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Association of diabetic retinopathy with plasma atherosclerotic index, visceral obesity index, and lipid accumulation products: NHANES 2005–2008

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Abstract

Background Abdominal obesity, a significant risk factor for the progression of diabetic retinopathy (DR), may lead to improved visual outcomes through early assessment. This study aims to evaluate any potential associations between DR and novel lipid metabolism markers, including the Atherogenic Index of Plasma (AIP), Visceral Adiposity Index (VAI), and Lipid Accumulation Product (LAP).

Methods This study aimed to elucidate the association between various lipid markers and DR by screening the National Health and Nutrition Examination Survey (NHANES) database in the United States from 2005 to 2008. To examine the correlation, multifactor logistic regression analysis, subgroup analysis, threshold effect analysis, interaction test, and smooth curve fitting were used.

Results Among the 2591 participants included, the incidence of DR was 13.6% and the mean age was 59.55 ± 12.26 years. After adjusting for important confounding covariates, logistic regression studies suggested a possible positive association between LAP, VAI, AIP, and DR occurrence (odds ratio [OR] = 1.004; 95% confidence interval [CI]: 1.002, 1.006; $P < 0.0001$; [OR] = 1.090; 95% [CI]: 1.037, 1.146; $P = 0.0007$; [OR] = 1.802; 95% [CI]: 1.240, 2.618; $P = 0.0020$). The nonlinear association between LAP and DR was further illustrated using an S-shaped curve by smoothing curve fitting, with the inflection point of the curve located at 63.4. Subgroup analyses and interaction tests were performed with full variable adjustment ($P > 0.05$ for all interactions).

Conclusion Studies have shown that elevated levels of LAP, VAI, and AIP increase the likelihood of DR, suggesting that they have the potential to be predictive markers of DR, emphasizing their potential utility in risk assessment and prevention strategies, and advocating for early intervention to mitigate the likelihood of DR.

Keywords DR, LAP, VAI, AIP, Cross-sectional study

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Introduction

Diabetic retinopathy (DR), as one of the most prevalent and devastating microvascular complications in the progression of diabetes mellitus, has become a major cause of visual function loss affecting middle-aged and elderly people. The International Diabetes Federation reported that the worldwide prevalence of diabetes was 463 million in 2019, with projections estimating it will rise to 700 million by 2045. The global prevalence of DR is as high as one-third of all people with diabetes. Thus, DR has become a global public health problem [1, 2].

Hyperglycemia, hypertension, and hyperlipidemia are risk factors for the systemic development of DR [3]. Obesity is closely related to it, and several clinical studies have identified a correlation between obesity and DR, but with varying accounts and no concrete conclusions. Some recent studies have suggested that the distribution of obesity may be associated with the risk of DR. Li et al. found a better correlation between abdominal obesity relative to BMI in the prediction of DR in 169 diabetic patients [4]. Obesity is categorized as either subcutaneous fat or visceral fat accumulation, and BMI as a conventional measure only provides a rough assessment of obesity status without distinguishing the type of fat. VAI, as a new type of obesity measurement index, can effectively assess visceral fat distribution and dysfunction and indirectly express visceral fat function. Moreover, the LAP, which is calculated from waist circumference (WC) and triglycerides (TG), can also be used to assess the status of abdominal lipid accumulation. AIP, as a better plasma atherosclerosis marker, can better reflect TG and high-density lipoprotein cholesterol (HDL-C) levels as well as the pathogenicity and specificity of dyslipidemia [5]. Current research indicates that AIP is associated with obesity and prediabetes, and it can serve as a predictive factor for diabetes [6–13]. These three indicators are all related to lipid metabolism and offer insights into various aspects of fat distribution and lipid abnormalities. Each indicator provides complementary information, contributing to a deeper understanding of the complex relationship between metabolic disorders and DR, as well as offering unique perspectives. This integrated approach enhances the robustness of findings and provides a more nuanced understanding of the associated risk factors.

However, no studies have been conducted to explore the relationship between these indicators and DR. This study further investigated this relationship using the NHANES 2005–2008 database.

Methods

Study population

This study included a total of 20,497 individuals with data from the NHANES database from 2005 to 2008, excluding data on certain demographic characteristics as follows: lack of eye exam data (14,793 individuals), lack of TG information (3049 individuals) and those lacking data on other covariate information (64 individuals). Finally, 2591 people met the inclusion criteria (Fig. 1).

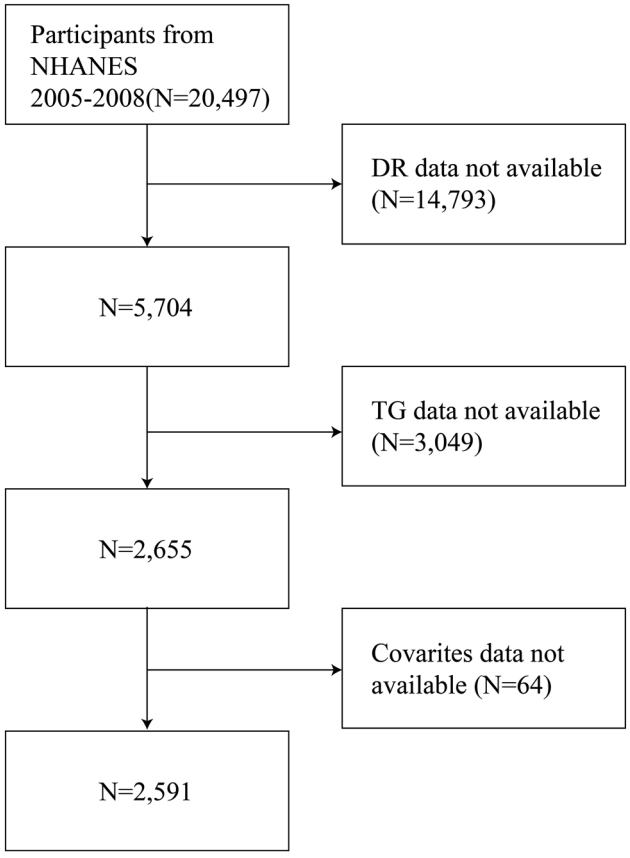

Fig. 1 Flow chart of patient screening. Abbreviations: NHANES: National Health and Nutrition Examination Survey; DR: diabetic retinopathy; TG: triglyceride

Assessment of DR

In this study, DR was used as a continuous variable to assess the fundus condition in both eyes with non-dilated pupils using a specialized digital imaging system and a fundus digital camera, and the fundus photographs were graded by an experienced expert. To differentiate the presence or absence of diabetic retinopathy.

Calculation of LAP, VAI, and AIP

LAP and VAI were calculated by gender using formulas established by Kahn and Amato, and AIP was calculated by mathematical derivation, with BMI in kg/m^2, WC in cm, and TG and HDL in mmol/L.

$$AIP = \lg\left(TG/HDL - c\right)$$

$$MALES:\ LAP = (WC - 65) * TG$$

$$FEMALES:\ LAP = (WC - 58) * TG$$

$$MALES:\ VAI = \left(\frac{WC}{39.68 + 1.88 * BMI}\right) * \left(\frac{TG}{1.03}\right) * \left(\frac{1.31}{HDL}\right)$$

$$FEMALES:\ VAI = \left(\frac{WC}{36.58 + 1.89 * BMI}\right) * \left(\frac{TG}{0.81}\right) * \left(\frac{1.52}{HDL}\right)$$

Covariates

Included routine demographic variables, physical measurements, and laboratory test indicators. such as age, race, gender, marital status, poverty-to-income ratio (PIR), education status, BMI, WC, TG, HDL-C, taking diabetic pills, taking insulin, Alcohol, HbA1c, and Total Cholesterol (TC). Daily health conditions such as smoking, alcohol consumption, and hypertension were assessed by self-report. In this way, the relationship between LAP, VAI, AIP, and DR was explored.

Statistical analysis

The study participants were stratified into two distinct groups, dichotomized according to their diagnosis of DR. To analyze the continuous variables, a weighted Student's t-test was employed, while for categorical variables, a chi-square test was utilized. To explore the correlation between LAP, VAI, AIP, and DR, independent associations were investigated using multifactor logistic regression models. Model 1, without covariate adjustment; Model 3 builds upon Model 2 by additionally incorporating marital status, PIR, educational level, smoking status, alcohol consumption, hypertension, diabetic medication use, insulin use, hemoglobin A1c (HbA1c), and TC as covariates. The nonlinear relationship between the three and DR was tested by smoothing curve fitting and testing. Finally, subgroup analyses and interaction tests were used to explore potential differences between different populations in depth. Statistical analyses were conducted using the EmpowerStats software package in conjunction with R (version 4.1.1). Statistical significance was established at a level of $P<0.05$.

Results

Demographic characteristics

A total of 2591 participants were screened for inclusion in the study between 2005 and 2008; the mean age of the participants was 59.55±12.26 years, 50.79% were male, and the overall prevalence of diabetic retinopathy was 13.6%. The population baseline table (Table 1) showed that participants in the DR group had higher AIP, VAI, and LAP values compared to the non-DR group ($P<0.01$). In addition, the DR group had elevated age, BMI, WC, and TG, while HDL-C and TC were significantly lower than the non-DR group ($P<0.01$).

Multivariate logistic regression modeling of the relationship between LAP, VAI, AIP, and DR in adults in NHANES 2005–2008

The correlations between the three indicators and DR were analyzed by constructing three multiple regression models (Table 2). The results were as follows: in the unadjusted model, there was a significant positive correlation between LAP, VAI, AIP, and DR, and this positive correlation persisted in the fully adjusted model III (OR=1.004,95% CI: 1.002, 1.006, $P<0.0001$; OR=1.090,95% CI: 1.037, 1.146, $P=0.0007$; OR=1.802,95% CI: 1.240, 2.618, $P=0.0020$), which suggests that the likelihood of DR prevalence increases by 0.4%, 9%, and 80% for each one-unit increase in LAP, VAI, and AIP, respectively ($P<0.05$).

Smoothed curve fitting under the fully adjusted model further revealed the nonlinear relationship between LAP, VAI, AIP, and DR (Fig. 2).

In Table 3 we further elucidated their relationship through a threshold effect analysis. The results showed a turning point of 63.4 for LAP (log-likelihood ratio=0.03), suggesting that the likelihood of DR was elevated by 1% for each unit increase in LAP when the LAP level was below 63.4. This correlation disappeared when the LAP level exceeded 63.4. However, in the likelihood ratio test, the *P*-values for VAI, AIP, and DR correlations were 0.213 and 0.065, respectively.

Subgroup analyses

The strength of the association between LAP, VAI, AIP, and DR was assessed by subgroup analysis, which showed that LAP, VAI, and AIP were statistically significant in men and those with a PIR of less than 1.3, with ORs for AIP of 2.82 (1.29, 6.16) and 2.81 (1.07, 7.38), respectively, suggesting that, in this subgroup, every time AIP rises by one unit, the likelihood of DR rises by 1.82-fold and 1.81-fold. However, the *P*-values for all subgroup interaction tests were not significantly different. This further implies that the significant covariates we included did not affect the association between them (Table 4).

Discussion

This cross-sectional study, which ultimately included 2,591 individuals, found a vital nonlinear positive correlation between VAI, LAP, AIP, and DR. All participants had saturation values of LAP (63.4), VAI inflection (0.54) and AIP inflection (0.78). This suggests a strong correlation between LAP, VAI, and AIP levels and a specific range of DR, and also suggests that maintaining ideal levels of LAP, VAI, and AIP has potential clinical significance in reducing the development of DR.

The progression of DR may be linked to these indices, suggesting a close association between lipid metabolism disorders and the development of DR. Multivariable

Table 1 Based on the baseline characteristics of the study population ascertained by NHANES from 2005 to 2008

Characteristics	Total (*N* = 2591)	Non-diabetic retinopathy (*N* = 2239)	diabetic retinopathy (*N* = 352)	*P*-value
Age (years)	59.55 ± 12.26	59.16 ± 12.32	62.01 ± 11.63	**< 0.001**
Poverty-to-income ratio	2.27 ± 1.53	2.28 ± 1.53	2.17 ± 1.53	0.204
Body mass index (kg/m^2)	29.15 ± 6.19	28.97 ± 6.12	30.26 ± 6.51	**< 0.001**
Hemoglobin A1c	5.67 ± 0.84	5.67 ± 0.84	5.70 ± 0.85	0.738
Waist circumference(cm)	100.97 ± 14.77	100.45 ± 14.77	104.26 ± 14.34	**< 0.001**
High-density lipoprotein cholesterol (mg/dL)	54.84 ± 16.30	55.19 ± 16.43	52.55 ± 15.26	**0.005**
Total cholesterol (mg/dL)	201.37 ± 42.07	202.31 ± 41.42	195.40 ± 45.59	**0.004**
Triglyceride (mg/dL)	144.31 ± 92.91	142.34 ± 90.13	156.82 ± 108.25	**0.007**
Gender (%)				0.103
Male	1316 (50.79%)	1123 (50.16%)	193 (54.83%)	-
Female	1275 (49.21%)	1116 (49.84%)	159 (45.17%)	-
Race(%)				0.131
Mexican American	578 (22.31%)	498 (22.24%)	80 (22.73%)	-
Other Hispanic	287 (11.08%)	248 (11.08%)	39 (11.08%)	-
Non-Hispanic White	1070 (41.30%)	929 (41.49%)	141 (40.06%)	-
Non-Hispanic Black	540 (20.84%)	473 (21.13%)	67 (19.03%)	-
Other Race	116 (4.48%)	91 (4.06%)	25 (7.10%)	-
Education Level(%)				0.335
Less Than 9th Grade	209 (8.07%)	186 (8.31%)	23 (6.53%)	-
9-11th Grade	268 (10.34%)	225 (10.05%)	43 (12.22%)	-
High School Grad	381 (14.70%)	338 (15.10%)	43 (12.22%)	-
Some College or AA degree	368 (14.20%)	320 (14.29%)	48 (13.64%)	-
College Graduate or above	269 (10.38%)	235 (10.50%)	34 (9.66%)	-
Other	1096 (42.30%)	935 (41.76%)	161 (45.74%)	-
Marital status(%)				0.559
Married	802 (30.95%)	706 (31.53%)	96 (27.27%)	-
Widowed	141 (5.44%)	119 (5.31%)	22 (6.25%)	-
Divorced	166 (6.41%)	141 (6.30%)	25 (7.10%)	-
Separated	57 (2.20%)	50 (2.23%)	7 (1.99%)	-
Never married	227 (8.76%)	201 (8.98%)	26 (7.39%)	-
Living with partner	102 (3.94%)	86 (3.84%)	16 (4.55%)	-
Other	1096 (42.30%)	936 (41.80%)	160 (45.45%)	-
Taking insulin				0.851
YES	55 (2.12%)	48 (2.14%)	7 (1.99%)	-
NO	2536 (97.88%)	2191 (97.86%)	345 (98.01%)	-
Take diabetic pills				0.956
YES	154 (5.94%)	132 (5.90%)	22 (6.25%)	-
NO	136 (5.25%)	117 (5.23%)	19 (5.40%)	-
Other	2301 (88.81%)	1990 (88.88%)	311 (88.35%)	-
Alcohol drinking(%)				0.627
YES	212 (8.18%)	179 (7.99%)	33 (9.38%)	-
NO	185 (7.14%)	162 (7.24%)	23 (6.53%)	-
Other	2194 (84.68%)	1898 (84.77%)	296 (84.09%)	-
Hypertension(%)				0.151
YES	534 (20.61%)	460 (20.54%)	74 (21.02%)	-
NO	1139 (43.96%)	1000 (44.66%)	139 (39.49%)	-
Other	918 (35.43%)	779 (34.79%)	139 (39.49%)	-
Smoking status(%)				0.273
YES	325 (12.54%)	284 (12.68%)	41 (11.65%)	-
NO	365 (14.09%)	324 (14.47%)	41 (11.65%)	-
Other	1901 (73.37%)	1631 (72.85%)	270 (76.70%)	-
Lipid accumulation product	67.28 ± 54.43	65.72 ± 52.50	77.19 ± 64.60	**< 0.001**

Table 1 (continued)

Characteristics	Total (*N* = 2591)	Non-diabetic retinopathy (*N* = 2239)	diabetic retinopathy (*N* = 352)	*P*-value
Visceral adiposity index	2.26 ± 2.04	2.22 ± 1.98	2.54 ± 2.33	**0.005**
Atherogenic index of plasma	0.37 ± 0.31	0.36 ± 0.31	0.42 ± 0.33	**0.003**

Note All values are presented as proportion (%) or mean (standard error); to analyze the continuous variables, a weighted Student's t-test was employed, while for categorical variables, a chi-square test was utilized

Significant values are in [bold]

Table 2 Multivariable logistic regression models for the association between lipid accumulation product(LAP), visceral adiposity index (VAI), atherogenic index of plasma (AIP), and diabetic retinopathy (DR) in adults in the NHANES 2005–2008

Exposure	Crude Model (Model 1)	Partially Adjusted Model (Model 2)	Fully Adjusted Model (Model 3)
	OR (95% CI) *P*-value	OR (95% CI) *P*-value	OR (95% CI) *P*-value
lipid accumulation product(LAP)	1.003 (1.002, 1.005) **0.0003**	1.003 (1.002, 1.005) **0.0002**	1.004 (1.002, 1.006) **< 0.0001**
visceral adiposity index(VAI)	1.070 (1.019, 1.122) **0.0060**	1.075 (1.024, 1.129) **0.0034**	1.090 (1.037, 1.146) **0.0007**
atherogenic index of plasma(AIP)	1.710 (1.201, 2.435) **0.0029**	1.691 (1.174, 2.436) **0.0048**	1.802 (1.240, 2.618) **0.0020**

Model 1, no covariates were adjusted

Model 2, age, gender, and race were adjusted

Model 3, age, gender, race, marital status, education level, income-to-poverty ratio, smoking status, hypertension, take diabetic pills, taking insulin, Alcohol, HbA1c, and TC were adjusted

All values are based on multivariate logistic regression analysis adjusting for [relevant confounders such as age, gender, etc.]. P-values for continuous variables were derived using Student's t-test, and for categorical variables, chi-square tests were applied

Significant values are in [bold]

Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval

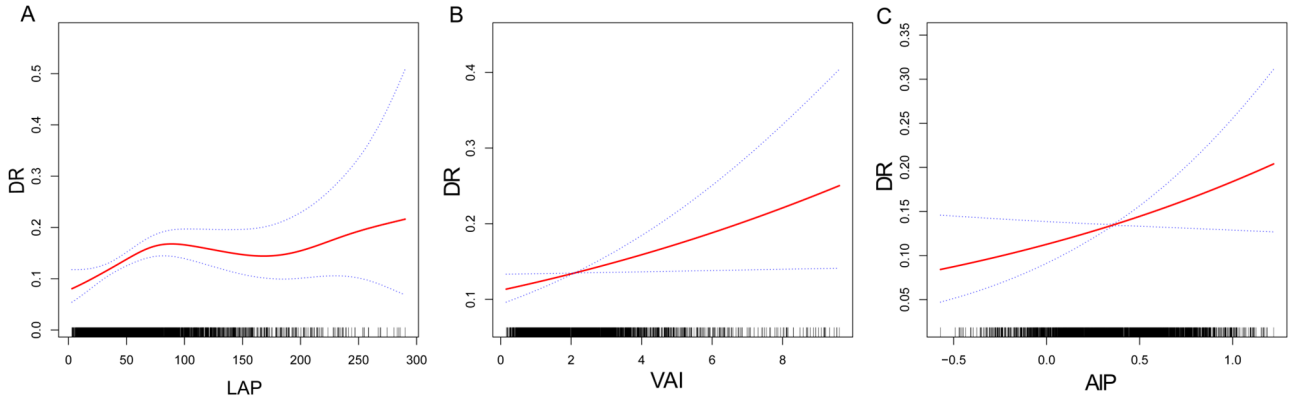

Fig. 2 The nonlinear associations between the lipid accumulation product (LAP)(**A**), visceral adiposity index (VAI)(**B**), atherogenic index of plasma (AIP) (**C**) and diabetic retinopathy (DR) The solid red line represents the smooth curve fit between variables. Blue bands represent the 95% confidence interval from the fit

logistic regression analysis indicates that after adjusting for all variables, the associations of LAP and VAI with DR are weaker than those of AIP. However, it is important to note that in clinical practice, we have observed that many DR patients exhibit higher body weight, BMI, waist circumference, and triglyceride levels compared to non-DR patients. Although LAP and VAI show weaker associations in the statistical models, these findings should not be disregarded, as they may reflect complex interactions between these indices and DR.

The interpretation of these results could be influenced by regional factors and temporal relationships, given that the data were collected from the U.S. region many years ago. Over the past decade or more, slight changes may have occurred. Additionally, fully adjusting the models might involve other unmeasured variables or interactions that could weaken the strength of associations within the regression model. The increase in these indices may still hold significant clinical relevance, suggesting that they may contribute to the underlying pathophysiological changes in DR. This nuanced understanding underscores the importance of considering these factors in both research and clinical settings, as they may offer valuable insights into the risk stratification and management of DR.

Obesity and diabetes are of great concern as globally prevalent public health problems. A series of studies have also shown that the pathogenesis of obesity and diabetes

Table 3 Threshold effect analysis of lipid accumulation product(LAP), visceral adiposity index (VAI) and atherogenic index of plasma (AIP) on diabetic retinopathy (DR) using a two-piecewise logistic regression model in adults in the NHANES 2005–2008

Threshold effect analysis	Diabetic retinopathy
	OR (95%CI) *P*-value
Lipid accumulation product(LAP)	
Fitting by the standard linear model	1.00 (1.00, 1.01) **< 0.0001**
Inflection point of LAP (K)	63.4
< K slope	1.01 (1.00, 1.02) **0.0018**
> K slope	1.00 (1.00, 1.01) 0.0651
Log-likelihood ratio test	**0.03**
visceral adiposity index(VAI)	
Fitting by the standard linear model	1.09 (1.04, 1.15) **0.0007**
Inflection point of VAI (K)	0.54
< K slope	15.49 (0.17, 1408.19) 0.2337
> K slope	1.08 (1.03, 1.14) **0.0019**
Log-likelihood ratio test	0.213
atherogenic index of plasma(AIP)	
Fitting by the standard linear model	1.80 (1.24, 2.62) **0.0020**
Inflection point of AIP (K)	0.78
< K slope	1.40 (0.89, 2.21) 0.1420
> K slope	6.52 (1.66, 25.69) **0.0073**
Log-likelihood ratio test	0.065

Age, gender, race, marital status, education level, income-to-poverty ratio, smoking status, hypertension, Alcohol, take diabetic pills, taking insulin, HbA1c, and TC were adjusted

Significant values are in [bold]

Non-linear relationships, including threshold and saturation effects, were explored using generalized additive models (GAMs)

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio

are closely related and are also involved in the development of its complications [14]. In previous studies, the association between obesity and DR has been inconsistent, and some studies have even shown that BMI is negatively associated with DR [15]. This suggests that the "obesity paradox" may exist between the two, with overweight or obesity being beneficial in preventing disease progression [16]. This further complicates the relationship between them. It is well known that BMI is a slightly poorer interpreter of fat distribution, and that abdominal fat correlates well with visceral fat accumulation [17]. Zheng et al. demonstrated that both generalized obesity and abdominal obesity are risk factors for DR through Mendelian randomization (MR) analysis [18]. severity was positively correlated [15]. This is also in line with our findings.

While visceral fat accumulation has traditionally been assessed using methods such as magnetic resonance imaging or tomography, VAI and LAP offer simpler, easier, and cheaper ways to assess visceral fat accumulation. Kahn et al. introduced LAP in 2005 and found that this metric better predicted the incidence of cardiovascular disease relative to traditional BMI [19]. The VAI, launched in 2010, also accurately utilizes metabolic markers to assess visceral fat distribution and metabolic abnormalities [20]. Lipid metabolism abnormalities are also associated with obesity, and Dobiásová and Frohlich proposed the AIP in 2001 using logarithmic transformation calculations, and Yin et al. showed that the AIP may be of greater value as a risk indicator for other diabetes mellitus [21, 22]. Currently, numerous studies have shown that VAI, LAP, and AIP exhibit significant advantages in predicting diabetes and cardiovascular disease risk. These indices provide a powerful tool for clinicians and researchers to assess risk factors associated with obesity and metabolic abnormalities, further enriching the existing risk assessment system [23, 24].

The present study revealed a nonlinear positive correlation between VAI, LAP, AIP, and DR after adjusting for confounders. This is consistent with the findings of Chen et al. Therefore, it is necessary to consider these three indices in the management of DR patients in clinical settings, and also suggests that these lipid indices have a role in the diagnosis and prediction of DR [25]. A previous longitudinal study also demonstrated that abdominal obesity increased the risk of DR in Chinese patients [26]. However, the underlying pathologic mechanism of the effect of abdominal obesity on DR is currently unknown. Previous studies have suggested that it may be related to insulin resistance and adipose tissue inflammation caused by visceral fat accumulation [27, 28]. In conclusion, VAI, LAP, and AIP are associated with diabetes and its small-vessel complications, but the results may vary in different study contexts. Thresholds for these lipid indices were also reported in the present study, but subsequent large-scale follow-up study investigations are needed if their optimal ranges need to be determined. In subgroup analyses, we found that all three metrics showed an increased likelihood of DR in men and populations with lower PIR. This may be due to metabolic and physiologic changes associated with men and women. In the U.S. population with lower PIR, they may be less attentive to the management of body fat.

Study strengths and limitations

This study leverages the nationally representative NHANES database to examine novel lipid markers—AIP, VAI, and LAP—and their relationship with DR. Employing advanced statistical analyses, we uncovered significant nonlinear associations, offering new insights for clinical risk stratification and potential early interventions. The study also has some shortcomings. First, this was a cross-sectional study in the United States region and did not have a longitudinal design for validation. In addition, this study has limited ability to explore the pathophysiologic aspects of the disease and has insufficient ability to test and extrapolate mechanistic

Table 4 Stratified analysis of the correlation between lipid accumulation product(LAP), visceral adiposity index (VAI), atherogenic index of plasma (AIP), and diabetic retinopathy (DR) in adults in the NHANES 2005–2008

Subgroup	OR(95%CI),*P*-value	*P* interaction	OR(95%CI),*P*-value	*P* interaction	OR(95%CI),*P*-value	*P* interaction
	lipid accumulation product(LAP)		**visceral adiposity index(VAI)**		**atherogenic index of plasma(AIP)**	
AGE		0.778		0.5861		0.9544
< 60	1.00 (1.00, 1.01) 0.0260		1.06 (0.98, 1.16) 0.1604		1.83 (0.80, 4.21) 0.1537	
≥ 60	1.00 (1.00, 1.01) 0.0057		1.10 (1.00, 1.20) 0.0469		1.77 (0.77, 4.07) 0.1755	
Gender		0.5017		0.1092		0.0689
Male	1.00 (1.00, 1.01) 0.0014		1.12 (1.04, 1.21)0.0037		2.82 (1.29, 6.16)0.0095	
Female	1.00 (1.00, 1.01) 0.0895		1.00 (0.88, 1.13)0.9539		0.86 (0.31, 2.38)0.7682	
Race		0.3614		0.9088		0.9574
Mexican American	1.01 (1.00, 1.01) 0.0082		1.11 (0.99, 1.24) 0.0725		2.67 (0.78, 9.12) 0.1174	
Other Hispanic	1.01 (1.00, 1.02) 0.0142		1.04 (0.78, 1.39) 0.7913		1.80 (0.22, 14.42) 0.5802	
Non-Hispanic White	1.00 (1.00, 1.01) 0.0426		1.04 (0.92, 1.19) 0.4984		1.40 (0.52, 3.80) 0.5077	
Non-Hispanic Black	1.00 (1.00, 1.01) 0.7152		1.13 (0.97, 1.30) 0.1160		1.94 (0.43, 8.71) 0.3878	
Other Race	1.00 (0.98, 1.02) 0.8883		0.98 (0.63, 1.52) 0.9231		2.13 (0.05, 90.04) 0.6924	
Education Level		0.4551		0.8002		0.3853
Less Than 9th Grade	1.00 (0.99, 1.01) 0.7552		1.04 (0.78, 1.39) 0.7648		0.36 (0.02, 5.66) 0.4675	
9-11th Grade	1.01 (1.00, 1.02) 0.0193		1.12 (0.92, 1.36) 0.2446		4.65 (0.67, 32.49) 0.1210	
High School Grad	1.00 (1.00, 1.01) 0.4437		0.98 (0.78, 1.23) 0.8628		1.88 (0.28, 12.72) 0.5156	
Some College or AA degree	1.00 (1.00, 1.01) 0.1350		1.19 (1.01, 1.41) 0.0389		6.67 (1.06, 41.92) 0.0431	
College Graduate or above	1.01 (1.00, 1.02) 0.2678		1.15 (0.90, 1.46) 0.2780		1.43 (0.17, 12.01) 0.7409	
Marital status		0.4482		0.5603		0.6869
Married	1.01 (1.00, 1.01) 0.0019		1.12 (1.03, 1.23) 0.0115		2.31 (1.00, 5.31) 0.0499	
Widowed	1.00 (0.99, 1.01) 0.5223		0.88 (0.65, 1.19) 0.3934		0.86 (0.19, 3.84) 0.8439	
Divorced	1.01 (1.00, 1.01) 0.0870		1.11 (0.93, 1.31) 0.2482		3.25 (0.82, 12.95) 0.0946	
Separated	1.01 (0.99, 1.03) 0.3077		1.15 (0.69, 1.94) 0.5864		7.74 (0.42, 142.52) 0.1683	
Never married	1.00 (0.99, 1.01) 0.9572		0.97 (0.79, 1.19) 0.7853		1.23 (0.31, 4.79) 0.7681	
Living with partner	1.00 (0.99, 1.01) 0.7018		0.99 (0.67, 1.46) 0.9554		1.13 (0.14, 9.05) 0.9114	
Poverty-to-income ratio		0.3584		0.0549		0.3153
< 1.3	1.01 (1.00, 1.01) 0.0034		1.20 (1.07, 1.34) 0.0020		2.81 (1.07, 7.38) 0.0355	
1.3–2.5	1.00 (1.00, 1.01) 0.0127		1.12 (1.00, 1.26) 0.0537		2.62 (0.94, 7.33) 0.0655	
≥ 2.5	1.00 (1.00, 1.01) 0.3164		0.98 (0.87, 1.12) 0.7877		1.08 (0.39, 3.00) 0.8868	
Smoke		0.8543		0.8097		0.946
YES	1.00 (1.00, 1.01) 0.0719		1.13 (0.95, 1.35) 0.1657		1.78 (0.32, 9.98) 0.5140	
NO	1.00 (1.00, 1.01) 0.3736		1.12 (0.94, 1.34) 0.2185		2.51 (0.52, 12.19) 0.2537	
Alcohol drinking		0.6199		0.3363		0.7461
YES	1.01 (0.99, 1.02) 0.3024		0.99 (0.70, 1.39) 0.9437		2.01 (0.14, 28.65) 0.6071	
NO	1.00 (0.99, 1.01) 0.9111		0.87 (0.63, 1.21) 0.4236		0.76 (0.06, 9.31) 0.8281	
Hypertension		0.3877		0.6113		0.7047
YES	1.01 (1.00, 1.01) 0.0243		1.12 (0.96, 1.31) 0.1538		2.76 (0.67, 11.40) 0.1606	
NO	1.00 (1.00, 1.01) 0.1369		1.05 (0.96, 1.15) 0.3148		1.43 (0.55, 3.70) 0.4581	
Taking insulin		0.2210		0.8922		0.7555
YES	1.01 (1.00, 1.03) 0.0714		1.12 (0.75, 1.66) 0.5739		2.66 (0.22, 31.96) 0.4406	
NO	1.00 (1.00, 1.01) < 0.0001		1.09 (1.04, 1.15) 0.0009		1.79 (1.22, 2.61) 0.0026	
Take diabetic pills		0.7546		0.5424		0.7819

Table 4 (continued)

Subgroup	OR(95%CI),*P*-value	*P* interaction	OR(95%CI),*P*-value	*P* interaction	OR(95%CI),*P*-value	*P* interaction
	lipid accumulation product(LAP)		visceral adiposity index(VAI)		atherogenic index of plasma(AIP)	
YES	1.01 (1.00, 1.01) 0.0720		1.18 (0.98, 1.42) 0.0885		2.51 (0.50, 12.64) 0.2645	
NO	1.00 (0.99, 1.01) 0.6098		0.96 (0.68, 1.35) 0.8077		0.96 (0.11, 8.03) 0.9679	

The results show that the subgroup analysis was adjusted for all presented covariates except the effect modifier

Stratified analysis were analyzed using generalized linear models (GLMs) with interaction terms

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio

hypotheses. It requires other cohort studies to verify the correlation between lipid markers and DR. Second, it is not possible to completely exclude the interference of all confounding factors. Due to regional limitations, the findings need to be validated in other countries. Finally, there was an imbalance in the sample sizes between the Non-DR and DR groups, with significantly fewer DR cases. Which could affect the robustness of the results. Additionally, due to the nature of the dataset, certain detailed clinical information, such as the staging and potential complications of DR, was not available. These missing details could influence the accuracy of the analysis and interpretation.

Conclusion

This study, based on NHANES data, revealed that elevated levels of LAP, VAI, and AIP were significantly associated with DR risk, confirming their potential as predictive markers of DR. It is recommended to reduce the levels of these markers through dietary modification and exercise to reach the optimal range to reduce the risk of DR. Meanwhile, it is emphasized that the assessment of LAP, VAI and AIP should be incorporated into clinical evaluation to optimize DR risk management and treatment strategies.

Abbreviations

DR	Diabetic Retinopathy
NHANES	National Health and Nutrition Examination Survey
LAP	Lipid Accumulation Product
VAI	Visceral Adiposity Index
AIP	Atherogenic Index of Plasma
BMI	Body Mass Index
WC	Waist Circumference
TG	Triglycerides
HDL-C	High-Density Lipoprotein Cholesterol
PIR	Poverty-Income Ratio
TC	Total Cholesterol
HbA1c	Hemoglobin A1c
OR	Odds Ratio
CI	Confidence Interval
MR	Mendelian randomization

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Author contributions

Bin Wei: Conceptualization, Methodology, Formal analysis, Writing – original draft, Visualization. Lin Zhou: Conceptualization, Software, Writing – review & editing. Benliang Shu、Qinyi Huang: Software, Visualization, Data curation,. Hua Chai: Validation, Data curation, Formal analysis,. Haoyu Yuan: Software, Visualization. Xiaorong Wu: Writing – review & editing, Supervision, Project administration.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

All participants submitted written informed consent and were approved by the National Ethics Board.

Consent to participate

Not applicable.

Consent to publish

Not applicable.

Competing interests

The authors declare no competing interests.

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