio.

Statistical Analysis

Continuous variables were summarized as mean ± standard deviation or median (interquartile range), depending on their distribution. Comparisons among groups were performed using 1-way analysis of variance for normally distributed variables and the Kruskal-Wallis test for non-normally distributed variables. Categorical variables are presented as frequencies and percentages; they were compared using the χ^2 test. Linear trends across eGDR quartiles were assessed by assigning the median value of each quartile as an ordinal variable. To evaluate potential selection bias resulting from large-scale exclusions, baseline characteristics were compared between included and excluded cohorts.

Logistic regression models were used to assess the association between eGDR and kidney stones, with results reported as odds ratios (ORs) and 95% confidence intervals (CIs). Covariate selection for multivariable adjustment was guided by a directed acyclic graph (DAG) to identify potential confounding pathways and minimize overadjustment (**Figure 2**). Variables included in the eGDR calculation (WC, hypertension, and HbA1c) were intentionally excluded from multivariable models to avoid overadjustment and multicollinearity. In the HMC-AHYU cohort, Model 1 was unadjusted. Model 2 adjusted for age, sex, fasting glucose, smoking status, alcohol consumption, and diabetes. Model 3 additionally adjusted for creatinine, uric acid, total cholesterol, HDL-C, LDL-C, TG, and BMI. The dose-response relationship between eGDR and kidney stones was evaluated using a generalized additive model with smoothing splines. Threshold-effect analyses were subsequently performed to identify inflection points at which the risk trajectory changed. Subgroup analyses were conducted

Table 2. Characteristics of participants in the Health Management Center, Affiliated Hospital of Yangzhou University cohort.

eGDR	Total	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P-value
Kidney stones						< 0.001
No	21 882 (93.01%)	4994 (84.92%)	5551 (94.37%)	5622 (95.60%)	5715 (97.14%)	
Yes	1645 (6.99%)	887 (15.08%)	331 (5.63%)	259 (4.40%)	168 (2.86%)	
Sex						< 0.001
Male	17 239 (73.27%)	4926 (83.76%)	5127 (87.16%)	4556 (77.47%)	2630 (44.71%)	
Female	6288 (26.73%)	955 (16.24%)	755 (12.84%)	1325 (22.53%)	3253 (55.29%)	
Age (years)	52.45 ± 14.69	61.09 ± 12.58	51.76 ± 14.80	49.93 ± 13.71	47.03 ± 13.66	< 0.001
Smoking status, n (%)						< 0.001
No	19 201 (81.61%)	4230 (71.93%)	4613 (78.43%)	4932 (83.86%)	5426 (92.23%)	
Yes	4326 (18.39%)	1651 (28.07%)	1269 (21.57%)	949 (16.14%)	457 (7.77%)	
Alcohol consumption, n (%)						< 0.001
No	18 200 (77.36%)	3886 (66.08%)	4374 (74.36%)	4667 (79.36%)	5273 (89.63%)	
Yes	5327 (22.64%)	1995 (33.92%)	1508 (25.64%)	1214 (20.64%)	610 (10.37%)	
Hypertension						< 0.001
No	17 449 (74.17%)	276 (4.69%)	5409 (91.96%)	5881 (100.00%)	5883 (100.00%)	
Yes	6078 (25.83%)	5605 (95.31%)	473 (8.04%)	0 (0.00%)	0 (0.00%)	
Diabetes						< 0.001
No	21 202 (90.12%)	4466 (75.94%)	5267 (89.54%)	5666 (96.34%)	5803 (98.64%)	
Yes	2325 (9.88%)	1415 (24.06%)	615 (10.46%)	215 (3.66%)	80 (1.36%)	
SBP (mm Hg)	128.49 ± 18.36	139.36 ± 17.86	130.89 ± 16.98	124.96 ± 15.97	118.75 ± 15.94	< 0.001
DBP (mm Hg)	79.87 ± 11.35	84.67 ± 11.15	82.02 ± 10.83	78.59 ± 10.35	74.20 ± 10.23	< 0.001
Height (cm)	170.06 ± 7.89	169.84 ± 7.40	172.49 ± 7.70	170.82 ± 7.75	167.08 ± 7.69	< 0.001
BMI (kg/m^2)	24.64 ± 3.13	25.60 ± 2.93	26.56 ± 3.28	24.40 ± 2.05	21.98 ± 1.97	< 0.001
WC (cm)	85.49 ± 8.49	88.85 ± 7.42	92.07 ± 8.26	84.77 ± 3.35	76.28 ± 3.69	< 0.001
WHtR	0.50 ± 0.05	0.52 ± 0.04	0.53 ± 0.04	0.50 ± 0.03	0.46 ± 0.03	< 0.001
Total cholesterol (mg/dL)	193.41 ± 38.07	191.12 ± 40.60	196.24 ± 38.03	194.74 ± 36.35	191.51 ± 36.91	< 0.001
Creatinine (μmol/L)	78.14 ± 21.60	82.66 ± 27.15	80.44 ± 21.10	78.73 ± 18.64	70.74 ± 16.00	< 0.001
Uric acid (μmol/L)	359.80 ± 86.61	378.98 ± 86.37	383.43 ± 86.35	363.64 ± 79.78	313.17 ± 74.91	< 0.001
HDL-C (mg/dL)	49.24 ± 11.79	47.33 ± 10.90	45.66 ± 10.29	48.45 ± 10.84	55.52 ± 12.55	< 0.001
LDL-C (mg/dL)	108.25 ± 29.39	104.87 ± 31.23	110.77 ± 29.55	110.96 ± 28.01	106.42 ± 28.19	< 0.001
Fasting glucose (mg/dL)	102.50 ± 23.26	111.36 ± 30.02	108.66 ± 27.48	97.29 ± 13.40	92.69 ± 9.42	< 0.001
TG (mg/dL)	167.38± 151.03	193.78 ±166.49	198.50 ±176.90	162.43 ±140.94	114.81 ± 88.99	< 0.001

Table 2 continued. Characteristics of participants in the Health Management Center, Affiliated Hospital of Yangzhou University cohort.

eGDR	Total	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P-value
HbA1c (%)	5.79 ± 0.79	6.10 ± 1.02	6.02 ± 0.93	5.60 ± 0.42	5.42 ± 0.32	< 0.001
TyG	8.83 ± 0.66	9.07 ± 0.64	9.06 ± 0.65	8.79 ± 0.58	8.42 ± 0.53	< 0.001
TyG-BMI	218.31 ± 36.57	232.58 ± 33.98	240.79 ± 36.13	214.52 ± 24.17	185.35 ± 22.04	< 0.001
TyG-WC	757.16 ±108.53	806.58 ± 95.51	834.45 ±100.00	744.80 ± 57.48	642.83 ± 55.21	< 0.001
TyG-WHTR	4.45 ± 0.61	4.75 ± 0.54	4.84 ± 0.55	4.37 ± 0.37	3.85 ± 0.36	< 0.001
TG/HDL-C	3.92 ± 4.79	4.61 ± 5.27	4.91 ± 5.71	3.79 ± 4.50	2.35 ± 2.66	< 0.001
METS-IR	37.69 ± 7.12	40.18 ± 6.64	42.03 ± 7.16	37.11 ± 4.92	31.45 ± 4.38	< 0.001
eGDR	9.40 ± 1.86	6.55 ± 0.63	9.28 ± 0.62	10.44 ± 0.23	11.31 ± 0.31	< 0.001

Continuous variables are presented as mean ± standard deviation. *P*-values for continuous variables were calculated using the Kruskal-Wallis rank-sum test. Categorical variables are presented as percentages (%), and *P*-values were calculated using the chi-square test. Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; eGDR, estimated glucose disposal rate; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; METS-IR, metabolic score for insulin resistance; SBP, systolic blood pressure; TG, triglycerides; TyG, triglyceride-glucose index; TyG-BMI, triglyceride-glucose-body mass index; TyG-WC, triglyceride-glucose-waist circumference; TyG-WHtR, triglyceride-glucose-waist-to-height ratio; WC, waist circumference; WHtR, waist-to-height ratio.

Table 3. Association between eGDR and kidney stones in the Health Management Center, Affiliated Hospital of Yangzhou University cohort.

	Model 1	*P*-value	Model 2	*P*-value	Model 3	*P*-value
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
eGDR (continuous)	0.70 (0.68-0.72)	< 0.001	0.82 (0.79-0.85)	< 0.001	0.84 (0.81-0.87)	< 0.001
eGDR (quartiles)						
Quartile 1	1.0 (Reference)		1.0 (Reference)		1.0 (Reference)	
Quartile 2	0.34 (0.29-0.38)	< 0.001	0.46 (0.39-0.53)	< 0.001	0.47 (0.41-0.55)	< 0.001
Quartile 3	0.26 (0.23-0.30)	< 0.001	0.49 (0.41-0.58)	< 0.001	0.56 (0.47-0.66)	< 0.001
Quartile 4	0.17 (0.14-0.20)	< 0.001	0.39 (0.32-0.48)	< 0.001	0.52 (0.41-0.65)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	

Model 1: Unadjusted. Model 2: Adjusted for age, sex, smoking status, alcohol consumption, and diabetes. Model 3: Adjusted for age, sex, creatinine, uric acid, total cholesterol, HDL-C, LDL-C, TG, BMI, smoking status, alcohol consumption, and diabetes. Abbreviations: BMI, body mass index; CI, confidence interval; eGDR, estimated glucose disposal rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; TG, triglycerides.

according to sex, age, BMI, and diabetes status; interaction terms were included to assess effect modification. To evaluate the robustness of the primary findings in the presence of missing data, sensitivity analysis was performed using multiple imputation by chained equations (MICE) with 5 imputed datasets. Results from the imputed datasets were compared with those from the complete-case analysis to assess the stability of observed associations. The discriminative performance of the 7 IR metrics was evaluated using receiver operating characteristic (ROC) curves. Differences in area under the curve (AUC) values were compared using the DeLong test. For each ROC curve, the optimal cutoff value was determined by maximizing

Table 4. Threshold effect analysis of the association between eGDR and kidney stone prevalence.

eGDR	ULR		PLR		LRT
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	*P*-value
< 9.02	0.78 (0.74-0.82)	< 0.001	0.59 (0.52-0.66)	< 0.001	< 0.001
≥ 9.02			1.07 (0.94-1.22)	0.319	
< 10.87	0.78 (0.65-0.93)	0.007	0.66 (0.53-0.82)	< 0.001	0.006
≥ 10.87			0.71 (0.44-1.14)	0.156	

All models were adjusted for covariates included in Model 3. Abbreviations: CI, confidence interval; eGDR, estimated glucose disposal rate; LRT, log-likelihood ratio test; OR, odds ratio; PLR, piecewise linear regression; ULR, unsegmented linear regression.

the sum of sensitivity and specificity; corresponding sensitivity and specificity values were reported. Additionally, internal validation was performed using 1000 bootstrap resamples to assess the robustness and stability of the predictive model. All statistical analyses were performed using EmpowerStats (X&Y Solutions, CA, USA) and R version 4.4.2. Statistical significance was defined as a 2-sided *P*-value < 0.05.

Results

Baseline Characteristics

Baseline characteristics were compared across eGDR quartiles among 23 527 participants from HMC-AHYU (mean age, 52.45 ± 14.69 years). As shown in **Table 2**, participants in the highest eGDR quartile were more likely to be women and tended to be older than those in lower quartiles. Across progressively higher eGDR quartiles, the prevalences of smoking, alcohol consumption, hypertension, and diabetes significantly decreased. Similarly, fasting glucose, creatinine, HbA1c, and TyG levels declined across quartiles (all $P < 0.001$).

Association Between eGDR and Kidney Stones

The results of multivariable logistic regression analyses are presented in **Table 3**. When eGDR was analyzed as a continuous variable, each 1-unit increase was associated with a significantly lower likelihood of kidney stones; this inverse association remained robust across all models ($P < 0.001$). After full adjustment for covariates, each 1-unit increase in eGDR was associated with a significant reduction in kidney stone risk (OR = 0.84, 95% CI: 0.81-0.87, $P < 0.001$). When participants were categorized into eGDR quartiles, those in the highest quartile (Q4) had a 48% lower risk of kidney stones than those in the lowest quartile (Q1) (OR = 0.52, 95% CI: 0.41-0.65, $P < 0.001$). Trend analyses demonstrated a progressive decrease in kidney stone risk with increasing eGDR quartile (P for trend < 0.001).

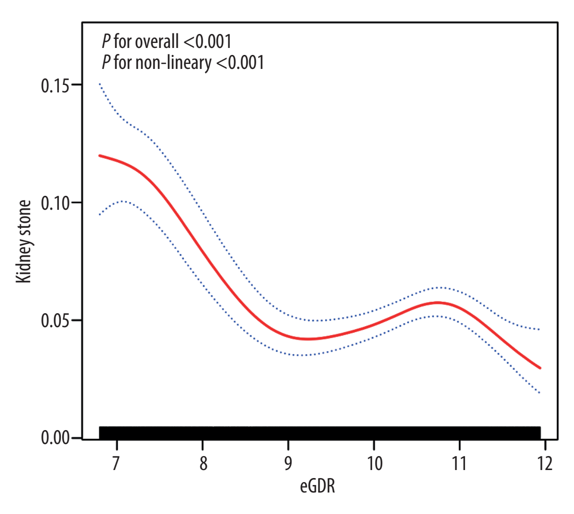

Figure 3. Smooth curve fitting of the association between eGDR and kidney stone risk. Solid red line represents the estimated prevalence of kidney stones, and blue dashed lines represent 95% confidence intervals. A significant inverse association was observed between eGDR and kidney stone risk. Abbreviation: eGDR, estimated glucose disposal rate.

Threshold Effect of eGDR on Kidney Stone Risk

Segmented regression analyses revealed nonlinear associations between eGDR and kidney stone risk (**Table 4, Figure 3**). Two significant inflection points were identified at eGDR values of 9.02 ($P_{LRT} < 0.001$) and 10.87 ($P_{LRT} = 0.006$). Using 9.02 as the cutoff, a protective effect was observed below the inflection point (OR = 0.59, 95% CI: 0.52-0.66, $P < 0.001$); no significant association was detected at eGDR of at least 9.02 (OR = 1.07, 95% CI: 0.94-1.22, $P = 0.319$). Using 10.87 as the cutoff, a protective effect was noted below the inflection point (OR = 0.66, 95% CI: 0.53-0.82, $P < 0.001$); no significant association was evident at eGDR of at least 10.87 (OR = 0.71, 95%

Table 5. Subgroup analysis of the association between eGDR and kidney stones.

eGDR	OR (95% CI)	*P*-value	*P* for Interaction
Sex			0.915
Male	0.84 (0.81-0.88)	<0.001	
Female	0.85 (0.78-0.91)	<0.001	
Age (years)			0.108
<40	0.79 (0.72-0.86)	<0.001	
40-60	0.87 (0.83-0.90)	<0.001	
≥60	0.87 (0.82-0.93)	<0.001	
BMI (kg/m^2)			0.518
<25	0.83 (0.79-0.87)	<0.001	
25-30	0.86 (0.81-0.90)	<0.001	
≥30	0.86 (0.74-1.00)	0.048	
Diabetes			<0.001
No	0.91 (0.87-0.95)	<0.001	
Yes	0.67 (0.62-0.72)	<0.001	

Models were adjusted for the covariates included in Model 3, excluding the corresponding stratification variable.
Abbreviations: BMI, body mass index; CI, confidence interval; eGDR, estimated glucose disposal rate; OR, odds ratio.

CI: 0.44-1.14, $P=0.156$). These inflection points were identified using 2-piecewise linear regression models and confirmed by log-likelihood ratio tests.

Subgroup Analysis

Table 5 summarizes the subgroup analyses, demonstrating that the inverse association between eGDR and kidney stone risk was statistically significant across several predefined subgroups. A significant interaction was observed between diabetes status and kidney stone risk (P for interaction <0.001). The protective association was stronger among individuals with diabetes (OR = 0.67, 95% CI: 0.62-0.72, $P<0.001$) than among individuals without diabetes (OR = 0.91, 95% CI: 0.87-0.95, $P<0.001$). Additionally, a significant protective association was observed among female participants (OR = 0.85, 95% CI: 0.78-0.91, $P<0.001$).

ROC Curve Analysis of IR Indices for Kidney Stones

The predictive performance of IR indices for kidney stone risk was evaluated through ROC curve analysis (**Figure 4, Table 6**). Among evaluated indices, eGDR demonstrated the highest discriminative ability, with an AUC of 0.692 (95% CI: 0.679-0.705), significantly outperforming conventional indices such as TyG (AUC = 0.597, 95% CI: 0.584-0.610) and METS-IR (AUC = 0.567, 95% CI: 0.554-0.581) (DeLong's test, all $P<0.001$). To assess model stability, internal validation was performed using 1000 bootstrap resamples. Bootstrap-derived 95% CIs closely matched the original estimates (eg, eGDR bootstrap 95% CI: 0.679-0.704), confirming the robustness of the predictive models.

Based on optimal threshold analysis using the maximum Youden index, TyG-WC yielded the highest cutoff value (719.24). Among all evaluated indices, TyG demonstrated the highest sensitivity (0.826), whereas eGDR exhibited the highest specificity (0.737). Although eGDR showed relatively lower sensitivity (0.597), its superior specificity and highest overall AUC support its potential utility as a screening metric for identifying individuals with elevated kidney stone risk.

Sensitivity Analysis

To assess the robustness of the primary complete-case analysis, sensitivity analysis was conducted using the MICE-imputed dataset (N = 23 900). As shown in **Table 7**, effect sizes and statistical significance remained highly consistent across the unadjusted, partially adjusted, and fully adjusted models. These findings indicate that missing data for secondary covariates did not materially influence the observed associations.

Discussion

To our knowledge, this is the first large-scale cross-sectional study in a Chinese population to investigate the association between eGDR and kidney stones. Our principal findings were as

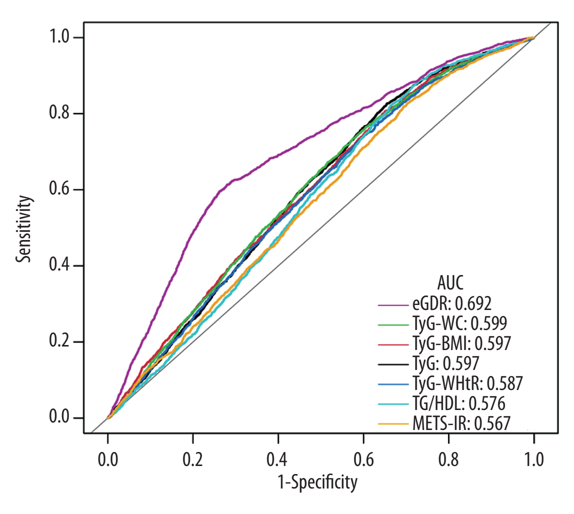

Figure 4. ROC curves of insulin resistance indices for kidney stones. Comparative analysis of the predictive performance of eGDR (AUC = 0.692) and TyG-related indices, TG/HDL-C, and METS-IR in the HMC-AHYU cohort. eGDR demonstrated the highest discriminative ability among all evaluated indices. Abbreviations: AUC, area under the curve; BMI, body mass index; eGDR, estimated glucose disposal rate; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HMC-AHYU, Health Management Center, Affiliated Hospital of Yangzhou University; METS-IR, metabolic score for insulin resistance; ROC, receiver operating characteristic; TG, triglycerides; TyG, triglyceride-glucose index; TyG-BMI, triglyceride-glucose-body mass index; TyG-WC, triglyceride-glucose-waist circumference; TyG-WHtR, triglyceride-glucose-waist-to-height ratio.

Table 6. Discriminative performance of insulin resistance indices for kidney stones.

Index	AUC (95% CI)	Bootstrap 95% CI	Cutoff threshold	Specificity	Sensitivity	*P*-value (vs eGDR)
eGDR	0.692 (0.679-0.705)	0.679-0.704	8.493	0.737	0.597	–
TyG	0.597 (0.584-0.610)	0.585-0.609	8.532	0.346	0.826	< 0.001
TyG-BMI	0.597 (0.584-0.611)	0.583-0.611	200.876	0.350	0.806	< 0.001
TyG-WC	0.599 (0.586-0.612)	0.586-0.612	719.243	0.394	0.766	< 0.001
TyG-WHtR	0.587 (0.574-0.601)	0.573-0.600	4.211	0.372	0.770	< 0.001
TG/HDL-C	0.576 (0.563-0.588)	0.562-0.588	1.997	0.336	0.822	< 0.001
METS-IR	0.567 (0.554-0.581)	0.553-0.581	33.555	0.307	0.818	< 0.001

Abbreviations: AUC, area under the curve; CI, confidence interval; eGDR, estimated glucose disposal rate; METS-IR, metabolic score for insulin resistance; TG/HDL-C, triglyceride-to-high-density lipoprotein cholesterol ratio; TyG, triglyceride-glucose index; TyG-BMI, triglyceride-glucose-body mass index; TyG-WC, triglyceride-glucose-waist circumference; TyG-WHtR, triglyceride-glucose-waist-to-height ratio. *P* values were calculated using DeLong's test comparing the AUC of each index with that of eGDR. Bootstrap 95% CIs were derived from 1000 resamples for internal validation.

follows: (1) lower eGDR levels were associated with a stepwise increase in kidney stone risk; (2) the association between eGDR and kidney stones followed a significant inverse dose-response pattern; (3) a significant interaction between eGDR and diabetes was observed, including a stronger protective association among individuals with diabetes; (4) threshold analyses identified eGDR inflection points at 9.02 and 10.87; and (5) eGDR demonstrated the strongest predictive performance among evaluated IR indices. These findings support the potential clinical utility of eGDR as a biomarker for kidney stone risk stratification.

Among commonly used surrogate markers of IR, all except eGDR have previously been linked to kidney stone risk. Prior studies have shown positive associations of the TyG index and related indices with kidney stone risk [21]. Similarly, TG/HDL-C and METS-IR have shown significant associations with kidney stone formation [22]. Although eGDR is a readily accessible and reliable indicator of IR, its association with kidney stones has not previously been investigated. By demonstrating an inverse dose-response relationship between eGDR and kidney stone risk, the present study addresses an important gap in the literature.

Previous studies have begun to clarify the metabolic mechanisms through which IR promotes kidney stone formation. Among patients with calcium-containing stones,

Table 7. Association between eGDR and kidney stone prevalence in the multiply imputed dataset (N = 23 900).

	Model 1 OR (95% CI)	*P*-value	Model 2 OR (95% CI)	*P*-value	Model 3 OR (95% CI)	*P*-value
eGDR (continuous)	0.70 (0.68-0.72)	< 0.001	0.82 (0.80-0.85)	< 0.001	0.84 (0.81-0.87)	< 0.001
eGDR (quartiles)						
Quartile 1	1.0 (Reference)		1.0 (Reference)		1.0 (Reference)	
Quartile 2	0.34 (0.30-0.39)	< 0.001	0.46 (0.40-0.53)	< 0.001	0.47 (0.41-0.55)	< 0.001
Quartile 3	0.26 (0.22-0.30)	< 0.001	0.48 (0.40-0.56)	< 0.001	0.53 (0.45-0.64)	< 0.001
Quartile 4	0.17 (0.14-0.20)	< 0.001	0.40 (0.33-0.48)	< 0.001	0.51 (0.40-0.64)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	

Multiple imputation by chained equations was used to handle missing data for secondary covariates, resulting in a complete dataset of 23 900 participants for sensitivity analyses. Model 1: Unadjusted. Model 2: Adjusted for age, sex, smoking status, alcohol consumption, and diabetes. Model 3: Adjusted for age, sex, creatinine, uric acid, total cholesterol, HDL-C, LDL-C, TG, BMI, smoking status, alcohol consumption, and diabetes. Abbreviations: BMI, body mass index; CI, confidence interval; eGDR, estimated glucose disposal rate; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; TG, triglycerides.

Cupisti et al [23] found that IR was associated with significantly lower urinary citrate excretion, suggesting that impaired insulin signaling can promote stone formation through changes in urinary composition. Additional studies have shown that IR can suppress renal ammonia production while increasing sodium and bicarbonate reabsorption, resulting in lower urinary pH [24]. Under acidic urinary conditions, a greater proportion of urate is converted to insoluble uric acid, thus increasing the risk of uric acid stone formation [25]. Furthermore, IR enhances renal citrate reabsorption and reduces urinary citrate excretion. Because citrate is a potent inhibitor of calcium crystallization, reduced urinary citrate levels may increase the risk of calcium-containing stones [26].

Our findings demonstrate that individuals in the lowest eGDR quartile exhibited elevated TG levels and reduced HDL-C levels, a lipid profile characteristic of the dyslipidemia associated with metabolic syndrome. This atherogenic profile may promote kidney stone formation through several mechanisms. Hypertriglyceridemia is closely linked to oxidative stress and a pro-inflammatory state, which can induce renal tubular injury and facilitate crystal nucleation and retention [27]. Concurrently, low levels of HDL-C diminish its anti-inflammatory and antioxidant effects, thus exacerbating renal tissue damage and enhancing stone risk. Individuals with diabetes exhibited a stronger inverse association between eGDR and kidney stone risk. We speculate that this finding reflects the greater impact of improved insulin sensitivity in this population, which may inhibit multiple lithogenic processes, including excessive urinary calcium excretion, urinary acidification, and disturbances in bone mineral metabolism [28,29].

Segmented regression analyses identified population-specific threshold effects in the association between eGDR and kidney stone risk. In the HMC-AHYU cohort, eGDR inflection points were identified at 9.02 and 10.87, suggesting that eGDR values above 10.87 confer additional renal protective effects. ROC analyses further demonstrated that eGDR had the strongest discriminative ability for kidney stone risk (AUC = 0.692), significantly outperforming conventional IR indices. Previous nutritional research has shown that plant-rich dietary patterns possess several protective characteristics [30]. Higher consumption of plant-based foods provides an alkaline load that may help counteract urinary acidification associated with IR [31].

Several limitations should be acknowledged. First, the cross-sectional nature of the study precludes causal inference, and longitudinal studies are needed to clarify temporal relationships. Second, because all participants were recruited from a single center, the generalizability of the findings to other populations may be limited. Third, the lack of detailed stone composition data prevented evaluation of subtype-specific associations with eGDR. Fourth, comprehensive dietary and lifestyle data were unavailable; these factors may influence the relationship between IR and kidney stone risk.

Conclusions

To our knowledge, this study is the first to demonstrate an association between eGDR and kidney stone risk in a large Chinese population. Given its ease of calculation and strong discriminative performance, eGDR may serve as a useful screening marker for kidney stone risk. Future multicenter prospective studies are needed to establish causal relationships, and interventional studies targeting insulin resistance should be undertaken.

Acknowledgements

We sincerely thank the Health Promotion Center of our institution for supporting this study and all research personnel involved in its conduct.

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Patient Consent

The requirement for informed consent was waived for this retrospective study by the Ethics Committee (Approval No. 2025-YKL06-K05).

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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