



Research paper

The association between red blood cell distribution width-to-albumin ratio and risk of depression: A cross-sectional analysis of NHANES

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Highlights

- Elevated RAR is independently linked to a great risk of depression.
- A linear relationship between RAR and depression was identified.
- RAR may serve as a novel biomarker for mental health risk assessment.

Abstract

Background

The red blood cell distribution width-to-albumin ratio (RAR) serves as an indicator of systemic inflammation and nutritional status. This study examines the relationship between RAR and depressive disorder in U.S. adults, utilizing data from the National Health and Nutrition Examination Survey (NHANES).

Methods

We applied logistic regression to evaluate the link between RAR and depressive risk, with its corresponding odds ratios (OR) and 95% confidence intervals (CI) calculated. Restricted cubic spline (RCS) was adopted to assess the potential linear association, while the receiver operating characteristic (ROC) curve was used to evaluate the ability of RAR to predict the depressive risk, with the result presented as an area under the curve (AUC).

Results

After adjusting for relevant covariates, a positive association between RAR and clinically relevant depression persisted (OR=1.33, 95% CI: 1.18–1.51, $P<0.001$). Participants in the highest RAR quartile exhibited a greater risk of clinically relevant depression than those in the lowest quartile (OR=1.36, 95% CI: 1.10–1.67, $P=0.005$). A linear relationship between RAR and clinically relevant depression was identified (P for non-linear=0.473), with RAR showing a strong predictive ability for depressive risk (AUC=0.7467). Stratified analysis showed significant interactions among smoking ($P=0.045$), marital status ($P<0.001$), and RAR's effect on depression outcome.

Conclusions

Elevated RAR is independently linked to clinically relevant depression, indicating its potential as a novel biomarker for mental health risk assessment. Further longitudinal studies are necessary to establish causality and evaluate its clinical relevance.

Introduction

Depression is a prevalent mental health issue with significant public health implications, affecting millions worldwide. Despite extensive research, its biological mechanisms remain largely unclear, though systemic inflammation has emerged as a crucial factor (Frank et al., 2021). Chronic low-grade inflammation is linked to changes in neurotransmitter systems, impaired neuroplasticity, and dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis (Hassamal, 2023; Leonard, 2018). Although traditional inflammatory markers like C-reactive

protein (CRP) and interleukin-6 are well-researched, alternative biomarkers reflecting both inflammatory and nutritional states could provide new insights.

Notably, the red blood cell distribution width (RDW)-to-albumin ratio (RAR) is gaining interest as a potential indicator of systemic inflammation (Sun et al., 2022). While RDW has typically been associated with erythrocyte disorders, recent studies suggest its involvement in broader pathological conditions, including cardiovascular diseases, diabetes, and depression (Arkew et al., 2022; Liu et al., 2024; Xi et al., 2024). Hypoalbuminemia, a common indicator of chronic illness or malnutrition, has also been associated with poor mental health outcomes (McFarland et al., 2022). However, research on the combined predictive power of RDW and albumin for depression remains limited.

RAR has been identified as a predictor of adverse outcomes in various studies, including one that linked RAR to all-cause mortality in the general population (Hao et al., 2024). Recent findings further suggest that RAR could reflect chronic inflammation, serving as a prognostic marker for conditions such as heart failure and diabetes (Chen et al., 2024; Zhou et al., 2024). These patterns hint at the value of RAR as a surrogate marker of inflammatory dysregulation, which could extend to psychiatric disorders such as depression. Elevated RDW indicates oxidative stress and inflammation, while low albumin levels may reflect a dysregulated acute-phase response. As a composite of these two indicators, RAR captures the combined effects of inflammation and metabolic stress, emerging as a promising yet underexplored marker in mental health research.

This study investigates the relationship between RAR and depression in U.S. adults using data from the National Health and Nutrition Examination Survey (NHANES). NHANES provides nationally representative health data, making it suitable for exploring novel biomarkers in diverse populations. We hypothesize that higher RAR values are positively associated with depression, even after adjusted for relevant covariates. Exploring the link between RAR and depression could enhance screening and early intervention, especially for at-risk populations. If RAR is confirmed as a reliable biomarker for depression, it could be incorporated into regular health assessments, providing a novel, cost-effective means to identify individuals who may need closer monitoring or preventive measures.

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Section snippets

Study design and population

This cross-sectional study utilizes publicly available data from the NHANES, a nationally representative survey designed to assess the health and nutritional status of the U.S. population. The NHANES is a comprehensive and nationally representative survey conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. The NHANES combines interviews, physical examinations, and laboratory tests to assess the health and nutritional status of the U.S. ...

Participant characteristics

A total of 23,657 adults from NHANES met the inclusion criteria. The majority were non-Hispanic White (70.29%), with 50.46% identifying as female. Among them, 2021 individuals screened positive for clinically relevant depression. As presented in Table 1, those with clinically relevant depression were more likely to be younger, female, smokers, physically inactive, obese, and had higher rates of chronic illnesses such as hypertension and diabetes compared to their non-depressed peers. ...

Discussion

This study reveals a significant link between the RAR and clinically relevant depression in U.S. adults, based on nationally representative NHANES data. After adjusting for demographic, lifestyle, and clinical factors, higher RAR values were associated with a greater risk of clinically relevant depression. These results indicate that RAR, an easily accessible biomarker, may reflect the inflammatory and metabolic processes underlying depression.

Current research on the link between RDW and ...

Conclusion

This study demonstrates a significant association between higher RAR levels and clinically relevant depression in U.S. adults, highlighting the impact of systemic inflammation and malnutrition on mental health. RAR may serve as a valuable biomarker for depression outcomes, aiding in early detection and personalized treatment approaches. ...

CRediT authorship contribution statement

Haobiao Liu: Writing – original draft, Visualization, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Rongqi Xiang:** Writing – original draft, Formal analysis, Data curation. **Zhuohang Chen:** Writing – review & editing, Visualization, Validation, Data curation. ...

Informed consent statement

Informed consent was obtained from all subjects involved in the study. ...

Institutional review board statement

This study is an analysis derived from publicly available NHANES data, which was acquired with the approval of the Ethics Review Board of the National Center for Health Statistics (<https://www.cdc.gov/nchs/nhanes/irba98.htm> ↗). Given that the NHANES public use data does not contain individually identifiable information, ethical review, and approval were waived for this study. ...

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Declaration of competing interest

The authors declare no conflict of interest. ...

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