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Association of atherogenic index of plasma with kidney dysfunction in diabetic individuals: findings from two national population-based studies

Lingling Zhu[1,2†], Tiansu Lv[1,2†], Siyuan Song[1,2], Ying Tan[1], Yun She[1,2], Xiqiao Zhou[1], Jiangyi Yu[1*] and Qianhua Yan[1*]

Abstract

Background Extensive evidence suggests that dyslipidemia is associated with endothelial dysfunction, oxidative stress, and inflammation, all of which can contribute to kidney dysfunction. The atherogenic index of plasma (AIP) is a novel marker of lipid metabolism disorder, but its role in kidney dysfunction in diabetic individuals remains controversial. This study aims to clarify the association of AIP with kidney dysfunction in diabetic individuals.

Methods This cross-sectional study analyzed a representative sample of participants aged 20 years and older from the United States ($n=2,386$, NHANES 2007–2018) and Korea ($n=698$, KNHANES 2012). Weighted multivariate logistic regression analyses and smoothed curve fitting were conducted to investigate the relationship between logarithmically transformed AIP (lgAIP) and multiple kidney dysfunction, including albuminuria and low estimated glomerular filtration rate (eGFR) in diabetic individuals. Additionally, we conducted interaction analyses and subgroup analyses to assess whether this relationship remained consistent across different populations. We utilized receiver operating characteristic (ROC) curves to assess and compare the diagnostic performance of AIP and other lipid indices for kidney dysfunction.

Results In both databases, higher lgAIP was significantly associated with the occurrence of albuminuria in diabetic individuals (NHANES: OR = 7.69, 95%CI: 2.90–20.40; KNHANES: OR = 6.00, 95%CI: 1.05–34.36) in the fully adjusted model. However, the OR (95% CI) for the association between lgAIP and low-eGFR was 1.22 (0.33, 4.53) in the NHANES database and 2.50 (0.16, 38.62) in the KNHANES database, indicating no statistically significant association. Subgroup analysis revealed that the association between lgAIP and albuminuria in diabetic individuals was influenced by age and BMI stratification in the NHANES database, and by BMI stratification in the KNHANES database (p for interaction < 0.05). Compared to other lipid indicators, AIP appears to be more precise and discriminatory in predicting albuminuria in diabetic individuals.

†Lingling Zhu and Tiansu Lv contributed equally to this work.

*Correspondence:
Jiangyi Yu
yjy202105@njucm.edu.cn
Qianhua Yan
1164487931@qq.com

Full list of author information is available at the end of the article

Conclusion Our findings highlight a strong association between lgAIP and albuminuria in diabetic individuals. Future research should explore the mechanisms that underlying this relationship.

Clinical trial number Not applicable.

Keywords Kidney dysfunction, Diabetic individuals, Atherogenic index of plasma, Cross-sectional study

Introduction

Diabetes mellitus (DM) is a critical global health challenge and one of the leading causes of mortality and disability worldwide. According to recent estimates, the global prevalence of diabetes reached 529 million cases in 2021, with projections suggesting an increase to 1.31 billion by 2050 [1]. Diabetes-related kidney disease, a severe complication of diabetes, affects approximately 20–40% of diabetic individuals during their lifetime [2]. Evidence indicates that factors such as estimated glomerular filtration rate (eGFR) and albuminuria are associated with an elevated risk of cardiovascular mortality in individuals with diabetes [3]. Previous studies have consistently identified dyslipidemia as a key risk factor for the development of kidney dysfunction in diabetic individuals [4]. Moreover, the progression of Diabetes-related kidney disease is often characterized by significant disruptions in lipid metabolism, including abnormalities in triglycerides (TG), cholesterol, sphingolipids, phospholipids, lipid droplets, and bile acids [5]. The identification of potential lipid biomarkers associated with the onset and progression of kidney dysfunction in diabetic individuals offers significant potential for improving prevention and treatment strategies.

The atherogenic index of plasma (AIP) was proposed by Dobiásová and Frohlich in 2001 as a reliable indicator of cardiovascular risk [6]. AIP is calculated as the logarithmic ratio of TG to high-density lipoprotein cholesterol (HDL-C), using the formula AIP = log (TG/HDL-C). The free fatty acids derived from TG hydrolysis can accumulate in peripheral tissues, including the liver, muscle, and pancreas, leading to lipid toxicity. This accumulation may induce inflammation, oxidative stress, and endoplasmic reticulum stress, ultimately contributing to insulin resistance. HDL-C is a lipoprotein particle rich in both lipids and proteins, with antioxidant and anti-inflammatory properties [7]. AIP, which reflects the balance between pro-atherosclerotic and anti-atherosclerotic lipids, as well as the size of lipoprotein particles relative to the esterification rate of cholesterol, offers a more comprehensive assessment of dyslipidemia than individual lipid markers [8]. Previous studies have demonstrated a strong association between AIP and various metabolic diseases, including diabetes [9], obesity [10], metabolic-associated fatty liver disease [11], and metabolic syndrome [12]. Recent studies have shown that elevated AIP is a sensitive indicator of early kidney injury in diabetic individuals [13–17]. However, a study conducted in a Chinese cohort found no significant association between AIP in the third tertile and diabetic nephropathy [18]. Clearly, the existing research findings are inconsistent.

Therefore, by integrating data from two public databases, this study performs a cross-national comparison between the United States (U.S.) and Korea, two countries with distinct cultural contexts and large heterogeneous populations, to comprehensively examine the association between AIP and kidney dysfunction in diabetic individuals.

Materials and methods

Study participants

We conducted a cross-sectional study using data from the U.S. National Health and Nutrition Examination Survey (NHANES) from 2007 to 2018 and the Korea NHANES (KNHANES) 2012. Both surveys employed similar study designs, utilizing stratified, multi-stage cluster probability sampling methods, and were conducted by the statistical divisions of the National Centers for Disease Control and Prevention in the U.S. and Korea, respectively [19]. The study was conducted in accordance with the 1975 Declaration of Helsinki, and written informed consent was obtained from all participants. As the dataset was anonymized to protect participant privacy, no additional ethical approval was required.

The exclusion criteria for the final sample analysis were as follows: (i) age < 20 years (NHANES, $N = 25{,}072$; KNHANES, $N = 1{,}829$); (ii) pregnancy (NHANES, $N = 372$; KNHANES, $N = 30$); (iii) missing data on UACR (NHANES, $N = 7{,}636$; KNHANES, $N = 859$); (iv) missing data on SCR (NHANES, $N = 1{,}443$; KNHANES, $N = 163$); (v) missing data on TG or HDL-C (NHANES, $N = 13{,}227$; KNHANES, $N = 0$); and (vi) absence of diabetes (NHANES, $N = 9{,}706$; KNHANES, $N = 4{,}479$). The final samples consisted of 2,386 and 698 participants, respectively (Fig. 1).

Exposure variable and outcome variable

The exposure variable was AIP, calculated as the logarithm of the ratio of TG (mmol/L) to HDL-C (mmol/L) [6]. Blood lipid levels were measured using peripheral blood samples collected in the morning after at least 8 h of fasting. TG concentrations were measured using an enzymatic method, and HDL-C was quantified using direct immunoassay or precipitation techniques.

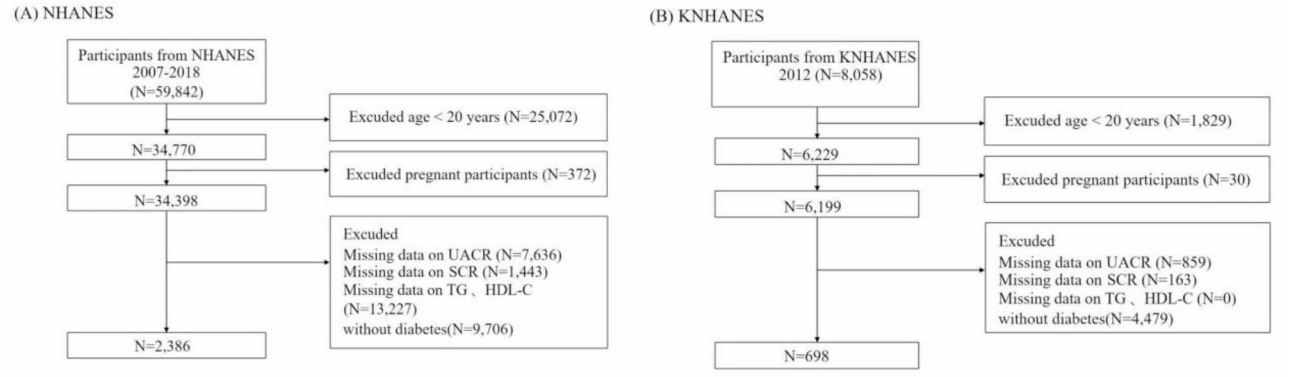

Fig. 1 Flowchart of participant selection

The outcome variable was kidney dysfunction in diabetic individuals, defined as albuminuria and low-eGFR. Diabetes was defined as meeting one or more of the following criteria: fasting blood glucose (FBG) ≥ 7.0 mmol/L, 2-hour post-load glucose during an oral glucose tolerance test (OGTT) ≥ 11.1 mmol/L, glycated hemoglobin (HbA1c) ≥ 6.5%, self-reported physician diagnosis, or current use of insulin or oral hypoglycemic agents [20]. Albuminuria was defined by UACR ≥ 30 mg/g, and low-eGFR was defined as eGFR < 60 ml/min/1.73 m^2. eGFR was calculated using the CKD-EPI 2021 formula, as recommended by the National Kidney Foundation [21]. Compared to the older MDRD equation, the CKD-EPI 2021 formula was developed using a more diverse population, offering improved calibration and greater applicability across different ethnic groups [22].

Covariates assessment

Based on previous studies, the following potential covariates were included: age, sex, race, education level, body mass index (BMI), hypertension, cardiovascular disease (CVD), smoking status, alcohol consumption status, alanine aminotransferase (ALT), and aspartate aminotransferase (AST).

Race was categorized into five groups in the NHANES database: Mexican Americans, other Hispanics, non-Hispanic whites, non-Hispanic blacks, and other races (including multiracial). Educational attainment was categorized into three levels: less than high school, high school graduate, and more than high school. BMI was calculated as weight (kg) divided by height squared (m^2). The American population was classified as normal weight (BMI < 25 kg/m^2), overweight (BMI 25–29.9 kg/m^2), and obese (BMI ≥ 30 kg/m^2), while the Korean population is defined as normal weight (BMI < 23 kg/m^2), overweight (BMI 23–24.9 kg/m^2), and obese (BMI ≥ 25 kg/m^2) according to World Health Organization criteria [23]. Hypertension was defined as a self-reported diagnosis, a mean systolic blood pressure (SBP) ≥ 130 mmHg and/or a mean diastolic blood pressure (DBP) ≥ 80 mmHg based on three separate measurements, or current use of antihypertensive medications [24].The presence of CVD was determined based on participants' self-reports on the medical condition questionnaire, including coronary heart disease, angina, myocardial infarction, and heart failure [25]. Smoking status was determined based on participants' lifetime smoking history, specifically whether they had smoked more than 100 cigarettes [26]. Participants were classified as drinkers if they had consumed at least 12 alcoholic beverages within a single year. Missing values in categorical variables were imputed using mode interpolation. For continuous variables with a normal distribution, mean interpolation was applied. For continuous variables with skewed distributions, median interpolation was used. The numbers and proportions of missing covariates are presented in Supplementary Table 1 (Table S1).

Statistical analysis

Since the NHANES and KNHANES data were obtained through multistage-clustered sampling, we incorporated survey weights to account for the complex sampling design, following the guidelines, and calculated weighted values for each merged dataset during the integration of yearly data [27]. Continuous variables were expressed as means with standard deviations, while categorical variables were reported as percentages with 95% confidence intervals (Cl). Participants were stratified into four groups based on AIP quartiles: Q1 (≤ 25th percentile), Q2 (> 25th to 50th percentile), Q3 (> 50th to 75th percentile), and Q4 (> 75th percentile). Differences among groups were assessed using weighted linear regression for continuous variables and weighted chi-square tests for categorical variables.

Weighted univariate logistic regression models (Model 1) and multivariate logistic regression models (Models 2 and 3) were used to estimate odds ratios (ORs) and corresponding 95% Cls for the association between lgAIP and kidney dysfunction in diabetic individuals. Model 1 was unadjusted, while Model 2 was adjusted for age, sex, and

race. Model 3 was further adjusted for age, sex, race, education level, BMI, ALT, AST, smoking status, alcohol consumption, hypertension, and CVD. To explore potential non-linear relationships, generalized additive models and smoothed curve fitting were performed after adjusting for covariates. This approach provided flexibility in modeling complex patterns that may not be captured by linear models and allowed for a more accurate representation of the relationship between lgAIP and kidney dysfunction across different ranges. To identify potential effect modifiers and further explore the association between AIP levels and kidney dysfunction, subgroup analyses were conducted based on age, sex, race, BMI, CVD, and hypertension. Interaction analyses were performed to examine the variability of associations across subgroups. The predictive performance of AIP and other lipid markers for kidney dysfunction was evaluated by calculating the area under the curve (AUC) using receiver operating characteristic (ROC) curves.

Due to the skewed distribution of AIP, we performed a logarithmic transformation of the index before analysis. All statistical analyses were conducted using R software (version 4.2.3) and Empower Stats (version 4.2). $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics

Table 1 presents the weighted characteristics of participants stratified by AIP quartiles. In NHANES, covariates with significant differences included age, gender, race, BMI, CVD, AST, ALT, UACR, eGFR, and smoking status, whereas in KNHANES, significant differences were observed for age, BMI, CVD, and ALT.

Association between LgAIP and albuminuria/low-eGFR

As shown in Table 2, multiple logistic regression analysis revealed a significant positive association between lgAIP and albuminuria in both the NHANES and KNHANES databases. Based on the smoothed curve fitting, lgAIP showed a positive relationship with both albuminuria and low-eGFR (Fig. 2).

NHANES: In the fully adjusted model (Model 3), a significant positive association was revealed between lgAIP and albuminuria (OR 7.69, 95%CI: 2.90–20.40). This association remained consistent across all models. Sensitivity analyses using lgAIP quartile categorization demonstrated a significant positive association between lgAIP and albuminuria across all three models ($p < 0.05$). In the fully adjusted model, the odds of albuminuria significantly increased across lgAIP quartiles compared to Q1 (Q2: 58%; Q3: 59%; Q4: 139%), with a significant trend observed for each unit increase in lgAIP (p for trend < 0.05). However, no significant association was observed between lgAIP and low eGFR, regardless of whether lgAIP was analyzed as a continuous or categorical variable.

KNHANES: A similar positive correlation was found. In Model 3, each one-unit increase in lgAIP was associated with a 500% increase in the odds of albuminuria (OR 6.00, 95% CI 1.05–34.36). When lgAIP was treated as a categorical variable, odds ratio for albuminuria for participants in the second, third, and fourth quartiles was 1.09, 0.68, and 1.83, respectively, with corresponding 95% CI of (0.57, 2.08), (0.40, 1.16), and (1.11, 3.01). The results showed a significant trend (p for trend < 0.05). No significant association was observed between lgAIP and low-eGFR, regardless of whether lgAIP was analyzed as a continuous or categorical variable.

We used receiver operating characteristic (ROC) curves and the area under the curve (AUC) to evaluate the predictive performance of AIP and other lipid markers, including LDL-C, HDL-C, and TG, for albuminuria. As shown in Supplementary Table 2 (Table S2), AIP demonstrated a slight advantage in predicting albuminuria (NHANES: AUC = 0.5546; KNHANES: AUC = 0.5352). Due to missing LDL-C data in over 50% of the cases in the KNHANES database, the comparison between AIP and LDL-C was excluded from the analysis.

Subgroup analysis

To assess whether the results of different subgroups were consistent with the findings in the general population, we conducted a subgroup analysis. Subgroup analyses revealed that the association between lgAIP and albuminuria was most prominent among participants younger than 60 years, those with obesity, and hypertensive individuals across all databases ($p < 0.05$). Interaction analyses showed that age and BMI significantly influenced the association between lgAIP and proteinuria in the NHANES database. Additionally, BMI significantly influenced the association between lgAIP and proteinuria in the KNHANES database (p for interaction < 0.05, Table 3).

Discussion

This study systematically investigated the association between AIP and kidney dysfunction in individuals with diabetes, utilizing large-scale population databases from the NHANES and KNHANES. Our results demonstrated that lgAIP are significantly associated with the development of albuminuria in diabetic individuals, and this association remained robust even after adjusting for potential confounders. Furthermore, our findings revealed that the relationship between lgAIP and albuminuria in diabetic individuals was moderated by BMI, with a strong positive correlation particularly observed among obese participants in both databases. In the NHANES database, the relationship was also moderated

Table 1 Baseline characteristics of participants. Continuous variables were listed as weighted mean (95% CI). Categorical variables were listed as weighted percentage (95% CI). BMI, body mass index; CVD, cardiovascular disease; ALT: Alanine transaminase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; BUN, blood Urea nitrogen; SCR, serum creatinine

Characteristics	NHANES(2007–2018)					KNHANES 2012				
	AIP				*P* Value	AIP				*P* Value
	Q1	Q2	Q3 (0.06,0.26)	Q4 (0.26,1.65)		Q1	Q2 (−0.06, 0.16)	Q3 (0.16, 0.36)	Q4 (0.36,1.56)	
Age (years)	60.61	61.08	59.49	56.85	< 0.0001	61.92	62.48	58.93	56.12	0.0007
Gender (%)					0.0120					0.7641
Male	46.85	48.63	54.50	60.53		52.74	50.04	57.13	53.77	
Female	53.15	51.37	45.50	39.47		47.26	49.96	42.87	46.23	
Race (%)					< 0.0001					
Mexican American	6.16 (4.53,8.32)	10.48 (7.59,14.30)	11.21 (8.00,15.50)	13.00 (9.92,16.85)						
Other Hispanic	4.95 (3.65,6.68)	7.65 (5.62,10.33)	6.35 (4.64,8.64)	7.62 (4.98,11.48)						
Non-Hispanic White	55.09	54.58	65.46	65.14						
Non-Hispanic Black	25.56	14.98	8.46 (6.11,11.61)	5.68 (4.05,7.91)						
Other Race	8.25 (6.11,11.05)	12.31 (9.18,16.31)	8.51 (6.41,11.21)	8.57 (5.61,12.87)						
Education Levels (%)					0.4430					0.0766
< high school	20.06	22.08	24.37	22.74		56.17	55.09	55.91	45.99	
=high school	22.77	25.17	27.34	23.83		25.61	25.59	17.43	36.33	
> high school	57.17	52.74	48.29	53.43		13.65 (8.08,22.14)	13.78 (8.82,20.87)	23.38	12.66 (8.21,19.03)	
Unclear						4.57 (1.46,13.43)	5.55 (2.22,13.20)	3.28 (1.63,6.47)	5.02 (2.71,9.10)	
BMI (kg/m^2)	30.94	32.44	34.18	34.10	< 0.0001	23.92	24.80	25.43	26.70	< 0.0001
Hypertension (%)					0.3720					0.3357
No	27.07	22.09	21.36	23.62		30.05	25.91	25.47	19.57	
Yes	72.93	77.91	78.64	76.38		69.95	74.09	74.53	80.43	
CVD (%)					0.0221					0.0046
No	85.78	78.11	81.19	77.35		87.77	89.54	97.06	95.66	
Yes	14.22	21.89	18.81	22.65		12.23 (7.90,18.46)	10.46 (5.98,17.67)	2.94 (1.29,6.56)	4.34 (1.93,9.45)	
Smoking status (%)					< 0.0001					0.2560
Yes	42.99	41.78	56.62	56.43		41.65	44.84	57.45	45.89	
No	57.01	58.22	43.38	43.57		53.77	47.36	38.99	49.09	
Unclear						4.57 (1.46,13.43)	7.80 (3.54,16.34)	3.56 (1.83,6.81)	5.02 (2.71,9.10)	
Drinking status (%)					0.1106					0.8025
Yes	64.71	66.69	72.91	72.44		18.22	19.19	12.84 (8.56,18.83)	16.26	
No	29.01	25.68	22.23	22.41		77.20	74.72	83.60	78.72	
Unclear	6.28 (4.62,8.49)	7.63 (5.22,11.02)	4.86 (3.11,7.52)	5.15 (3.72,7.09)		4.57 (1.46,13.43)	6.09 (2.60,13.59)	3.56 (1.83,6.81)	5.02 (2.71,9.10)	
AST (U/L)	24.13	26.23	26.21	27.99	0.0008	25.19	25.97	26.46	28.51	0.5745

Table 1 (continued)

Characteristics	NHANES(2007–2018)					KNHANES 2012				
	AIP				*P* Value	AIP				*P* Value
	Q1	Q2	Q3 (0.06,0.26)	Q4 (0.26,1.65)		Q1	Q2 (−0.06, 0.16)	Q3 (0.16, 0.36)	Q4 (0.36,1.56)	
ALT (U/L)	23.39	26.59	28.55	31.41	< 0.0001	22.40	27.46	30.25	33.15	0.0007
BUN (mmol/L)	5.87 (5.59,6.14)	5.71 (5.45,5.97)	5.73 (5.41,6.04)	5.76 (5.44,6.07)	0.8669	5.80 (5.51,6.10)	5.90 (5.35,6.45)	5.49 (5.20,5.78)	5.51 (5.11,5.91)	0.2605
UACR (mg/g)	69.09	119.79	122.50	181.19	0.0091	53.19	47.44	30.56	106.62	0.1208
SCR (μmol/L)	85.89	82.25	82.70	84.24	0.8476	80.59	81.80	78.94	79.35	0.9466
eGFR (ml/min/1.73 m^2)	86.19	85.23	88.22	89.82	0.0371	87.30	87.70	90.04	91.51	0.2423

Table 2 Association between lgAIP and albuminuria/low-eGFR. Data are presented as odds ratios, 95% confidence intervals, and *P*-value. Model 1: no covariates were adjusted. Model 2: age, sex, and race were adjusted. Model 3: age, sex, race, education level, BMI, ALT, AST, smoking status, alcohol consumption status, hypertension, and CVD were adjusted

Exposure	NHANES			KNHANES		
	Model 1 OR (95% CI), *P* value	Model 2 OR (95% CI), *P* value	Model 3 OR (95% CI), *P* value	Model 1 OR (95% CI), *P* value	Model 2 OR (95% CI), *P* value	Model 3 OR (95% CI), *P* value
Albuminuria						
lgAIP (continuous)	5.83 (2.58, 13.15) 0.0001	10.20 (4.01, 25.93) < 0.0001	7.69 (2.90, 20.40) 0.0001	3.77 (0.75, 18.86) 0.1086	5.60 (1.08, 28.93) 0.0414	6.00 (1.05, 34.36) 0.0460
lgAIP (categories)						
Q1	Reference	Reference	Reference	Reference	Reference	Reference
Q2	1.59 (1.12, 2.27) 0.0112	1.63 (1.14, 2.34) 0.0092	1.58 (1.09, 2.29) 0.0195	1.16 (0.63, 2.15) 0.6303	1.15 (0.62, 2.12) 0.6537	1.09 (0.57, 2.08) 0.7980
Q3	1.52 (1.09, 2.12) 0.0147	1.70 (1.21, 2.39) 0.0033	1.59 (1.12, 2.26) 0.0118	0.66 (0.40, 1.08) 0.0997	0.69 (0.43, 1.12) 0.1394	0.68 (0.40, 1.16) 0.1562
Q4	2.17 (1.53, 3.08) < 0.0001	2.61 (1.80, 3.79) < 0.0001	2.39 (1.62, 3.53) < 0.0001	1.68 (1.03, 2.76) 0.0410	1.90 (1.18, 3.05) 0.0092	1.83 (1.11, 3.01) 0.0196
P for trend	0.0002	< 0.0001	0.0003	0.1185	0.0404	0.0439
Low-eGFR						
lgAIP(continuous)	0.42 (0.18, 1.01) 0.0566	1.80 (0.54, 5.96) 0.3383	1.22 (0.33, 4.53) 0.7703	0.26 (0.03, 2.47) 0.2448	0.56 (0.04, 7.97) 0.6675	2.50 (0.16, 38.62) 0.5127
lgAIP (categories)						
Q1	Reference	Reference	Reference	Reference	Reference	Reference
Q2	0.93 (0.63, 1.39) 0.7352	1.08 (0.67, 1.74) 0.7529	1.02 (0.63, 1.65) 0.9344	0.71 (0.26, 1.95) 0.5089	0.62 (0.22, 1.73) 0.3606	0.90 (0.32, 2.51) 0.8401
Q3	0.90 (0.59, 1.38) 0.6379	1.22 (0.77, 1.95) 0.3983	1.10 (0.67, 1.81) 0.6968	0.33 (0.11, 0.99) 0.0506	0.37 (0.13, 1.08) 0.0696	0.53 (0.18, 1.57) 0.2542
Q4	0.67 (0.43, 1.04) 0.0801	1.18 (0.68, 2.07) 0.5597	1.05 (0.58, 1.91) 0.8722	0.70 (0.27, 1.85) 0.4772	0.99 (0.40, 2.45) 0.9910	1.54 (0.60, 3.97) 0.3726
P for trend	0.0739	0.4519	0.7988	0.3716	0.8272	0.5283

by age, with a strong positive association observed among participants under 60 years of age.

AIP, reflecting the ratio of TG to HDL-C, is an emerging lipid index for assessing atherosclerosis risk. TG is a conventional marker of atherosclerosis, whereas HDL-C is recognized for its anti-inflammatory and anti-atherosclerotic properties [28]. Therefore, AIP may reflect a balance between atherogenesis and anti-atherogenesis within the body. We reviewed previous studies examining the association between AIP and diabetes-related kidney disease. However, the findings were inconsistent. Several studies suggested that AIP could be a valuable predictor of albuminuria in patients with T2DM, indicating early kidney damage [13–17]. However, a study conducted in a Chinese cohort found no significant association between AIP in the third tertile and diabetic nephropathy [18].

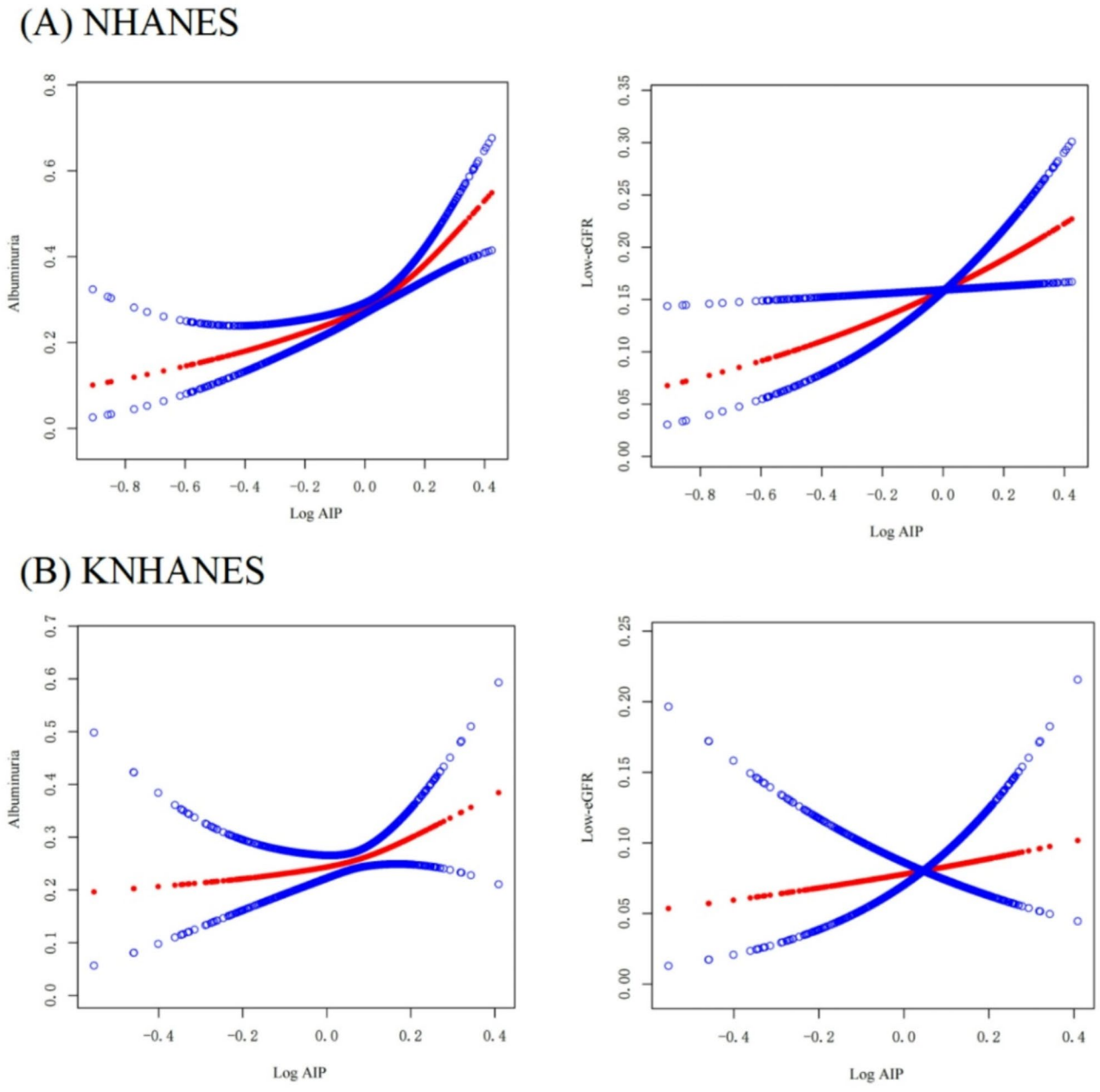

Fig. 2 The relationship between lgAIP and albuminuria/low-eGFR. Red line represents the smooth curve fit between variables. Blue lines represent the 95% confidence interval from the fit

These conflicting results may stem from variations in lipid measurement techniques (e.g., fasting versus non-fasting samples) and laboratory methods, resulting in inconsistent AIP values. Different approaches to calculating eGFR may lead to discrepancies in defining kidney disease. Variations in demographic characteristics, such as age, sex, and ethnicity, as well as differences in comorbidities and lipid-lowering therapies, may modify and confound the relationship. Therefore, our study leverages a large cohort from the U.S. and the Korean populations. It provides robust evidence that elevated lgAIP is independently associated with an increased prevalence of albuminuria in diabetic individuals, even after adjusting for other potential confounding factors. This research extends and complements previous studies, further validating AIP as a reliable marker of kidney dysfunction in diabetic individuals.

In our subgroup analysis, a significant association between lgAIP and albuminuria in diabetic individuals was observed only in patients with a BMI ≥ 25 kg/m^2. In contrast, no significant association was observed in individuals with a normal BMI. Several factors may explain

Table 3 Association between LgAIP and albuminuria/low-eGFR in subgroups. Age, sex, race, education level, BMI, ALT, AST, smoking status, alcohol consumption status, hypertension, and CVD were adjusted were adjusted. In the subgroup analyses, the model is not adjusted for the stratification variable itself

Subgroups	NHANES				KNHANES			
	Albuminuria		Low-eGFR		Albuminuria		Low-eGFR	
	OR(95%CI)	*P* for interaction	OR (95%CI)	*P* for interaction	OR (95%CI)	*P* for interaction	OR (95%CI)	*P* for interaction
Gender		0.7936		0.6684		0.7963		0.9130
Male	6.94 (2.06, 23.44)		1.62 (0.22, 11.82)		8.46 (0.65, 110.11)		2.46 (0.10, 63.52)	
Female	8.71 (2.19, 34.61)		0.92 (0.17, 4.95)		5.27 (0.44, 63.37)		1.88 (0.03, 115.94)	
Age(year)		0.0243		0.1756		0.0924		0.7013
<60	21.30 (5.75, 78.90)		6.96 (0.23, 211.47)		75.56 (2.06, 2765.96)		7.58 (0.00, 12060.58)	
≥60	3.10 (0.89, 10.74)		0.59 (0.16, 2.19)		1.75 (0.21, 14.94)		1.61 (0.09, 29.94)	
Race		0.0690		0.0545				
Mexican American	4.09 (0.56, 29.94)		0.32(0.00, 23.43)					
Other Hispanic	204.56 (18.49, 2262.83)		8.40 (0.08, 830.25)					
Non-Hispanic White	7.77 (1.43, 42.13)		0.46 (0.08, 2.55)					
Non-Hispanic Black	5.86 (1.11, 30.88)		14.56 (2.00, 106.26)					
Other Race	3.21 (0.50, 20.74)		11.44 (0.19, 689.32)					
BMI (kg/m^2)		0.0024		0.9378		0.0429		0.6683
normal	0.88 (0.18, 4.18)		1.09 (0.08, 15.15)		4.16 (0.14, 122.78)		1.12 (0.06, 22.33)	
overweight	7.08 (1.69, 29.56)		1.76 (0.30, 10.35)		0.11 (0.00, 4.32)		0.59 (0.00, 245.41)	
obesity	27.33 (6.26, 119.41)		1.20 (0.19, 7.39)		62.28 (2.72, 1423.87)		14.06 (0.10, 2065.20)	
Hypertension		0.3792		0.9489		0.2346		0.7487
No	18.15 (2.34, 140.53)		1.13 (0.09, 13.63)		1.08 (0.03, 43.66)		4.00 (0.07, 221.38)	
Yes	6.34 (2.09, 19.25)		1.23 (0.29, 5.31)		12.35 (1.95, 78.11)		1.74 (0.06, 52.85)	
CVD		0.5705		0.9895		0.8007		0.5425
No	8.81 (3.03, 25.67)		1.22 (0.24, 6.11)		6.30 (0.91, 43.60)		1.58 (0.09, 29.19)	
Yes	4.84 (0.71, 32.86)		1.21 (0.23, 6.44)		12.41 (0.10, 1515.17)		12.45 (0.02, 6689.15)	

this discrepancy. First, patients with a BMI ≥ 25 kg/m^2 often exhibit more pronounced metabolic disturbances, including insulin resistance, elevated TG levels, and decreased HDL-C levels due to the synergistic effects of lipid metabolism and obesity. These metabolic abnormalities can exacerbate the negative effects of AIP on kidney dysfunction by promoting glomerular hyperfiltration, inflammation, and lipid toxicity. In contrast, normal-weight individuals generally have a lower metabolic burden, which may attenuate the direct effect of lipid metabolism abnormalities on kidney function, thus reducing statistical significance. Additionally, obesity may enhance the effects of AIP through intricate metabolic pathways, including visceral fat accumulation and chronic low-grade inflammation—synergistic factors that are likely absent in individuals with a normal BMI. Despite the lack of a significant association in our study, previous researches have suggested that normal-weight individuals with dyslipidemia, particularly those classified as Metabolically Obese Normal Weight (MONW), may still be at an elevated risk for kidney dysfunction [29, 30]. In the subgroup analysis stratified by age, a

notable association between AIP and albuminuria in diabetic individuals was identified exclusively in individuals under the age of 60 in the NHANES database. This finding indicates that the predictive capacity of AIP for kidney dysfunction in diabetic individuals may exhibit greater sensitivity and specificity within younger age groups. Therefore, stringent control of AIP in younger diabetic patients may serve as an effective preventive measure against the development of kidney dysfunction. The lack of a significant association between AIP and albuminuria in elderly diabetic individuals may be attributed to age-related changes in lipid metabolism, including increased LDL-C levels and decreased HDL-C levels. However, these changes tend to be more uniform across individuals, reducing inter-individual variability and potentially diminishing the impact of AIP in older populations. Aging is frequently associated with chronic low-grade inflammation, which significantly contributes to the decline in kidney function and may confound the effect of AIP on albuminuria in older diabetic individuals. Additionally, the widespread use of statins as a standard lipid-lowering therapy may diminish the sensitivity of AIP as an indicator of lipid metabolism abnormalities.

However, the exact mechanisms underlying the link between AIP and kidney dysfunction in diabetic individuals remain poorly understood. Oxidative stress, inflammatory responses, endothelial dysfunction, and insulin resistance may underlie this biological connection. AIP reflects an imbalance between TG and HDL-C, with high TG and low HDL-C levels being characteristic of dyslipidemia. High TG levels contribute to the accumulation of lipoproteins, such as VLDL-C, in the bloodstream. These lipoproteins are prone to oxidation, resulting in the formation of oxidized lipids, such as malondialdehyde and 4-HNE. This process induces mitochondrial dysfunction in kidney cells and increases the production of reactive oxygen species (ROS), promoting oxidative stress [31]. Increased ROS can disrupt the integrity of the glomerular filtration barrier, induce podocyte apoptosis or shedding, and damage renal tubular epithelial cells, impairing their ability to reabsorb proteins and ultimately leading to albuminuria in diabetic individuals [32]. ROS can also damage cells and tissues, leading to a pro-inflammatory environment [33]. High TG levels and low HDL-C levels contribute to an increase in pro-inflammatory lipids, such as oxidized low-density lipoprotein, within the renal microenvironment. This accumulation activates the nuclear factor κB signalling pathway through interactions with macrophages, triggering the release of pro-inflammatory cytokines, including TNF-α, IL-6, and MCP-1, and resulting in a chronic inflammatory state [34]. Both oxidative stress and inflammation are essential in the development of albuminuria in diabetic individuals [35]. In addition, elevated levels of AIP indicate a increased risk of atherosclerosis, which is associated with endothelial cell damage through mechanisms such as reduced bioavailability of nitric oxide (NO) and increased oxidative stress [36]. Endothelial dysfunction disrupts the glomerular filtration barrier, leading to proteinuria and the progression of kidney disease [37]. AIP is strongly associated with insulin resistance, a key feature of T2DM [9]. Insulin resistance exacerbates hyperglycemia, promotes the release of free fatty acids, and consequently worsens lipid metabolism abnormalities. The interaction between insulin resistance and lipid abnormalities accelerates the development of kidney dysfunction in diabetic individuals by inducing podocyte damage, mesangial dilation, and extracellular matrix deposition.

Our study suggests that AIP may serve as a novel biomarker for clinicians to assess kidney dysfunction in diabetic individuals. This research highlights the significance of monitoring lipid profiles, especially in obese diabetic individuals aged under 60 years, as AIP can serve as an effective indicator for assessing kidney dysfunction in diabetic individuals in this specific population. Identifying elevated AIP serves as an early warning for timely intervention, potentially aiding in preventing kidney dysfunction in diabetic individuals through proactive lipid management.

Strengths and limitations

This study offers several strengths. First, we employed two large, representative population databases from the U.S. and Korea, thereby improving the generalizability of our findings. Second, through stratification and subgroup analysis, we examined the association between AIP and kidney dysfunction in diabetic individuals, identifying specific populations in which the association was significant. However, this study has several limitations. First, as a cross-sectional observational study, it does not establish a causal relationship. Second, although we accounted for various covariates, potential confounding factors, such as differences in healthcare access, genetic predispositions, and measurement errors (e.g., self-reported diabetes diagnoses) may still influence the observed relationship. Future prospective longitudinal studies should be conducted to explore the biological mechanisms underlying the observed associations, and explore interventions that can modulate AIP levels.

Conclusions

The findings of this study clearly demonstrate a robust positive correlation between lgAIP and albuminuria in diabetic patients. Notably, this relationship persists whether lgAIP is regarded as a continuous variable or divided into quartiles. This research offers a crucial means for the early detection of kidney dysfunction among diabetic individuals. In the future, prospective

longitudinal studies are essential. By conducting such studies, we can delve into the underlying biological mechanisms of the observed associations. This exploration will not only deepen our understanding of these relationships but also offer a more comprehensive view of the significance of this study, potentially guiding more targeted research and clinical interventions.

Abbreviations

AIP	Atherogenic index of plasma
DM	Diabetes mellitus
U.S.	United States
CVD	Cardiovascular disease
NHANES	National Health and Nutrition Examination Survey
KNHANES	Korea National Health and Nutrition Examination Survey
TG	Triglyceride
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
UACR	Urine albumin-to-creatinine ratio
eGFR	Estimated glomerular filtration rate
BMI	Body mass index
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
BUN	Blood urea nitrogen
SCR	Serum creatinine
CI	Confidence intervals
OR	Odds ratios
AUC	Area under the curve
ROC	Receiver operating characteristic
ROS	Reactive oxygen species

Supplementary Information

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Supplementary Material 1

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Author contributions

L.L.Z. conducted database search, prepared extracted data for NHANES and KNHANES databases, and was mainly responsible for writing this paper. T.S.L. and Y.S.participated in the processing and analysis of the data. S.Y.S. and Y.T provided language polishing for the article. X.Q.Z, J.Y.Y. and Q.H.Y jointly supervised the study. All authors contributed to the article and approved the submitted version.

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Data availability

Publicly available datasets were analyzed in this study. The data can be found on the NHANES official website at http://www.cdc.gov/nchs/nhanes.htm and on the Korea Disease Control and Prevention Agency (KDCA) website at https://knhanes.kdca.go.kr.

Declarations

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by National Center for Health Statistics Institutional Review Board. KNHANES was approved by Institutional Review Board of Korea Disease Control and Prevention Agency(2012-01EXP-01–2 C). All participants provided their written informed consent to participate in this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Endocrinology, Jiangsu Province Hospital of Chinese Medicine, Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, China
[2]The First Clinical Medical College, Nanjing University of Chinese Medicine, Nanjing, China

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