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Red cell distribution width/albumin ratio as a marker for metabolic syndrome: findings from a cross-sectional study

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Abstract

Background Metabolic syndrome (MetS) imposes a significant health burden on patients globally. Chronic low-grade inflammation is pivotal in the onset and progression of this condition. However, the role of the novel inflammatory marker, red cell distribution width to albumin ratio (RAR), in the development of MetS remains unclear.

Methods This population-based cross-sectional study utilized data from the 2011–2020 National Health and Nutrition Examination Survey (NHANES). Participants included individuals over 18 years old with complete data on serum albumin concentration, red cell distribution, and MetS and its components. MetS was defined using the criteria established by the National Cholesterol Education Program Adult Treatment Panel III. The calculation formula for RAR is: RAR = Red cell distribution width (%)/serum albumin (g/dL). Study participants were stratified into four quartiles based on RAR levels. Logistic regression analysis and subgroup analysis were employed to explore the independent interaction between RAR and MetS, as well as investigate the relationship between RAR levels and the specific components of MetS. Finally, the receiver operating characteristic (ROC) curve was used to assess the predictive efficacy of RAR for MetS.

Results A total of 4899 participants were included in this study, comprising 2450 males and 2449 females; 1715 individuals (35.01%) were diagnosed with MetS. As the quartile of RAR increased, the proportion of individuals with MetS also increased. Spearman correlation analysis indicated a positive correlation between RAR and the insulin resistance index HOMA-IR. Logistic regression analysis, adjusting for multiple confounding factors, showed that each standard deviation increase in RAR was associated with a significant 1.665-fold increase (95% CI, 1.404–1.975; $P < 0.001$) in the odds of MetS prevalence. In logistic regression analysis stratified by quartiles of RAR, the risks of MetS in Q1-Q4 were 1.372 (95% CI, 1.105–1.704; $P = 0.004$), 1.783 (95% CI, 1.434–2.216; $P < 0.001$), and 2.173 (95% CI, 1.729–2.732; $P < 0.001$), respectively. Subgroup analyses and interaction tests demonstrated that gender, age, race, education, smoking status, and physical activity modified the positive association between RAR and MetS (p for interaction < 0.05). Additionally, analysis of the area under the receiver operating characteristic (ROC) curve showed that the optimal cutoff value for predicting MetS using RAR was 3.1348 (sensitivity: 59.9%; specificity: 60.6%; and AUC: 0.628).

Conclusions Increasing RAR levels are associated with a higher risk of MetS. Therefore, greater attention should be given to patients with high RAR levels for improved prevention and treatment of MetS.

Keywords Red cell distribution width to albumin ratio, Metabolic syndrome, NHANES, Inflammation

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Introduction

Metabolic syndrome (MetS) is associated with an increased risk of cardiovascular disease and all-cause mortality [1, 2]. A previous study reported a stable prevalence of 33% in adults from 2007 to 2012 [3]. In 2016, the prevalence of MetS among adults aged 20 and older in the United States was 34.7% according to statistics. MetS contributes to the development of conditions such as type 2 diabetes, coronary heart disease, stroke, and other disabilities [4–8]. Also referred to as X syndrome, insulin resistance syndrome, Reaven syndrome, and "fatal quartet," metabolic syndrome comprises clinical symptoms such as central and abdominal obesity, systemic hypertension, insulin resistance (or type 2 diabetes), and dyslipidemia with atherogenic lipid profiles. It is characterized by promoting thrombosis and a pro-inflammatory state, marked by increased activity of inflammatory cytokines [9].

Typically, patients with Metabolic Syndrome (MetS) are obese and present with insulin resistance, which can result in hyperglycemia, hypertension, dyslipidemia, visceral obesity, hyperuricemia, increased inflammatory markers, endothelial dysfunction, and thrombosis, all of which may contribute to MetS through various complex mechanisms [10]. Insulin resistance induces systemic oxidative stress, which in turn activates inflammatory responses, thereby promoting chronic low-grade inflammation and elevated levels of pro-inflammatory cytokines [11, 12]. Both inflammation and oxidative stress play significant roles in the development of metabolic complications [13].

Red Cell Distribution Width (RDW) is a marker routinely examined in laboratories, reflecting the heterogeneity of red blood cell volume. Impaired red blood cell production and abnormal red blood cell survival lead to an increase in RDW, which is associated with systemic inflammation and various diseases such as cardiovascular diseases, venous thromboembolism, cancer, diabetes, community-acquired pneumonia, chronic obstructive pulmonary disease, and liver and kidney failure [14]. Serum albumin is the most abundant circulating protein in blood, serving as a crucial marker of nutritional status and inflammatory response [13]. The physiological characteristics of albumin include anti-inflammatory, antioxidant, anticoagulant, antiplatelet aggregation activities, and colloid osmotic pressure [15]. Several studies have reported a negative correlation between serum albumin concentration and the incidence of functional impairments, diseases, and mortality rates [16–18]. Additionally, RDW is positively correlated with chronological age, while serum albumin is negatively correlated with chronological age [19].

RDW and serum albumin concentration are both considered comprehensive biomarkers of multidimensional dysfunction related to inflammation, oxidative stress, and nutrition. Integrating these two markers may be valuable in predicting mortality. Recently, RAR has emerged as a potential risk biomarker for adverse outcomes in various diseases, including acute myocardial infarction, atrial fibrillation, diabetes, heart failure, chronic kidney disease, and stroke [20–24]. However, the relationship between RAR and MetS remains unclear. Therefore, this cross-sectional study aims to investigate the correlation between RAR and the risk of MetS. The goal is to identify a simple indicator for assessing MetS risk, enabling early intervention to reduce its occurrence.

Methods

Data extraction and cleaning process

Data source and extraction method

The data for this study were extracted from the National Health and Nutrition Examination Survey (NHANES), a publicly available and nationally representative dataset. NHANES provides comprehensive health and nutritional information through a combination of interviews, physical examinations, and laboratory tests.

The datasets were accessed and downloaded from the official NHANES website (https://www.cdc.gov/nchs/nhanes/index.htm). We identified relevant variables from the NHANES questionnaires, examination, and laboratory files based on the study's objective to investigate the relationship between Red Cell Distribution Width (RDW), albumin levels, and Metabolic Syndrome (MetS). The years of the data cycle were selected based on the availability of variables required for the study.

Data merging and integration

Once the relevant files were downloaded, we used SPSS (version 26.0) for data integration. Each file from the NHANES database is typically stored in separate datasets categorized by survey components, such as demographics, examination, and laboratory results. These datasets were merged using the unique participant identifier (SEQN), which is consistently used across all NHANES files to link participant data. This process ensured the correct integration of demographic, biochemical, and questionnaire data for each participant.

Data cleaning and preprocessing

After merging the datasets, the following steps were undertaken to clean the data:

Handling Missing Data: Variables with significant missing data (more than 20%) were excluded from further analysis. For variables with less than 20% missing values, missing data points were handled by

multiple imputation, a method recommended for minimizing bias in health data.

Outlier Detection: Continuous variables, such as RDW and albumin levels, were visually inspected using box plots, and extreme outliers were identified using the 1.5 IQR rule. Identified outliers were either winsorized or removed if deemed implausible based on medical literature.

Categorical Variable Coding: Categorical variables, including MetS components, were coded as binary variables based on established clinical definitions.

Normalization: Certain continuous variables, including RDW and albumin, were standardized to z-scores to ensure comparability between variables with different measurement units.

Exclusion Criteria: Participants under 18 years of age, pregnant women, and those with incomplete data necessary for the diagnosis of MetS were excluded from the analysis.

Study subjects

Figure 1 illustrates the process of selecting study subjects from the National Health and Nutrition Examination Survey (NHANES). We excluded 3,568 participants due to missing age data, 17,800 participants who were under 18 years old, 279 pregnant women, 2648 participants with cardiovascular disease (including angina, myocardial infarction, stroke, congestive heart failure, or coronary heart disease were included. Since there is no comprehensive cardiovascular disease questionnaire for participants under 40 years old, those with symptoms of typical chest pain were also excluded), 16,499 participants with incomplete MetS data, and 28 participants with incomplete blood routine and blood biochemical examination data. Ultimately, the study included 4,899 participants.

Data collection

Interviewer-administered questionnaires were used to obtain information on demographics (age, gender, race) and educational attainment. These questionnaires also collected data on lifestyle factors, including cigarette use, alcohol intake, and physical activity. Cigarette use was classified as never, former, or current. Participants self-reported the frequency and duration of moderate and vigorous physical activity across work, transportation, and leisure-time domains. Using these data, we derived a dichotomous variable to indicate whether or not the participant met the 2008 U.S. national physical activity guidelines of $\geq$150 min of moderate activity, $\geq$75 min of vigorous activity per week, or an equivalent combination [25].

Definition

RAR was calculated as follows: RAR = Red cell distribution width (%) / serum albumin (g/dL) [26].

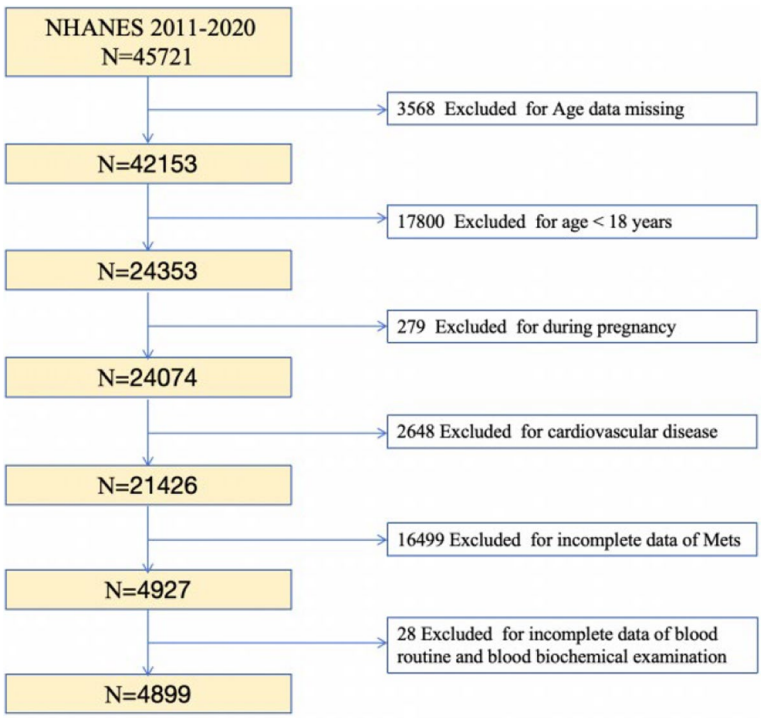

Fig. 1 Flowchart for the selection of the analyzed study sample from the NHANES

Body mass index (BMI) was calculated based on the weight in kilograms and the height in meters.

Waist-to-height ratio (WtHR) was calculated as waist circumference (cm) / height (cm).

Insulin resistance was assessed using the HOMA method with the following equation: HOMA-IR = [Fasting insulin (μU/mL) × Fasting glucose (mmol/L)] / 22.5 [27].

MetS definition

MetS is diagnosed using the criteria from the Adult Treatment Program III of the National Cholesterol Education Program [28]. To meet the MetS diagnosis, an individual must exhibit any three of the following five criteria: (1) triglycerides (TG) ≥ 150 mg/dL; (2) high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL in men and < 50 mg/dL in women; (3) fasting plasma glucose (FPG) ≥ 100 mg/dL; (4) waist circumference (WC) > 102 cm in men and > 88 cm in women; (5) systolic blood pressure (SBP) ≥ 130 mmHg and/or diastolic blood pressure (DBP) ≥ 85 mmHg. Fasting blood samples were collected in the morning after a 9-hour fast, and blood pressure was measured three times by a physician to determine the average value.

Statistical analysis

The characteristics of study participants were presented as either mean (standard deviation) or median (interquartile range), depending on the distribution of continuous variables. Categorical variables were expressed as count (proportion). Continuous variable comparisons were conducted using the Student's t-test, Mann-Whitney U test, Kruskal-Wallis H test, or one-way ANOVA, depending on the normality of the data. Chi-square tests were employed for between-group comparisons of categorical variables. The association between RAR and MetS and its components was assessed through logistic regression models, presenting results as odds ratios (OR) with corresponding 95% confidence intervals (CI). Subgroup analysis of the association between RAR and MetS was performed using stratified factors, including sex, age, race, education, smoking status, and physical activity. These stratification variables were also considered as pre-specified possible impact modifiers. To test for heterogeneity of associations between subgroups, an interaction term was also introduced. Lastly, the predictive validity of RAR for the presence of MetS was determined using receiver operating characteristic (ROC) curves and the area under the curve (AUC) in all subjects. All statistical analyses considered two-tailed *p*-values, with significance set at $p < 0.05$. The statistical software SPSS (version 26.0) was used for all analyses, and Forest plots were generated using GraphPad Prism (version 9.0.0).

Results

Clinical characteristics of the participants

Clinical and laboratory characteristics of the subjects are detailed in Table 1. This study included a total of 4,899 participants, with 2,450 males and 2,449 females, and a mean age of 43 years. The diagnosis rate of Metabolic Syndrome (MetS) was 35.01%. Participants were divided into four groups (Q1-Q4) based on RAR quartiles, and their clinical and laboratory characteristics were compared. The results indicated a gradual increase in the proportion of females as RAR quartiles increased from Q1 to Q4. Additionally, there was a statistically significant increase in the proportion of current smokers and individuals consuming > 3 drinks per day as RAR quartiles increased from the lowest to the highest ($P < 0.05$). Moreover, BMI, WHtR, and HOMA-IR showed a gradual increase with statistically significant differences ($P < 0.05$). The proportions of Diabetes, Hypertension, Hyperuricemia, MetS, Elevated BP, Low HDL-C, and Elevated WC also increased gradually with statistically significant differences ($P < 0.05$).

Association between RAR and Clinical/Laboratory characteristics

Spearman correlation analysis (Table 2) revealed several significant associations. RAR showed a positive correlation with age, female gender, WC, BMI, WHtR, FPG, 2hPG, HbA1c, HOMA-IR, WBC, PLT, GGT, and MetS ($P < 0.05$). Conversely, RAR was negatively correlated with TC, LDL-C, RBC, Hb, ALT, AST, uric acid, and serum creatinine ($P < 0.05$).

Univariate analysis of determinants of MetS of the participants

Table 3 displays the associations of RAR and other variables with the risk of MetS presence. The univariate analysis revealed that age, gender, ethnicity, education, smoking status, alcohol consumption, physical activity, PIR, WBC, RBC, PLT, ALT, GGT, TC, LDL-C, uric acid, and RAR were significantly associated with MetS.

Association of RAR with MetS and its components

The results of the logistic regression analysis of the RAR and MetS are shown in Table 4. This relationship was significant in both our unadjusted crude model (model 1) (odds ratio (OR) = 2.261; 95% confidence interval (CI), 1.986–2.574; $P < 0.001$) and the least adjusted model (model 2) (OR = 2.140; 95% CI, 1.852–2.472; $P < 0.001$). In the fully adjusted model (model 3), there was still a positive association between RAR and MetS (OR = 1.665; 95% CI, 1.404–1.975; $P < 0.001$). This indicates that each SD increase in RAR was associated with a significant 1.665-fold increase in the odds of MetS prevalence. For

Table 1 Clinical characteristics of the participants based on RAR categories

Variable	Total	Q1[2.33-2.8696]	Q2(2.8696–3.0952]	Q3(3.0952-3.400]	Q4(3.4–7.48]	*P* value
Age, years	43.00(30.00,61.00)	33.00(24.00,49.00)	41.00(29.00,60.00)	52.00(35.00,65.00)	50.00(35.00,65.00)	< 0.001
Gender %						< 0.001
Male	2450	827(33.80%)	649(26.50%)	579(23.60%)	395(16.10%)	
Female	2449	413(16.90%)	544(22.20%)	672(27.40%)	820(33.50%)	
Ethnicity %						< 0.001
Mexican American	695	165(23.70%)	191(27.50%)	179(25.80%)	160(23.00%)	
Other Hispanc	579	127(21.90%)	147(25.40%)	179(30.90%)	126(21.80%)	
Non-Hispanic White	1776	510(28.70%)	461(26.00%)	447(25.20%)	358(20.20%)	
Non-Hispanic Black	1035	142(13.70%)	165(15.90%)	289(27.90%)	439(42.40%)	
Other race	814	296(13.70%)	229(15.90%)	157(27.90%)	132(42.40%)	
Education %						< 0.001
Less than high school diploma	1007	200(19.90%)	231(22.90%)	307(30.50%)	269(26.70%)	
High school graduate or equivalent	1031	230(22.30%)	239(23.20%)	242(23.50%)	320(31.00%)	
More than high school	2558	680(26.60%)	640(25.00%)	657(25.70%)	581(22.70%)	
Smoking status %						< 0.001
Never smoker	2877	788(27.40%)	701(24.40%)	703(24.40%)	685(23.80%)	
Former smoker	1070	245(22.90%)	269(25.10%)	305(28.50%)	251(23.50%)	
Current smoker	952	207(21.70%)	223(23.40%)	243(25.50%)	279(29.30%)	
Alcohol consumption %						< 0.001
0–1 cup/day	2789	631(22.60%)	655(23.50%)	744(26.70%)	759(27.20%)	
2–3 cups/day	1358	356(26.20%)	335(24.70%)	345(25.40%)	322(23.70%)	
> 3 cups/day	752	253(33.60%)	203(27.00%)	162(21.50%)	134(17.80%)	
BMI	27.80(24.00,32.60)	25.30(22.00,28.90)	27.20(23.80,31.10)	28.90(24.90,33.68)	31.30(26.10,37.30)	< 0.001
WHtR	0.58(0.52,0.65)	0.53(0.47,0.59)	0.57(0.52,0.63)	0.60(0.54,0.67)	0.64(0.56,0.72)	< 0.001
HOMA-IR	2.45(1.45,4.38)	1.99(1.27,3.44)	2.34(1.41,3.79)	2.66(1.56,4.82)	3.05(1.63,5.53)	< 0.001
TC	183.00(158.00,211.00)	183.00(157.00,212.00)	184.00(159.00,210.00)	185.00(161.00,213.00)	179.00(153.00,209.00)	0.040
LDL-C	107.00(85.00,132.00)	106.00(85.00,133.00)	107.00(87.00,132.75)	110.00(86.00,133.00)	105.00(81.00,130.00)	0.040
PIR	1.99(1.02,3.88)	2.20(1.09,4.19)	2.26(1.07,4.19)	1.98(1.04,3.88)	1.68(0.90,3.27)	< 0.001
Physically active %						< 0.001
No	3172	678(21.40%)	750(23.60%)	861(27.10%)	883(27.80%)	
Yes	1727	562(32.50%)	443(25.70%)	390(22.60%)	332(19.20%)	
Diabetes %	941	133(14.10%)	185(19.70%)	291(30.90%)	332(35.30%)	< 0.001
Hypertension %	1988	389(19.60%)	447(22.50%)	553(27.80%)	599(30.10%)	< 0.001
Hyperlipidemia %	3322	755(22.70%)	775(23.30%)	913(27.50%)	879(26.50%)	< 0.001
Hyperuricemia %	1012	214(21.10%)	231(22.80%)	266(26.30%)	301(29.70%)	< 0.001
MetS %						< 0.001
No	3184	968(30.40%)	825(25.90%)	748(23.50%)	643(20.20%)	
Yes	1715	272(15.90%)	368(21.50%)	503(29.30%)	572(33.40%)	
Elevated BP %						< 0.001
No	2730	796(29.20%)	712(26.10%)	635(23.30%)	587(21.50%)	
Yes	2169	444(20.50%)	481(22.20%)	616(28.40%)	628(29.00%)	
Elevated WC %						< 0.001
No	2286	862(37.70%)	619(27.10%)	477(20.90%)	328(14.30%)	
Yes	2613	378(14.50%)	574(22.00%)	774(29.60%)	887(33.90%)	
Elevated FPG %						< 0.001
No	2363	716(30.30%)	569(24.10%)	554(23.40%)	524(22.20%)	
Yes	2536	524(20.70%)	624(24.60%)	697(27.50%)	691(27.20%)	

Table 1 (continued)

Variable	Total	Q1[2.33-2.8696]	Q2(2.8696–3.0952]	Q3(3.0952-3.400]	Q4(3.4–7.48]	*P* value
Elevated TG %						0.030
No	3823	947(24.80%)	944(24.70%)	955(25.00%)	977(25.60%)	
Yes	1076	293(27.20%)	249(23.10%)	296(27.50%)	238(22.10%)	
Low HDL-C %						< 0.001
No	3361	928(27.60%)	846(25.20%)	836(24.90%)	751(22.30%)	
Yes	1538	312(20.30%)	347(22.60%)	415(27.00%)	464(30.20%)	

BMI Body mass index, *WtHR* Waist-to-height ratio, *HOMA-IR* Homeostasis model assessment of insulin resistance, *TC* Total cholesterol, *LDL-C* Low-density lipoprotein cholesterol, *PIR* Family income to poverty ratio, *MetS* Metabolic syndrome, *BP* Blood pressure, *WC* Waist circumference, *TG* Triglycerides, *FPG* Fasting plasma glucose, *HDL-C* High-density lipoprotein cholesterol

Table 2 Association between RAR and other parameters

	r	*p*
Age, years	0.283**	< 0.001
Gender	0.251**	< 0.001
WC, cm	0.339**	< 0.001
BMI	0.344**	< 0.001
WHtR	0.401**	< 0.001
SBP, mm Hg	0.013	0.395
DBP, mm Hg	-0.005	0.726
FPG, mg/dL	0.139**	< 0.001
2hPG	0.140**	< 0.001
HbA1c, %	0.340**	< 0.001
HOMA-IR	0.188**	< 0.001
TC, mg/dL	-0.041**	0.005
TG, mg/dL	-0.016	0.251
LDL-C, mg/dL	-0.029*	0.046
HDL-C, mg/dL	-0.02	0.163
WBC, $\times 10^9$/L	0.143**	< 0.001
RBC, $\times 10^{12}$/L	-0.145**	< 0.001
Hb, mg/dL	-0.430**	< 0.001
PLT, $\times 10^9$/L	0.130**	< 0.001
ALT, U/L	-0.182**	< 0.001
AST, U/L	-0.167**	< 0.001
GGT, U/L	0.030*	0.035
Uric acid, mg/dL	-0.056**	< 0.001
Serum creatinine, mg/dL	-0.073**	< 0.001
MetS	0.212**	< 0.001

WC Waist circumference, *BMI* Body mass index, *WHtR* Waist-to-Height Ratio, *SBP* Systolic blood pressure, *DBP* Diastolic blood pressure, *FPG* Fasting plasma glucose, *2hPG* Postprandial 2-hour plasma glucose, *HbA1c* Glycated hemoglobin, *HOMA-IR* Homeostasis model assessment of insulin resistance, *TG* Triglycerides, *TC* Total cholesterol, *HDL-C* High-density lipoprotein cholesterol, *LDL-C* Low-density lipoprotein cholesterol, *WBC* White blood cell, *RBC* Red blood cell, *HB* Hemoglobin, *PLT* Platelet, *ALT* Alanine aminotransferase, *AST* Aspartate aminotransferase, *GGT* Gamma-glutamyl transferase, *MetS* Metabolic syndrome

**Correlation is significant at the 0.01 level (2-tailed); *Correlation is significant at the 0.05 level (2-tailed)

sensitivity analysis, we converted RAR from a continuous variable to a categorical variable (quartiles). Participants in the highest RAR quartile (Q4) had a statistically significant 2.173-fold increased risk of MetS compared to those in the lowest RAR quartile (Q1) (OR = 2.173; 95% CI, 1.729–2.732; $P < 0.001$). Compared to the Q1 group, participants in the Q2 and Q3 groups also showed a higher risk of MetS prevalence, with 1.783-fold (OR = 1.783; 95% CI, 1.105–1.704; $P = 0.004$) and 1.372-fold (OR = 1.372; 95% CI, 1.434–2.216; $P < 0.001$) increased risks, respectively, all of which were statistically significant.

In addition, Table 4 depicts the association between RAR and the five MetS-related biochemical indicators in various models. Using multivariate regression analysis with a complex sampling design, we found that RAR levels were substantially and positively linked with increased FPG, BP, and WC levels and reduced HDL-C levels. For BP, the risk increased by 1.235-fold (95% CI, 1.025–1.488), 1.771-fold (95% CI, 1.464–2.142), and 1.966-fold (95% CI, 1.605–2.409) in the Q2, Q3, and Q4 groups, respectively, with *P*-values < 0.05. For WC, the risk increased by 1.677-fold (95% CI, 1.356–2.072), 2.445-fold (95% CI, 1.965–3.042), and 3.109-fold (95% CI, 2.452–3.943) in the Q2, Q3, and Q4 groups, respectively, with *P*-values < 0.001. For FPG, the risk increased by 1.299-fold (95% CI, 1.063–1.587) and 1.291-fold (95% CI, 1.034–1.611) in the Q2 and Q4 groups, respectively, with *P*-values < 0.05.

Due to the absence of cardiovascular disease survey data for individuals under 40 in the NHANES database, a logistic regression analysis was performed specifically for subjects aged 40 and older, excluding those with cardiovascular disease (Table 5). The association between RAR and MetS was statistically significant in both the unadjusted crude model (model 1) (OR = 1.660; 95% CI, 1.406–1.961; $P < 0.001$) and the minimally adjusted

Table 3 Univariate analysis of determinants of MetS in study subjects

Variable	Total	Non-Mets	Mets	Univariate analysis	
				Statistic	*P*
Age	43.00(30.00,61.00)	39.00(26.00,58.00)	52.00(36.00,65.00)	-15.159	< 0.001
Gender%				9.957	0.002
Male	2450 (50%)	1645(67.10%)	805(32.90%)		
Female	2449 (50%)	1539(62.80%)	910(37.20%)		
Ethnicity %				65.296	< 0.001
Mexican American	695(14.20%)	397(57.10%)	298(42.90%)		
Other Hispanc	579(11.80%)	350(60.40%)	229(39.60%)		
Non-Hispanic White	1776(36.30%)	1112(62.60%)	664(37.40%)		
Non-Hispanic Black	1035(21.10%)	734(70.90%)	301(29.10%)		
Other race	814(16.60%)	591(72.60%)	223(27.40%)		
Education %				35.287	< 0.001
Less than high school diploma	1007(21.90%)	577(57.30%)	430(42.70%)		
High school graduate or equivalent	1031(22.40%)	626(60.70%)	405(39.30%)		
More than high school	2558(55.70%)	1719(67.20%)	839(32.80%)		
Smoking status %				37.491	< 0.001
Never smoker	2877(58.70%)	1968(68.40%)	909(31.60%)		
Former smoker	1070(21.80%)	629(58.80%)	441(41.20%)		
Current smoker	952(19.40%)	587(61.70%)	365(38.30%)		
Alcohol consumption %				11.975	0.003
0–1 cup/day	2789(56.90%)	1756(63.00%)	1033(37.00%)		
2–3 cups/day	1358(27.70%)	914(67.30%)	444(32.70%)		
> 3 cups/day	752(15.40%)	514(68.40%)	238(31.60%)		
Physically active %				96.360	< 0.001
No	3172(64.70%)	1905(60.10%)	1267(39.90%)		
Yes	1727(35.30%)	1279(74.10%)	448(25.90%)		
PIR	1.99(1.02,3.88)	2.10(1.02,4.09)	1.88(1.00,3.50)	-2.763	0.006
WBC, $\times 10^9$/L	6.50(5.40,7.80)	6.20(5.20,7.40)	7.10(5.90,8.40)	-15.034	< 0.001
RBC, $\times 10^{12}$/L	4.72(4.39,5.05)	4.69(4.38,5.03)	4.75(4.43,5.07)	-3.574	< 0.001
Hb, mg/dL	14.10(13.10,15.20)	14.10(13.10,15.10)	14.20(13.10,15.20)	-0.73	0.465
PLT, $\times 10^9$/L	230.00(195.00,272.00)	226.00(192.00,265.00)	239.00(201.00,284.00)	-7.501	< 0.001
ALT, U/L	20.00(15.00,28.00)	19.00(15.00,26.00)	23.00(17.00,32.00)	-11.252	< 0.001
AST, U/L	22.00(19.00,27.00)	22.00(19.00,27.00)	22.00(18.00,27.00)	-1.386	0.166
GGT, U/L	19.00(14.00,29.00)	17.00(13.00,26.00)	23.00(17.00,36.00)	-15.836	< 0.001
TC, mg/dL	183.00(158.00,211.00)	180.00(156.00,208.00)	189.00(161.00,219.00)	-6.755	< 0.001
LDL-C, mg/dL	107.00(85.00,132.00)	104.00(84.00,128.00)	113.00(88.00,139.25)	-6.763	< 0.001
Uric acid, mg/dL	5.40(4.40,6.40)	5.20(4.30,6.10)	5.70(4.80,6.70)	-12.767	< 0.001
Serum creatinine, mg/dL	0.83(0.69,0.98)	0.83(0.70,0.98)	0.82(0.69,0.98)	-0.574	0.566
RAR	3.10(2.87,3.40)	3.05(2.83,3.32)	3.23(2.98,3.51)	-14.851	< 0.001

PIR family income to poverty ratio, *WBC* White blood cell, *RBC* Red blood cell, *Hb* Hemoglobin, *PLT* Platelet, *ALT* Alanine aminotransferase, *AST* Aspartate aminotransferase, *GGT* Gamma-glutamyl transferase, *TC* Total cholesterol, *LDL-C* Low-density lipoprotein cholesterol, *RAR* Red cell distribution width to albumin ratio

model (model 2) (OR = 1.744; 95% CI, 1.460–2.084; $P < 0.001$). Even in the fully adjusted model (model 3), a positive association between RAR and MetS remained (OR = 1.366; 95% CI, 1.112–1.677; $P = 0.003$). This suggests that for each SD increase in RAR, the odds of MetS prevalence increased by a significant 1.366-fold.

In the sensitivity analysis, RAR was transformed from a continuous variable into a categorical variable (quartiles). Participants in the highest RAR quartile (Q4) demonstrated a statistically significant 1.660-fold higher risk of MetS compared to those in the lowest quartile (Q1) (OR = 1.660; 95% CI, 1.241–2.220; $P = 0.001$). Additionally,

Table 4 Association of RAR with MetS and its components

	Model1		Model2		Model3	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
MetS						
Continous	2.261(1.986,2.574)	< 0.001	2.140(1.852,2.472)	< 0.001	1.665(1.404,1.975)	< 0.001
Q1	Ref.		Ref.		Ref.	
Q2	1.587(1.323,1.905)	< 0.001	1.390(1.152,1.676)	0.001	1.372(1.105,1.704)	0.004
Q3	2.393(2.008,2.853)	< 0.001	1.948(1.616,2.349)	< 0.001	1.783(1.434,2.216)	< 0.001
Q4	3.166(2.656,3.773)	< 0.001	2.814(2.318,3.415)	< 0.001	2.173(1.729,2.732)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	
Elevated BP						
Continous	1.568(1.387,1.772)	< 0.001	1.590(1.391,1.819)	< 0.001	1.530(1.312,1.785)	< 0.001
Q1	Ref.		Ref.		Ref.	
Q2	1.211(1.028,1.427)	0.022	1.232(1.042,1.455)	0.014	1.235(1.025,1.488)	0.026
Q3	1.739(1.481,2.042)	< 0.001	1.790(1.509,2.123)	< 0.001	1.771(1.464,2.142)	< 0.001
Q4	1.918(1.632,2.255)	< 0.001	2.020(1.690,2.414)	< 0.001	1.966(1.605,2.409)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	
Elevated WC						
Continous	4.813(4.107,5.642)	< 0.001	2.938(2.479,3.483)	< 0.001	2.408(1.960,2.958)	< 0.001
Q1	Ref.		Ref.		Ref.	
Q2	2.115(1.791,2.496)	< 0.001	1.680(1.405,2.009)	< 0.001	1.677(1.356,2.072)	< 0.001
Q3	3.700(3.134,4.370)	< 0.001	2.404(2.002,2.886)	< 0.001	2.445(1.965,3.042)	< 0.001
Q4	6.167(5.176,7.347)	< 0.001	3.695(3.037,4.495)	< 0.001	3.109(2.452,3.943)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	
Elevated FPG						
Continous	1.427(1.263,1.613)	< 0.001	1.308(1.132,1.512)	< 0.001	1.083(0.917,1.280)	0.348
Q1	Ref.		Ref.		Ref.	
Q2	1.498(1.277,1.759)	< 0.001	1.274(1.069,1.517)	0.007	1.299(1.063,1.587)	0.011
Q3	1.719(1.467,2.014)	< 0.001	1.236(1.030,1.482)	0.022	1.178(0.958,1.449)	0.121
Q4	1.802(1.536,2.114)	< 0.001	1.550(1.280,1.877)	< 0.001	1.291(1.034,1.611)	0.024
P for trend	< 0.001		< 0.001		0.063	
Elevated TG						
Continous	0.827(0.712,0.960)	0.013	0.961(0.812,1.137)	0.642	1.025(0.827,1.270)	0.822
Q1	Ref.		Ref.		Ref.	
Q2	0.853(0.704,1.032)	0.102	0.825(0.677,1.005)	0.057	0.922(0.717,1.184)	0.523
Q3	1.002(0.833,1.205)	0.985	1.009(0.826,1.233)	0.927	1.166(0.905,1.503)	0.235
Q4	0.787(0.649,0.955)	0.015	0.936(0.755,1.161)	0.546	1.028(0.779,1.356)	0.845
P for trend	0.078		0.986		0.459	
Low HDL-C						
Continous	1.729(1.524,1.960)	< 0.001	2.067(1.792,2.385)	< 0.001	1.267(1.059,1.517)	0.010
Q1	Ref.		Ref.		Ref.	
Q2	1.220(1.020,1.459)	0.030	1.294(1.077,1.554)	0.006	1.045(0.832,1.313)	0.704
Q3	1.477(1.241,1.757)	< 0.001	1.736(1.441,2.092)	< 0.001	1.209(0.959,1.524)	0.109
Q4	1.838(1.546,2.184)	< 0.001	2.320(1.913,2.815)	< 0.001	1.262(0.988,1.612)	0.062
P for trend	< 0.001		< 0.001		0.035	

Model1: There are no covariates were adjusted

Model 2: Age, gender, and ethnicity were adjusted

Model 3: Age, gender, ethnicity, education levels, smoking status, alcohol consumption, physical activity, poverty income ratio, WBC, RBC, PLT, ALT, GGT, TC, LDL-C and uric acid were adjusted

Table 5 Logistic regression analysis of RAR and MetS and its components in subjects aged 40 and older, excluding those with a history of heart disease

	Model1		**Model2**		**Model3**	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
MetS						
Continous	1.660(1.406,1.961)	< 0.001	1.744(1.460,2.084)	< 0.001	1.366(1.112,1.677)	0.003
Q1	Ref.		Ref.		Ref.	
Q2	1.200(0.931,1.548)	0.159	1.164(0.900,1.506)	0.247	1.143(0.856,1.527)	0.365
Q3	1.592(1.253,2.022)	< 0.001	1.559(1.218,1.995)	< 0.001	1.451(1.098,1.917)	0.009
Q4	2.035(1.602,2.585)	< 0.001	2.124(1.652,2.731)	< 0.001	1.660(1.241,2.220)	0.001
P for trend	< 0.001		< 0.001		< 0.001	
Elevated BP						
Continous	1.598(1.353,1.887)	< 0.001	1.669(1.401,1.988)	< 0.001	1.661(1.364,2.024)	< 0.001
Q1	Ref.		Ref.		Ref.	
Q2	1.106(0.861,1.419)	0.43	1.144(0.889,1.471)	0.296	1.198(0.914,1.571)	0.191
Q3	1.557(1.231,1.969)	< 0.001	1.667(1.309,2.122)	< 0.001	1.686(1.297,2.192)	< 0.001
Q4	1.946(1.537,2.463)	< 0.001	2.103(1.643,2.691)	< 0.001	2.148(1.632,2.828)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	
Elevated WC						
Continous	2.491(2.037,3.047)	< 0.001	1.996(1.607,2.479)	< 0.001	1.568(1.219,2.018)	< 0.001
Q1	Ref.		Ref.		Ref.	
Q2	1.339(1.049,1.710)	0.019	1.205(0.925,1.569)	0.166	1.071(0.793,1.447)	0.653
Q3	1.999(1.581,2.528)	< 0.001	1.628(1.260,2.103)	< 0.001	1.603(1.194,2.152)	0.002
Q4	3.011(2.362,3.840)	< 0.001	2.321(1.774,3.036)	< 0.001	1.836(1.341,2.513)	< 0.001
P for trend	< 0.001		< 0.001		< 0.001	
Elevated FPG						
Continous	1.006(0.850,1.191)	0.946	1.098(0.916,1.315)	0.312	0.927(0.754,1.139)	0.470
Q1	Ref.		Ref.		Ref.	
Q2	1.415(1.097,1.826)	0.007	1.361(1.047,1.767)	0.021	1.387(1.038,1.852)	0.027
Q3	1.452(1.142,1.847)	0.002	1.369(1.064,1.761)	0.015	1.296(0.980,1.715)	0.069
Q4	1.306(1.028,1.659)	0.029	1.397(1.081,1.806)	0.011	1.197(0.894,1.603)	0.228
P for trend	0.088		0.028		0.476	
Elevated TG						
Continous	0.654(0.534,0.801)	< 0.001	0.816(0.663,1.005)	0.056	0.837(0.646,1.086)	0.182
Q1	Ref.		Ref.		Ref.	
Q2	0.674(0.516,0.879)	0.004	0.688(0.524,0.902)	0.007	0.808(0.581,1.124)	0.206
Q3	0.669(0.520,0.860)	0.002	0.758(0.584,0.985)	0.038	0.934(0.680,1.283)	0.672
Q4	0.526(0.406,0.681)	< 0.001	0.677(0.516,0.889)	0.005	0.711(0.504,1.002)	0.051
P for trend	< 0.001		0.025		0.126	
Low HDL-C						
Continous	1.549(1.308,1.833)	< 0.001	1.737(1.448,2.084)	< 0.001	1.044(0.829,1.316)	0.713
Q1	Ref.		Ref.		Ref.	
Q2	1.115(0.844,1.474)	0.443	1.150(0.867,1.526)	0.333	0.866(0.618,1.213)	0.402
Q3	1.309(1.008,1.699)	0.044	1.446(1.104,1.895)	0.007	1.007(0.729,1.391)	0.968
Q4	1.598(1.233,2.070)	< 0.001	1.892(1.440,2.486)	< 0.001	0.970(0.693,1.358)	0.859
P for trend	< 0.001		< 0.001		0.812	

Model1: There are no covariates were adjusted

Model 2: Age, gender, and ethnicity were adjusted

Model 3: Age, gender, ethnicity, education levels, smoking status, alcohol consumption, physical activity, poverty income ratio, WBC, RBC, PLT, ALT, GGT, TC, LDL-C and uric acid were adjusted

participants in the Q3 group also showed an elevated risk of MetS, with a 1.451-fold increase (OR = 1.451; 95% CI, 1.098–1.917; $P = 0.009$) compared to the Q1 group.

Moreover, Table 5 illustrates the association between RAR and the five MetS-related biochemical indicators across various models. Using multivariate regression analysis with a complex sampling design, we observed that RAR levels were significantly and positively correlated with increased BP, elevated WC levels, and reduced HDL-C levels. For BP, the risk increased by 1.686-fold (95% CI, 1.297–2.192) and 2.148-fold (95% CI, 1.632–2.828) in the Q3 and Q4 groups, respectively, with P-values < 0.001. For WC, the risk rose by 1.603-fold (95% CI, 1.194–2.152) and 1.836-fold (95% CI, 1.341–2.513) in the Q3 and Q4 groups, respectively, with P-values < 0.05.

Subgroup analysis

Our subgroup analysis(Fig. 2) revealed that when stratified by gender, smoking status, and physical activity, the relationship between RAR levels and MetS was consistent, with the risk of MetS increasing as RAR levels increased ($P < 0.05$). In the subgroup analyses based on age, ethnicity, and education levels, only participants who were under 60 years old, Non-Hispanic White, Non-Hispanic Black, or had a high school education or higher showed statistical significance ($P < 0.05$). Although it was not statistically significant ($P > 0.05$), RAR was positively correlated with MetS in participants who were 60 years or older, Mexican American, Other Hispanic, and of other races.

The interaction analysis revealed that the interaction between RAR levels and variables such as age, gender, ethnicity, smoking status, and physical activity was significant ($P < 0.05$), whereas the interaction with education levels was not significant ($P > 0.05$).

The subgroup analysis was conducted based on age (< 60 years and ≥ 60 years), sex (male and female), ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Other race), education level (less than high school diploma, high school graduate or equivalent, more than high school), smoking status (never smoker, former smoker, current smoker), and physical activity (no/yes).

For the age subgroups, adjustments were made for gender, ethnicity, education level, smoking status, alcohol consumption, physical activity, poverty income ratio, WBC, RBC, PLT, ALT, GGT, TC, LDL-C, and uric acid.

In the sex subgroups, the analysis adjusted for age, ethnicity, education level, smoking status, alcohol consumption, physical activity, poverty income ratio, WBC, RBC, PLT, ALT, GGT, TC, LDL-C, and uric acid.

When analyzing ethnic subgroups, adjustments were made for age, gender, education level, smoking status,

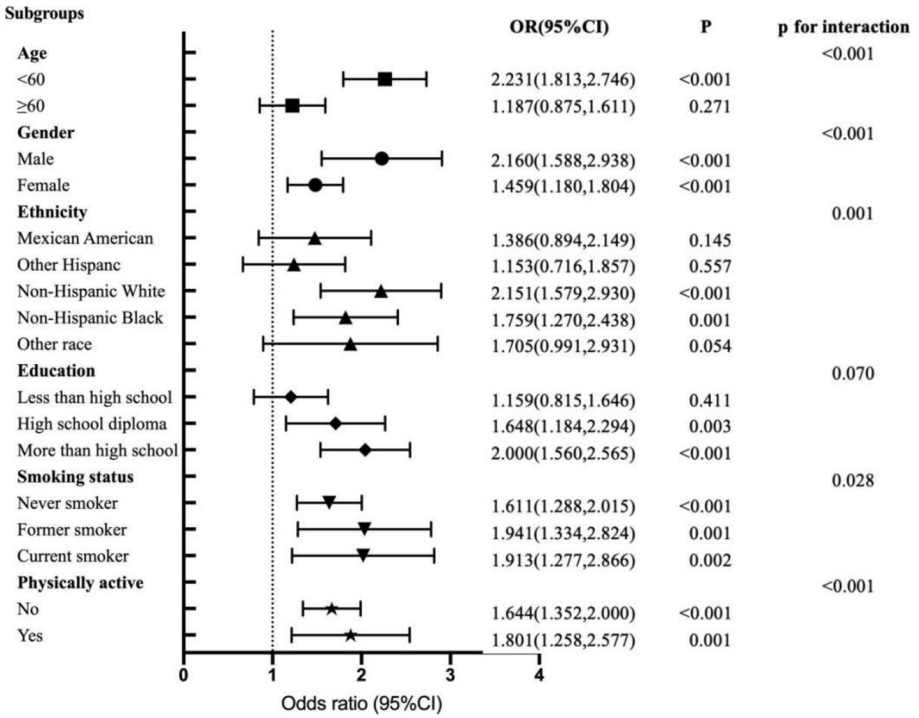

Fig. 2 Subgroup analysis of the association between RAR and MetS

alcohol consumption, physical activity, poverty income ratio, WBC, RBC, PLT, ALT, GGT, TC, LDL-C, and uric acid.

In the education level subgroups, adjustments were made for age, gender, ethnicity, smoking status, alcohol consumption, physical activity, poverty income ratio, WBC, RBC, PLT, ALT, GGT, TC, LDL-C, and uric acid.

For the smoking status subgroups, the analysis was adjusted for age, gender, ethnicity, education level, alcohol consumption, physical activity, poverty income ratio, WBC, RBC, PLT, ALT, GGT, TC, LDL-C, and uric acid.

Finally, when analyzing the physical activity subgroups, adjustments were made for age, gender, ethnicity, education level, smoking status, alcohol consumption, poverty income ratio, WBC, RBC, PLT, ALT, GGT, TC, LDL-C, and uric acid.

Predictive value of RAR in screening for the presence of MetS

To further explore the predictive value of RAR for MetS, ROC curve analysis was performed. As shown in Fig. 3, the best cut-off value for RAR to predict the presence of MetS was 3.1348 (sensitivity: 59.9%; specificity: 60.6%; AUC: 0.628; Fig. 1A) for all study subjects, 2.9529 (sensitivity: 69.2%; specificity: 47.7%; AUC: 0.614; Fig. 1B) for male subjects, and 3.1379 (sensitivity: 70.8%; specificity: 51.9%; AUC: 0.637; Fig. 1C) for female subjects.

Discussion

In this study, we investigated the association between RAR and MetS in adults using data from the NHANES. To our knowledge, this is the first study to explore this relationship. We found that RAR levels are significantly higher in patients with MetS, and that RAR levels are positively correlated with the risk of MetS. Even after controlling for confounding variables, this correlation remained evident. Consistent results were observed in both continuous and categorical analyses.

The divergence observed between RAR's positive association with MetS and its negative correlation with specific biomarkers like LDL-C, ALT, AST, uric acid, and serum creatinine can be attributed to several factors: (1) Multifactorial Nature of Metabolic Syndrome (MetS): MetS is a cluster of risk factors, including insulin resistance, dyslipidemia, hypertension, and abdominal obesity. RAR, being an inflammatory marker, may be strongly influenced by systemic inflammation and oxidative stress, which are prominent in MetS. However, individual biomarkers such as LDL-C, ALT, and AST can reflect specific aspects of metabolic dysfunction that do not always directly parallel the inflammatory state. (2) Different Roles of Inflammatory Markers and Metabolic Parameters: RAR is primarily an indicator of systemic inflammation, while biomarkers like LDL-C, ALT, AST, and others reflect lipid metabolism, liver function, or kidney health. The inverse relationship between RAR and these biomarkers could suggest that while inflammation (high RAR) is linked to the overall presence of MetS, certain metabolic parameters may behave differently due to compensatory or regulatory mechanisms within the body. For instance, liver enzymes (ALT, AST) might decrease in some stages of liver dysfunction even as systemic inflammation increases. (3) Complexity of Spearman Correlation: Spearman correlation measures the monotonic

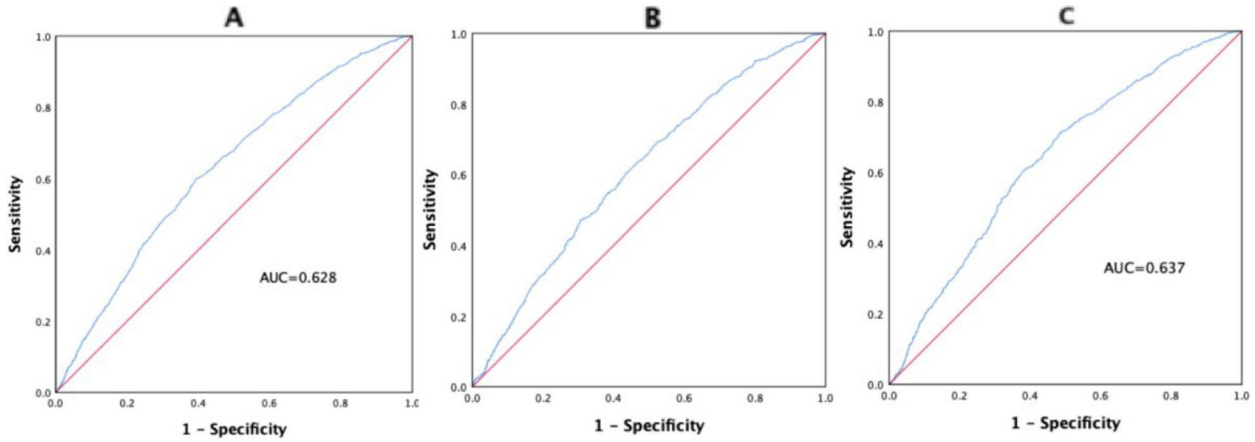

Fig. 3 ROC curve analysis of the predictive value of RAR for metabolic syndrome and its components. **A** ROC analysis of RAR to indicate Mets for study subjects. AUC = 0.628; 95% CI: 0.612 ~ 0.644; $P < 0.001$; identified RAR cutoff value = 3.1348; Youden index = 0.205;sensitivity: 59.9%; specificity: 60.6%. **B** ROC analysis of RAR to indicate Mets for male study subjects. AUC = 0.614; 95% CI: 0.591 ~ 0.637; $P < 0.001$; identified RAR cutoff value = 2.9529; Youden index = 0.169; sensitivity: 69.2%; specificity:47.7%. **C** ROC analysis of RAR to indicate Mets for female study subjects. AUC = 0.637; 95% CI: 0.615 ~ 0.660; $P < 0.001$; identified RAR cutoff value = 3.1379; Youden index = 0.227; sensitivity: 70.8%; specificity:51.9%

relationship between variables, which can sometimes reflect unexpected patterns. In complex conditions like MetS, where multiple processes are interacting (e.g., inflammation, lipid metabolism, liver function), such correlations may not capture the full biological context. The negative correlation with LDL, ALT, and other markers does not necessarily negate RAR's role as an inflammatory marker but rather reflects distinct relationships with these individual biomarkers. (4) Differential Influence of RAR: RAR's positive association with MetS may be more representative of its role in inflammation-driven pathways (e.g., insulin resistance, central obesity) rather than direct associations with lipid or liver metabolism. The negative correlations seen with LDL-C, ALT, etc., might indicate that in individuals with higher RAR, there is a compensatory mechanism that lowers these specific markers despite the presence of MetS.

The subgroup analysis interaction showed that the interaction between RAR levels and variables such as age, gender, ethnicity, smoking status, and physical activity was significant ($P<0.05$), while the interaction with education levels was not ($P>0.05$). This discrepancy can be explained by various biological, social, and behavioral factors: (1) Age: As people age, inflammatory processes tend to increase due to a phenomenon known as "inflammaging," which is associated with MetS. In our subgroup analysis, RAR levels were significantly associated with MetS in individuals under 60 years of age, and this association became more pronounced with increasing age. Additionally, residual and unobserved heterogeneity may lead to an attenuation of hazard rates with age and an underestimation of hazard ratios [29]. (2) Gender: Men and women have different hormonal profiles that influence their risk of MetS. For instance, estrogen has a protective effect in premenopausal women, thereby reducing their risk of MetS [30]. (3) Ethnicity: Different ethnic groups exhibit varying susceptibilities to MetS due to genetic, environmental, and lifestyle factors. These differences could explain why RAR, a marker of systemic inflammation, shows a significant interaction with ethnicity. (4) Smoking Status: Smoking increases oxidative stress and systemic inflammation, both of which are central to the development of MetS. Smokers and former smokers may have higher RDW levels and lower albumin levels, leading to elevated RAR [31]. (5) Physical Activity: Physical activity has anti-inflammatory effects and can reduce the risk of MetS by improving insulin sensitivity, lowering blood pressure, and enhancing lipid profiles [32]. (6) Education Level: Education level may not directly influence biological pathways such as inflammation and oxidative stress, which are central to the relationship between RAR and MetS.

This study found that RAR levels are significantly positively correlated with the MetS components of elevated blood pressure (BP) and elevated waist circumference (WC). Although the specific mechanisms are not yet fully understood, several factors may be associated with RAR levels and MetS risk: 1)RAR as a Marker of Inflammation: RDW and albumin levels are linked to systemic inflammation. RDW reflects the variability in red blood cell size, which can be influenced by oxidative stress and inflammatory cytokines. 2) Hypoalbuminemia is a negative acute-phase response observed in chronic inflammation. Elevated RAR indicates increased inflammation, a key feature of MetS. MetS is characterized by chronic low-grade inflammation, with elevated levels of pro-inflammatory markers such as TNF-α, IL-6, and CRP. These cytokines may impair erythropoiesis and cause alterations in red blood cell turnover, leading to increased RDW. Low albumin levels further reflect the systemic inflammatory state, connecting elevated RAR to the inflammatory pathways driving MetS [33]. (3) Oxidative Stress as a Common Link: Oxidative stress plays a central role in the pathophysiology of MetS, contributing to endothelial dysfunction, insulin resistance, and dyslipidemia. Elevated RDW is associated with oxidative damage to red blood cells, indicating increased oxidative stress. This stress, coupled with decreased albumin (which has antioxidant properties), can exacerbate the metabolic dysregulation seen in MetS [34]. (4) Endothelial Dysfunction in MetS: Oxidative stress leads to endothelial cell damage, reduced nitric oxide bioavailability, and vascular inflammation. These processes contribute to hypertension, insulin resistance, and dyslipidemia—core features of MetS. Thus, increased RAR may serve as a marker of oxidative stress, which underlies both MetS and associated cardiovascular risk [35].

Inflammation is a complex biological process involving various cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP). Dysregulation of this process can lead to chronic inflammation and tissue damage [36]. Existing research indicates that MetS is associated with chronic low-grade inflammation in the body, which is closely related to the incidence of diabetes and hypertension [37, 38]. Obesity, particularly abdominal obesity as indicated by increased waist circumference or waist-to-height ratio, is a common manifestation of MetS and serves as a marker of "dysfunctional adipose tissue" [39]. These "dysfunctional adipose tissues" are closely associated with inflammatory responses. Animal studies have shown that macrophages in obese adipose tissue are polarized to a pro-inflammatory phenotype, a condition associated with metabolic complications [40–42]. Similarly, white adipose tissue from patients

with metabolic abnormalities, such as those with T2DM, is characterized by adipocyte hypertrophy and high rates of pro-inflammatory macrophage infiltration [43].

Additionally, we found that after adjusting for multiple variables, the associations between RAR and FPG, TG, and HDL-C were not significant. We hypothesize that this lack of significance may be related to interactions among different immune cells under stress and potential selection bias. In a retrospective case-control study, Wang et al. found no significant difference in total neutrophil count between pregnant women with diabetes and the control group [44]. A cross-sectional survey in Brazil also showed no significant difference in neutrophil-to-lymphocyte ratio scores between normal and hyperglycemic subjects [45], which is consistent with our observations to date. Similar reports are increasingly frequent. Another factor to consider is that previous diagnoses (such as hyperglycemia and dyslipidemia) may lead to changes in patient lifestyle, and pharmacological interventions could influence the observed results.

In summary, RAR, as assessed through routine laboratory tests, may be a promising indicator. It is simple, reliable, and cost-effective, making it a valuable tool for identifying individuals at high risk for MetS in clinical practice.

However, several limitations of our study should be acknowledged. Firstly, the cross-sectional design of this study precludes determining a causative link between RAR and MetS. Secondly, the potential mechanisms underlying the association between RAR and MetS warrant further investigation through prospective large-scale studies. Despite these limitations, the relatively large sample size enhances the robustness of our findings. Given that RAR can be easily derived from routine indicators, it is readily applicable in clinical practice, especially for large-scale screening procedures.

Conclusions

Increasing RAR levels are associated with a higher risk of MetS. Therefore, greater attention should be given to patients with high RAR levels for improved prevention and treatment of MetS.

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Clinical trial number
Not applicable.

Authors' contributions
Hao Guo analyzed the data and performed the data curation, and drafted the manuscript. Yu Wang and Ying Miao analyzed the data and data curation. Qiang Lin participated in data curation, Oversaw the study design and revised the paper.

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Data availability
The National Health and Nutrition Examination Survey dataset is publicly available at the National Center for Health Statistics of the Center for Disease Control and Prevention (https://www.cdc.gov/nchs/nhanes/index.htm).

Declarations

Ethics approval and consent to participate
NHANES is conducted by the Centers for Disease Control and Prevention (CDC) and the National Center for Health Statistics (NCHS). The NCHS Research Ethics Review Committee reviewed and approved the NHANES study protocol. All participants signed written informed consent.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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