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Association between red blood cell distribution width-to-albumin ratio and depression: a cross-sectional analysis among US adults, 2011–2018

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Abstract

Background Red blood cell distribution width (RDW)-to-albumin ratio (RAR) is a novel index. Its relationship with depression, a common and complex psychiatric disorder, remains unclear. This study utilized the National Health and Nutrition Examination Survey (NHANES) database to investigate this relationship.

Methods Multivariate logistic regression, restricted cubic spline (RCS) regression, receiver operating characteristic (ROC) analysis, and sensitivity analyses were used to examine the relationship between RAR and depression based on NHANES data from 2011–2018. The study also used subgroup analyses and interaction tests to explore whether the relationship was stable across populations.

Results RAR was positively associated with depression in 18,150 participants aged ≥ 20 years. In fully adjusted models, each one-unit increase in RAR was associated with a 22% increase in the likelihood of depression [1.22 (1.05, 1.41)]. Participants in the highest quartile of RAR had a 30% higher risk of depression than those in the lowest quartile of RAR [1.30 (1.04, 1.63)]. Subgroup analyses revealed that the association between RAR and depression was significantly stronger among men, alcohol-drinking and high-income groups.

Conclusions Higher baseline RAR was associated with an increased risk of depression in US adults and was more informative than RDW, albumin, and hemoglobin-to-RDW ratio (HRR). Further large-scale prospective studies are needed to analyze the role of RAR in depression. These findings emphasize that RAR can be a simple, reliable and cost-effective predictor of depression in clinical practice.

Keywords RAR, Depression, NHANES, Cross-sectional study

Introduction

Depression, a common mental disorder characterized by persistent low mood, diminished pleasure and decreased motivation, is associated with premature death from other illnesses and suicide [1, 2]. Depression has a high prevalence and high recurrence rate [3]. According to the World Health Organization (WHO), depression affects approximately 280 million people globally [4]. The prevalence of depression is increasing among young people, especially in high-income areas [5]. It is projected that

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depression will surpass cancer and cardiovascular disease as the top global burden of disease by 2030 [6]. Existing evidence supports the association of inflammation with the pathophysiology of depression [7, 8]. Patients with depression tend to have higher levels of serum biomarkers associated with inflammation, including high-sensitivity c-reactive protein (hs-CRP), interleukin (IL)−6, IL-12, IL-18, and TNF-α [9]. Besides, inflammation may be the cause of disease, not just the result of it [10, 11]. Studies have shown that early recognition and prevention of depression is crucial [12]. However, despite the abundance of clinical studies related to depression, there are still relatively few definitive biomarkers for depression.

Red blood cell distribution width (RDW) is a simple laboratory test that reflects the degree of heterogeneity in erythrocyte volume. Elevated RDW reflects a severe dysregulation of erythrocyte homeostasis, including impaired erythropoiesis and abnormal erythrocyte survival [13]. Studies have reported a strong relationship between inflammatory response and elevated RDW [13, 14] and that RDW is associated with the progression and mortality of various diseases, including stroke [13, 15]. A recent research has shown that the hemoglobin-to-RDW ratio (HRR), a combined indicator of RDW and hemoglobin, is a more accurate predictor of depression than RDW alone in people over 65 years of age [16]. Serum albumin is the most abundant circulating protein in the blood, synthesized by the liver, reflecting nutritional status [17] and anti-inflammatory effects [18]. Albumin is also an important non-enzymatic antioxidant [19]. Previous studies have linked low blood albumin levels to depressive symptoms in patients with different types of psychiatric disorders, including patients with schizophrenia and those who have attempted suicide [20–22]. The RDW and albumin concentrations convey information about inflammation, oxidative stress and nutritional-related information from different perspectives [13, 23, 24] and are both easily accessible from laboratory tests. Hence, the RDW-to-albumin ratio (RAR) generated by the combination of these two markers may be more valuable in predicting depression than either metric alone.

Therefore, we hypothesized that elevated RAR may be associated with increased depression. Potential correlations between RAR and depression were then explored using data obtained from NHANES from 2011 to 2018. Additionally, we conducted a comparative analysis of RAR, RDW, albumin, and HRR.

Methods

This study followed the reporting guidelines of the Strengthening Reporting of Observational Studies in Epidemiology (STROBE). It used a nationwide cross-sectional design with secondary analysis of publicly accessible and de-identified data from NHANES. Therefore, the study did not require any supplemental institutional review board approval or informed consent.

Study population

The NHANES database is a comprehensive national survey conducted since 1999. It assesses the health, nutrition, and social status of the U.S. population using complex, multistage, and stratified sampling techniques. For more information about the data, visit (https://www.cdc.gov/nchs/nhanes/index.htm). Comprehensive information on the design, methods, and weighting of NHANES has been published previously [25]. All study procedures were authorized by the National Center for Health Statistics Ethics Review Board prior to data collection, and all participants signed informed consent forms. Surveys used household questionnaires, telephone interviews, and examinations conducted by healthcare professionals and trained personnel to collect data.

Data used in this cohort study were from NHANES from 2011 to 2018 and included demographic information, physical examination results, laboratory measurements, and questionnaire items. Exclusion criteria for the analysis included participants younger than 20 years of age (N= 16,539), pregnant women (N= 247), participants with missing RAR data (N= 2,342), and participants with missing data from the PHQ-9 questionnaire (N= 1,878). The final analysis included 18,150 eligible participants, as shown in Fig. 1.

RAR

RAR was extracted from blood samples. To ensure validity and comparability of data, rigorous laboratory tests were performed according to standardized sampling protocols. In the mobile examination centers, RDW (percentage) was measured by a Coulter analyzer using peripheral blood. Serum albumin concentration was measured by bromocresol violet method using a Roche Cobas 6000 chemistry analyzer.

RAR was calculated based on the above metric: RAR = RDW (%)/Albumin (g/dL).

Depression

Assessment of depression was assessed using the Patient Health Questionnaire-9 (PHQ-9), a self-report depression screening tool based on nine items reflecting major depressive disorder from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. It is a reliable and valid measure of depression severity and is used to ask how often depressive symptoms have occurred in the past two weeks. Scores for each item on the questionnaire are defined as 0 (not at all) to 3 (almost daily) points, with a total score range of 0–27. Scores of 10 or

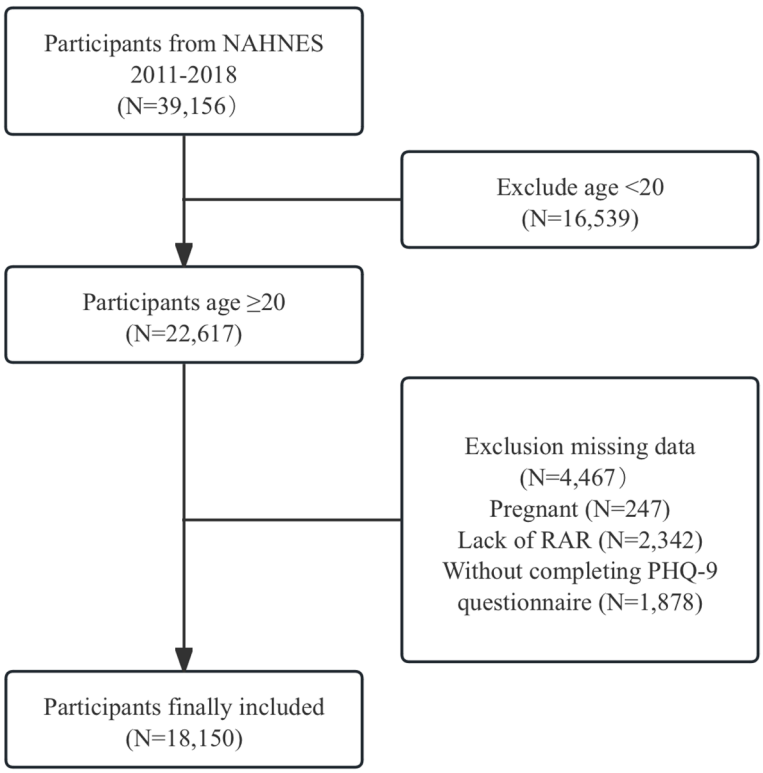

Fig. 1 Flowchart of the sample selection from NHANES 2011–2018

more indicated the presence of depression, and the sensitivity and specificity of this screening tool is good (88%) [26, 27].

Covariables

In this study, covariates included demographic characteristics, lifestyle factors, and clinical information. Demographic characteristics comprised baseline age, sex, race/ethnicity, education level, marital status, and the poverty income ratio (PIR). Lifestyle factors included body mass index (BMI), sleep duration, smoking status, and drinking status. Drinking status was determined through two 24-h dietary recall interviews. Participants were classified as drinkers if they reported alcohol consumption in at least one of the 24-h dietary recalls. Smoking status was determined based on the criterion of smoking at least 100 cigarettes during a person's lifetime. Information on other demographic characteristics and lifestyle factors was collected through self-report questionnaires. Clinical information, including the status of hypertension, diabetes, coronary heart disease, and stroke, was obtained through self-reports from participants or proxies.

Statistical analysis

In accordance with the NHANES analysis guidelines, we included a complex sampling design and test sample weights for mobile examination centers in our study. Prior to data analysis, baseline variables were checked for missing values. The percentage of missing data in the variables ranged from 0% to 9.1% (Supplementary Fig. 1). In order to include these data in the analysis, we interpolated the missing data using multiple imputations by chained equations (MICE), using the `mice` package in the R language. The predictive mean matching method was used, and the default interpolation number was 5 ($k = 5$).

In the descriptive statistics, continuous variables were presented as weighted means (weighted standard errors), while categorical variables were presented as unweighted counts (weighted percentages). Analysis of variance (ANOVA) and chi-square tests were used to examine baseline characteristics of participants across the quartiles of RAR. Weighted multivariable linear regression and logistic regression analyses were employed to assess the linear relationship between RAR and depression. The linear relationship between RAR and depression was tested using the trend test after converting RAR from a continuous variable to a categorical variable (quartiles). In addition, potential nonlinear associations between RAR and depression were assessed using restricted cubic spline (RCS) regression in fully adjusted models, and the diagnostic value of RAR for depression was assessed

using receiver operating characteristic (ROC) analysis. Furthermore, stratified subgroup analyses were performed for all covariates. Interaction effects were tested by adding interaction terms in the fully adjusted model. To validate the robustness of the research findings, we conducted sensitivity analyses in the study. First, we repeated the analysis after excluding participants with missing covariates (N= 2,604). Second, PHQ-9 scores were analyzed as a continuous variable using multivariate linear regression. Statistical analyses were performed using R Studio (version 4.2.0) and EmpowerStats (version 4.2). A two-sided p-value of less than 0.05 was considered statistically significant for this study.

Results

Baseline characteristics

A total of 21,006 participants were excluded from this study, leaving a final sample as presented in Fig. 1. The weighted mean age of the participants was 48.20 (0.32) years, with women accounting for a weighted proportion of 50.70% and non-Hispanic White individuals for 66.45%. Among these participants, 1,627 (representing a weighted proportion of 8.06%) had a PHQ-9 score ≥10. We divided RAR into quartiles: Q1 (2.21–2.93), Q2 (2.93–3.16), Q3 (3.16–3.46), and Q4 (3.46–9.62). Compared with those in lower quartiles, participants in higher RAR quartiles were more likely to be female, non-Hispanic Black, less educated, and be separated/divorced/widowed. They were more to likely have longer sleep duration and higher prevalence rates of hypertension, diabetes, coronary heart disease, and stroke, and yet were less likely to drink alcohol. Additionally, individuals with higher RAR had lower levels of PIR, albumin, and HRR but higher levels of BMI and RDW (Table 1).

Association between RAR and depression

In this study, the unadjusted (Model 1) linear correlation analyses indicated a positive association between RAR and depression (OR =1.69, 95% CI: 1.51, 1.89). This association was also consistently observed in Models 2 and 3. In the fully adjusted model that accounted for all confounders (Model 3), the association between RAR and depressive symptoms remained consistent (OR =1.22, 95% CI: 1.05, 1.41). It suggested that for every unit increase in RAR, the likelihood of developing depressive symptoms increased by 22% (Table 2). The correlation between RAR and depression was stronger when compared to RDW (OR =1.05, 95% CI: 0.99, 1.11) (Supplementary Table 1). Furthermore, the above associations remained statistically significant after categorizing RAR into quartiles (P for trend =0.024). Participants in the highest quartile of RAR had a 30% increased risk of depression compared to participants in the lowest quartile of RAR (OR =1.30, 95% CI: 1.04, 1.63).

We used RCS regression to model and visualize the relationship between predicted RAR and the odds ratio (OR) (Fig. 2). After adjusting for all covariates, there was a linear positive correlation between RAR and depression (p for nonlinear =0.673), with a threshold of 3.16. In addition, ROC analysis showed that among depressed individuals, the area under the curve (AUC) of RAR was 0.583, exceeding that of albumin (AUC =0.575), RDW (AUC =0.562) and HRR (AUC =0.560) (Supplementary Fig. 2).

Subgroup analyses

To investigate the potential association between RAR and depression in specific populations, we performed subgroup analyses and interaction tests for all baseline characteristics with reference to previous studies [28–31]. The interactions for age, race/ethnicity, education level, marital status, BMI, sleep duration, smoking status, and prior disease history was not significant after stratified analysis (all P-interaction >0.05). However, the association between RAR levels and depression may be moderated by sex (P-interaction$N$= 0.031), alcohol drinking status (P-interaction$N$= 0.040), and PIR (P-interaction$N$= 0.002). These data suggest that the effect of RAR on depression remained relatively stable across most subgroups (Fig. 3).

Sensitivity analyses

After excluding participants with missing covariates (N= 2,604), we still observed that elevated RAR levels were associated with a higher risk of depression (OR =1.22, 95% CI: 1.03, 1.45). When linear regression was performed with PHQ-9 scores as a continuous variable, all models were statistically significant, indicating that RAR levels were positively associated with PHQ-9 scores (β =0.49, 95% CI: 0.30, 0.67) (Supplementary Table 2).

Discussion

This study explored the relationship between RAR and depression among U.S. adults based on data from a large-scale cross-sectional survey. First, the prevalence of depression among study participants was 8.96%, a finding consistent with the national average of 7.5%−11.0% for the prevalence of major depressive disorder (MDD) as reported by the National Comorbidity Survey (NCS) [32]. Second, our study revealed for the first time a positive association between high RAR and increased depression. Specifically, for each unit increase in RAR, the odds of depression increased by 22% (adjusted OR =1.22, 95% CI: 1.05–1.41). Further analysis showed a linear relationship between RAR and depression with a threshold of 3.16. ROC analysis validated the superior

Table 1 Basic characteristics of participants by RAR quartile (weighted)

	RAR				***P*-value**
	Q1 (2.21–2.93)	**Q2 (2.93–3.16)**	**Q3 (3.16–3.46)**	**Q4 (3.46–9.62)**	
	***N* = 4,462**	***N* = 4,549**	***N* = 4,571**	***N* = 4,568**	
Age (years)	41.42 (0.48)	48.19 (0.40)	51.66 (0.49)	53.84 (0.42)	< 0.001
Sex (%)					< 0.001
Male	2824 (61.92)	2466 (52.65)	2099 (44.76)	1614 (32.21)	
Female	1638 (38.08)	2083 (47.35)	2472 (55.24)	2954 (67.79)	
Race/ethnicity (%)					< 0.001
Mexican American	604 (8.09)	705 (9.38)	637 (8.37)	561 (8.44)	
Other Hispanic	426 (5.59)	507 (6.24)	547 (6.73)	401 (6.05)	
Non-Hispanic white	1964 (72.05)	1844 (68.73)	1711 (64.95)	1498 (57.21)	
Non-Hispanic black	525 (4.93)	724 (7.31)	1096 (12.15)	1614 (20.52)	
Other race/multiracial	943 (9.33)	769 (8.33)	580 (7.79)	494 (7.77)	
Education level (%)					< 0.001
Below high school	788 (10.94)	950 (13.13)	1001 (14.14)	1068 (16.48)	
High school or equivalent	882 (19.41)	1004 (22.54)	1045 (22.65)	1154 (28.16)	
Above high school	2792 (69.65)	2595 (64.33)	2525 (63.22)	2346 (55.36)	
Marital status (%)					< 0.001
Married/living with partner	2719 (62.89)	2851 (65.91)	2660 (63.21)	2429 (58.61)	
Separated/divorced/widowed	596 (11.86)	882 (17.23)	1162 (21.47)	1379 (26.42)	
Never married	1147 (25.25)	816 (16.86)	749 (15.31)	760 (14.98)	
PIR	3.16 (0.06)	3.10 (0.06)	2.95 (0.05)	2.61 (0.05)	< 0.001
BMI (kg/m^2)	26.81 (0.14)	28.60 (0.16)	30.38 (0.21)	32.78 (0.19)	< 0.001
Sleep duration (hours)	7.21 (0.03)	7.27 (0.03)	7.29 (0.03)	7.34 (0.03)	0.049
Smoking status (%)					0.015
No	2648 (58.65)	2581 (55.47)	2532 (54.00)	2510 (55.57)	
Yes	1814 (41.35)	1968 (44.53)	2039 (46.00)	2058 (44.43)	
Alcohol drinking status (%)					< 0.001
No	2934 (59.87)	3195 (64.67)	3410 (71.48)	3631 (77.50)	
Yes	1528 (40.13)	1354 (35.33)	1161 (28.52)	937 (22.50)	
Hypertension (%)					< 0.001
No	3337 (76.48)	3034 (69.16)	2688 (62.46)	2256 (53.60)	
Yes	1125 (23.52)	1515 (30.84)	1883 (37.54)	2312 (46.40)	
Diabetes (%)					< 0.001
No	4075 (93.52)	3921 (89.01)	3714 (84.48)	3354 (77.29)	
Yes	303 (4.49)	521 (9.03)	715 (12.91)	1050 (19.26)	
Borderline	84 (1.99)	107 (1.96)	142 (2.61)	164 (3.45)	
Coronary heart disease (%)					< 0.001
No	4382 (98.70)	4395 (96.92)	4353 (95.19)	4257 (93.35)	
Yes	80 (1.30)	154 (3.08)	218 (4.81)	311 (6.65)	
Stroke (%)					< 0.001
No	4395 (98.75)	4414 (97.77)	4388 (97.12)	4262 (94.10)	
Yes	67 (1.25)	135 (2.23)	183 (2.88)	306 (5.90)	
RDW (%)	12.63 (0.02)	13.13 (0.01)	13.58 (0.02)	14.96 (0.04)	< 0.001
Albumin (g/dL)	4.59 (0.01)	4.32 (0.00)	4.13 (0.01)	3.87 (0.01)	< 0.001
HRR	1.17 (0.00)	1.10 (0.00)	1.04 (0.00)	0.89 (0.01)	< 0.001
PHQ-9	2.60 (0.08)	2.84 (0.08)	3.28 (0.10)	3.81 (0.08)	< 0.001
Depressive symptoms					< 0.001
< 10	4165 (93.99)	4215 (92.93)	4142 (91.37)	4001 (88.35)	
≥ 10	297 (6.01)	334 (7.07)	429 (8.63)	567 (11.65)	

Table 1 (continued)

Mean ± SE for continuous variables: the *P* value was calculated by the weighted linear regression model

N (%) for categorical variables: the *P* value was calculated by the weighted chi-square test

Table 2 Association of RAR with depression

Exposure	OR (95% CI)		
	Model 1	**Model 2**	**Model 3**
RAR	1.69 (1.51, 1.89)	1.60 (1.40, 1.82)	1.22 (1.05, 1.41)
RAR quartile			
Quartile 1	Reference	Reference	Reference
Quartile 2	1.19 (0.94, 1.51)	1.18 (0.93, 1.50)	1.10 (0.87, 1.40)
Quartile 3	1.48 (1.17, 1.86)	1.44 (1.14, 1.83)	1.17 (0.91, 1.53)
Quartile 4	2.06 (1.70, 2.51)	1.93 (1.55, 2.42)	1.30 (1.04, 1.63)
P for trend	< 0.001	< 0.001	0.024

Model 1: no covariates were adjusted

Model 2: age, sex, and race/ethnicity were adjusted

Model 3: age, sex, race/ethnicity, education level, marital status, PIR, BMI, sleep duration, smoking status, alcohol drinking status, hypertension status, diabetes status, coronary heart disease status and stroke status were adjusted. 95% CI, 95% confidence interval

diagnostic potential of RAR in the diagnosis of depression compared to RDW, albumin, and HRR. In addition, subgroup analyses revealed that the association between RAR and depression may manifest differently in specific populations.

The presence of a chronic inflammatory cellular environment contributes to an increase in apoptosis at the molecular level, leading to dysregulation of red blood cell (RBC) homeostasis and even inducing inflammatory anemia [33]. Depression is a common and difficult-to-treat condition associated with a chronic low-grade inflammatory response, cell-mediated immune activation, and activation of the compensatory anti-inflammatory reflex system (CIRS), accompanied by increased oxidative and nitrosative stress (O&NS) [34, 35]. The manifestations of inflammation may present a duality, and this complexity stems from the multifaceted and dynamic nature of the inflammatory process. Although inflammation may be a good acute protective response, it may also perform poorly in chronic states such as depression. Whether this chronic systemic inflammation stems from psychosocial stress, poor diet, physical inactivity, obesity, smoking, altered intestinal permeability, or sleep and vitamin D deficiency, early detection and control of inflammation can help to prevent disease progression and improve prognosis [34, 36, 37].

Previous studies have shown that RDW can be used as an indicator of chronic inflammation [13, 38]. Inflammatory response can affect erythropoiesis, life cycle half-life and deformability, which in turn promotes erythrocyte expansion, leading to elevated RDW levels [39]. Additionally, albumin, an important indicator for assessing nutritional status, is also capable of reflecting inflammation levels [40]. Low albumin levels have been shown to be associated with an increased

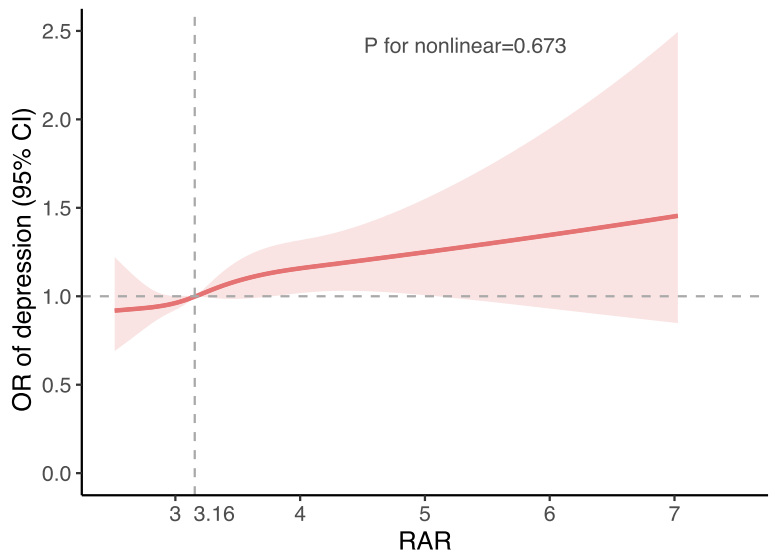

Fig. 2 The association between RAR and depression. Adjusted for age, sex, race/ethnicity, education level, marital status, PIR, BMI, sleep duration, smoking status, alcohol drinking status, hypertension status, diabetes status, coronary heart disease status and stroke status

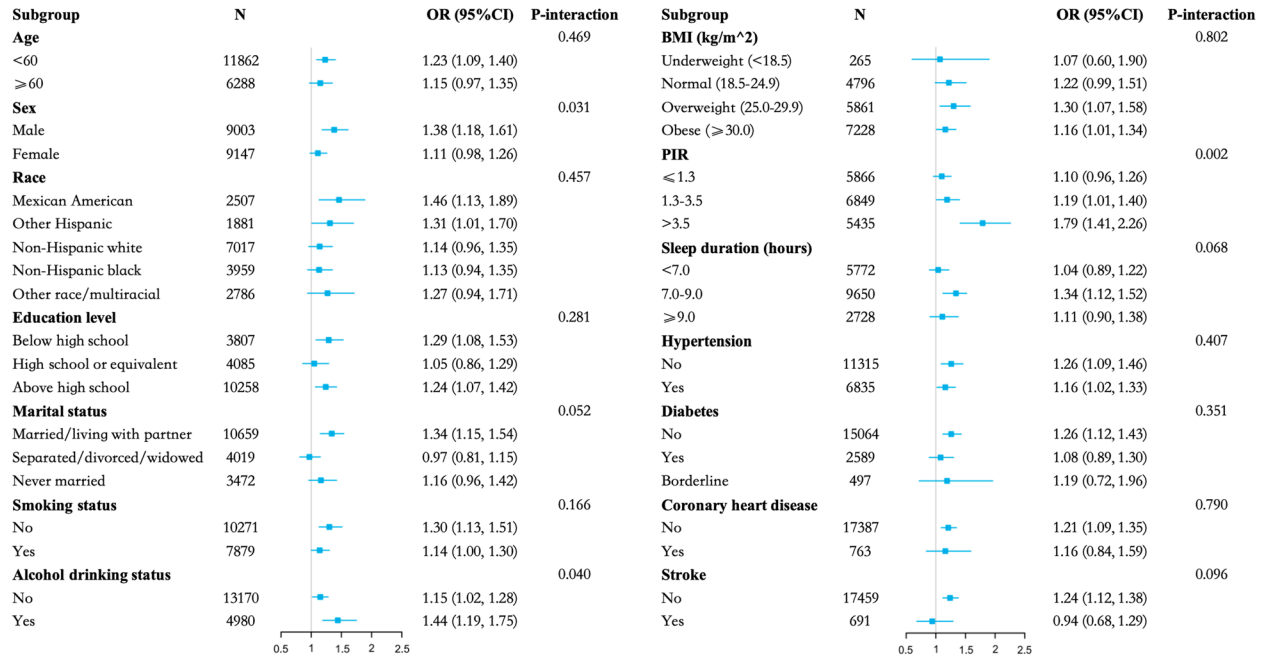

Fig. 3 Subgroups analyses of the association between RAR and depression

risk of depression [41, 42]. RAR, as a combined indicator of RDW and albumin, reflects the combined information of inflammatory status and nutritional status of a patient. It is a potential novel biomarker, and can be obtained quickly and easily by laboratory tests. Many studies have explored the association of RAR with various diseases, including diabetic kidney disease (DKD) [43], rheumatoid arthritis [44], and pancreatitis [45]. For example, in diabetic patients, studies have found a causal relationship between sterile low-grade inflammation and DKD, and high RAR is positively associated with DKD risk [43]. In addition, RAR can be used to predict all-cause mortality as well as the risk of death due to various chronic diseases including cardiovascular diseases and cancer [46]. The results of our ROC analysis showed that the combined indicator RAR was superior to RDW or albumin alone in its ability to assess depression. This may be related to the fact that RAR integrates information on multiple aspects such as inflammation, oxidative stress, nutrition, and thus assesses the physiological state of multidimensional dysfunction [13, 47]. In addition, the area under the curve of RAR (AUC = 0.583) was also higher than that of another novel inflammation indicator, HRR (AUC = 0.560). HRR has been shown to be an independent risk factor for depression in people older than 65 years of age [16]. These results suggest that RAR may have greater potential as a potential biomarker for early detection and assessment of the risk of depression in adults.

The association of high RDW with an increased risk of developing depression has gained increasing attention in recent years [48, 49]. A predictive models of depression constructed on the basis of blood biomarkers has emphasized RDW as one of the important features [50]. Interestingly, Shafiee M et al. found that the association between RDW and depression was more significant in men [49]. This is similar to our observation in subgroup analysis that the association between RAR and depression was significantly stronger in males than females. Jiang R et al. also found that the association between inflammation and depression was more pronounced in males when they examined the association between frailty and depression [51]. We hypothesize that this phenomenon may be related to gender-related hormonal dysregulation. It has been shown that males and females differ in the expression of immune responses and inflammatory mediators [9, 52], and that inflammation levels may differ due to changes in sex hormones [53, 54]. However, it has also been shown that higher levels of inflammation are more strongly associated with the course of chronic depression in women only [55]. This issue still requires further research. In subgroup analyses, we also observed that the association between RAR and depression was stronger in alcohol-drinking and high-income populations. Alcohol addiction has been shown to be a

risk factor for depression [56], and alcohol withdrawal can lead to an increase in immune signaling molecules and neuroinflammation in the brain [57]. In addition, patients with alcohol use disorder (AUD) typically have lower serum albumin levels [58], which may further exacerbate the risk of depression. In addition, high-income groups may face stressors such as a fast pace of life and social competition, which exacerbate various chronic diseases [59–61]. Behavioral factors such as sedentary lifestyle are also strongly associated with increased risk of depression and are moderated by inflammation [56, 62]. A global epidemiologic study showed that residents of high-income regions have the highest prevalence of immune-mediated inflammatory diseases (IMIDs), including atopic dermatitis, inflammatory bowel disease, and others [63], which may be associated with environmental exposures and lifestyle factors [64, 65]. Whereas the risk of depression in low-income groups may be influenced by multiple and complex factors, RAR fails to effectively capture risk or its role is partially masked.

Although the exact mechanisms underlying the association between elevated RAR levels and the risk of depression are not yet fully understood, the relationship between RDW and inflammation, as well as the findings of RAR and inflammation-related diseases, may at least in part explain the associations we found between depression and RAR. In particular, low levels of albumin, an important indicator of nutritional status, may play an important role in the development of depression, further reinforcing the potential of RAR as a comprehensive biomarker in depression screening.

Our study has several strengths. First, to our knowledge, it is the first study to identify a positive correlation between the RAR and depression. The rigorous quality control and sophisticated sampling design of the NHANES database allowed us to assess this association in a nationwide sample of adults. In addition, subgroup analyses revealed that the association between RAR and depression was significantly stronger among men, alcohol-drinking, and high-income groups. Sensitivity analyses further enhanced the robustness and reliability of the results.

However, it also has some limitations. First, as a cross-sectional study, it cannot establish a causal relationship between RAR and depression. Second, the study relied on self-reported questionnaires to assess depression rather than clinical diagnoses, which may introduce reporting bias. Although the PHQ-9 is a highly reliable tool for assessing the severity of depressive symptoms, it does not capture the full complexity and nuances of depression. Third, despite adjustments for various factors and conducting sensitivity analyses, unmeasured confounders, such as medication use and diet, may still influence the results. Future longitudinal studies could further explore the causal relationship between RAR and depression and evaluate other potential confounding factors.

Conclusions

Our study demonstrated a positive correlation between higher RAR and higher prevalence of depression in US adults. RAR can be assessed quickly and easily by routine laboratory tests and may serve as a simple and practical parameter for the early detection of depression, which may be important for the prevention of depression and improvement of prognosis. Further studies are needed to validate and explore the underlying mechanisms.

Abbreviations

RDW	Red blood cell distribution width
RAR	Red blood cell distribution width-to-albumin ratio
NHANES	National Health and Nutrition Examination Survey
HRR	Hemoglobin-to-red blood cell distribution width ratio
WHO	World Health Organization
hs-CRP	High-sensitivity c-reactive protein
STROBE	Strengthening Reporting of Observational Studies in Epidemiology
CDC	Centers for Disease Control and Prevention
BMI	Body mass index
PIR	Family poverty income ratio
PHQ-9	Patient Health Questionnaire-9
SE	Standard error
OR	Odds Ratio
95% CI	95% Confidence interval
AUC	Area under the curve
RBC	Red blood cell
MDD	Major depressive disorder
NCS	National Comorbidity Survey
CIRS	Compensatory anti-inflammatory reflex system
O&NS	Oxidative and nitrosative stress
DKD	Diabetic kidney disease

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12888-025-06907-z.

Supplementary Material 1.

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Authors' contributions

Y.Z. and S.Q. conceived the study design. Y.Z. and L.Z. performed the data analyses, and Y.T. collected the data and helped to perform the data analysis. Y.Z. wrote the manuscript. S.Q. reviwed and provided the critical revision. All authors approved the submitted and final versions.

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Data availability

The datasets generated and analyzed in the current study are available at NHANES website: https://www.cdc.gov/nchs/nhanes/index.htm.

Declarations

Ethics approval and consent to participate

The protocols of NHANES were approved by the institutional review board of the National Center for Health Statistics, CDC (https://www.cdc.gov/nchs/nhanes/irba98.htm). NHANES has obtained written informed consent from all participants before enrolment.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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