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# Association between Neutrophil Percentage-to-Albumin ratio and anemia risk: a population-based study

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**Anemia remains a significant global health challenge, driven by complex inflammatory mechanisms. This study investigated the association between neutrophil percentage-to-albumin ratio (NPAR) and anemia risk, utilizing data from 24,938 participants in the National Health and Nutrition Examination Survey (2005–2018). Multivariable logistic regression analysis revealed a significant association between NPAR and anemia risk (OR = 1.16; 95% CI 1.13–1.18, $p < 0.0001$). Two-piecewise regression analysis identified a nonlinear relationship with a threshold at NPAR 11.96: below this threshold, an inverse association was observed (OR = 0.88; 95% CI 0.79–0.98, $p = 0.0249$), while above it, a positive association was evident (OR = 1.21; 95% CI 1.18–1.25, $p < 0.0001$). Subgroup analyses demonstrated stronger associations in males, non-Hispanic Whites, diabetic patients, and individuals who were married or living with a partner. These findings highlight the potential of NPAR as a novel biomarker for assessing anemia risk in clinical practice.**

**Keywords** NPAR, Anemia, NHANES, Inflammation marker

Anemia is a common condition characterized by reduced hemoglobin concentration resulting in impaired oxygen-carrying capacity[1]. It is often a manifestation of underlying causes, such as nutritional deficiencies, chronic diseases, or other health conditions, and may present with symptoms like fatigue, dizziness, weakness, and palpitations[2]. In severe cases, it may lead to organ damage or other serious health complications[3–5]. Anemia may result in a range of adverse effects, including impaired cognitive function, compromised immune system, and diminished work capacity[6]. In 2021, the global prevalence of anemia was 24.3%, approximately 1.92 billion people, and It is more common in female of reproductive age and children younger than 5 year[7]. The widespread impact of this health issue necessitates urgent global action to mitigate its occurrence and effects.

Inflammation is pivotal in anemia, with inflammatory anemia being the second most common type after iron deficiency anemia[8]. Inflammatory processes can contribute to anemia through mechanisms such as the suppression of erythropoiesis and the disruption of iron metabolism[9]. Specifically, in chronic inflammatory conditions, increased levels of cytokines can lead to reduced iron availability and impaired red blood cell production, resulting in anemia[10].

NPAR emerging as a cost-effective inflammatory biomarker, integrates two routinely measured parameters that reflect both immune response and nutritional status[11]. While NPAR has demonstrated prognostic value in cardiovascular diseases, kidney disorders, and various cancers[12–14], its relationship with anemia—a condition closely linked to inflammation—remains unexplored. Understanding this association could provide valuable insights into anemia's inflammatory mechanisms and potentially identify NPAR as a novel predictor for anemia risk in clinical practice. Here, we conducted a large-scale population-based study to investigate the relationship between NPAR and anemia, aiming to establish whether this accessible biomarker could serve as an early warning signal for anemia risk assessment.

## Methods

### Study population

The National Health and Nutrition Examination Survey (NHANES) is a cornerstone U.S. health surveillance program. This complex, multistage probability sampling study gathers comprehensive health data from the

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non-institutionalized civilian population. NHANES combines in-home interviews, mobile examination center assessments, and laboratory analyses. This study utilized publicly available data from NHANES, which has been approved by the National Center for Health Statistics Research Ethics Review Board, and all NHANES participants provided informed consent. As this study uses publicly available NHANES data, it was exempt from additional institutional review board approval. All methods were performed in accordance with the relevant guidelines and regulations.

Data for this analysis were sourced from seven biennial cycles of NHANES conducted between 2005 and 2018. Of the 70,190 participants who completed the interviews, 42,143 were aged ≥ 18 years. Exclusions were made for individuals lacking data on hemoglobin (Hgb), NPAR values, relevant covariates, as well as pregnant women. Consequently, the final cross-sectional study sample comprised 24,938 participants. Figure 1 illustrates the sample selection process in detail.

## Anemia ascertainment

The World Health Organization's criteria were utilized to establish the definition of anemia in this study[15]. Anemia was defined by hemoglobin levels under 13 g/dL in males and under 12 g/dL in non-pregnant women. The prevalence of anemia was the primary outcome variable in this study.

## Definition of NPAR

Hematological indices were evaluated using the NHANES CBC protocol, employing a Beckman Coulter DxH 900 automated system (Brea, CA, USA). NPAR was determined by the formula: Neutrophil percentage (%) × 100/Albumin (g/dL). NPAR served as the exposure variable in this study.

## Covariates

Potential confounding factors affecting the NPAR-anemia association were incorporated into the analysis. These included age, gender, race/ethnicity (Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, other race), education level (less than high school, high school, more than high school), marital status (married/living with partner, widowed/divorced/separated, never married), poverty-to-income ratio (income to poverty ratio), body mass index (BMI), smoking status (current, former, never), drinking status, and chronic medical conditions such as diabetes, hypertension, kidney disease, congestive heart failure, stroke, thyroid disease, and cancer. Additionally, white blood cell (WBC) counts, red blood cell (RBC) counts, platelet counts, and albumin levels were included. Chronic medical conditions were identified based on affirmative responses to whether a doctor had previously diagnosed the condition, as recorded in the questionnaire.

## Statistical analysis

The demographic and clinical characteristics were presented as median (Q25, Q75) and weighted percentages. The differences in general characteristics were assessed using the weighted $\chi^2$ test and weighted linear regression models. Univariable and multivariable logistic regression analyses were performed to investigate the NPAR-anemia relationship. In the multivariable analysis, NPAR was treated as a continuous or tertile categorical variable. Model 1 included no covariates; Model 2 adjusted for age, gender, and race; Model 3 further adjusted for education, marital status, income to poverty ratio, BMI, smoking and drinking status, diabetes, hypertension,

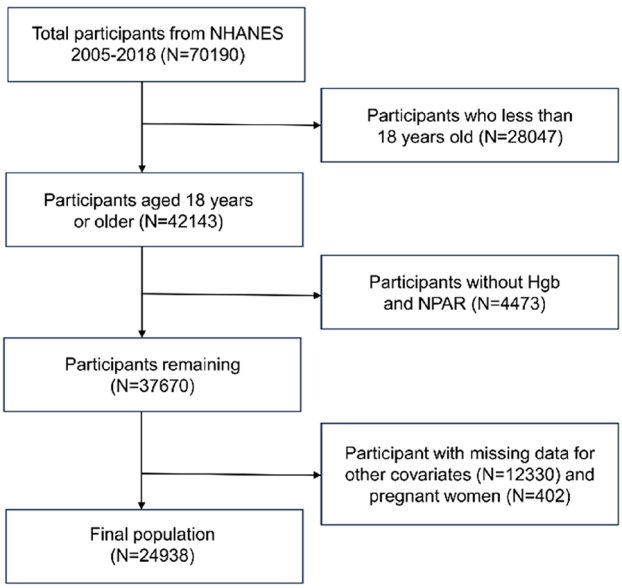


**Fig. 1**. Flowchart of participant selection. NHANES, National Health and Nutrition Examination Survey; Hgb, hemoglobin; NPAR, neutrophil percentage-to-albumin ratio.

and other chronic diseases. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, with a P-value of < 0.05 denoting statistical significance.

Regression analysis was performed to investigate the association between NPAR and anemia, stratified by factors such as age, gender, race, education, marital status, income to poverty ratio, BMI, smoking and drinking status, diabetes, hypertension, kidney disease, congestive heart failure, stroke, thyroid disease, and cancer. Interaction P-values were also calculated for these subgroups.

The nonlinear relationship between NPAR and anemia was explored using generalized additive models and smooth curve fitting. Upon identifying nonlinearity, a recursive method was employed to determine the inflection point in the NPAR-anemia association. A two-piecewise linear regression model was then applied to each side of this point. All analyses were performed using R (version 4.2.0) and EmpowerStats (version 4.2), with statistical significance set at $P < 0.05$.

## Results

### Baseline characteristics

Substantial disparities were observed between participants with and without anemia (Table 1). Anemic individuals were older (median age 51 vs. 46 years, $p < 0.0001$) and predominantly female (66.38% vs. 47.31%, $p < 0.0001$). Non-Hispanic Blacks were more prevalent in the anemic group (28.73% vs. 8.42%, $p < 0.0001$). Anemia associated with lower socioeconomic status (median income to poverty ratio 2.37 vs. 3.26, $p < 0.0001$) and higher rates of diabetes, hypertension, and kidney disease (all $p < 0.0001$). These findings highlight the complex relationship between anemia and various health and socioeconomic factors.

Analysis of NPAR quartiles revealed significant demographic and health characteristic variations (Table 2). Higher NPAR quartiles associated with increased age (median age: 43 to 50 years, $p < 0.0001$) and a greater proportion of females (39.36–57.88%, $p < 0.0001$). Non-Hispanic Whites predominated in higher quartiles (65.33–74.73%, $p < 0.0001$). Prevalence of diabetes, hypertension, kidney disease and anemia increased with higher NPAR (all $p < 0.0001$). Hematological parameters showed distinct trends: WBC and PLT counts increased, while RBC, Hb concentration decreased with rising NPAR (all $p < 0.0001$). Additionally, serum albumin levels decreased as NPAR increased. These findings highlight the intricate relationship between NPAR and diverse health indicators.

### Association between NPAR and anemia

Multivariable logistic regression assessed the NPAR-anemia association. Table 3 displays outcomes from both crude and adjusted analyses. We identified a consistent positive association between NPAR and anemia across all models. Even after adjusting for all covariates in Model 3, this association remained robust (OR = 1.16; 95% CI, 1.13–1.18; $p < 0.0001$), suggesting that each unit increase in NPAR is linked to a 16% higher risk of anemia. When analyzing NPAR by tertiles, the fourth quartile showed a markedly higher prevalence of anemia in Model 1 (OR = 2.57; 95% CI, 2.16–3.05; $p < 0.0001$), Model 2 (OR = 2.54; 95% CI, 2.12–3.03; $p < 0.0001$), and Model 3 (OR = 2.50; 95% CI, 2.09–2.98; $p < 0.0001$) compared to the first quartile. All models showed a significant upward trend in anemia prevalence with increasing NPAR levels (p for trend < 0.0001). However, further covariate-adjusted smoothed curve analysis revealed a more nuanced, non-linear relationship between NPAR and anemia prevalence, specifically an inverted U-shaped association (Fig. 2).

Table 4 illustrates a significant positive association between NPAR values and anemia risk in the standard linear model (OR = 1.16, 95% CI 1.13–1.18, $P < 0.0001$). Two-piecewise regression revealed a pivotal NPAR threshold of 11.96. Below this value, NPAR inversely associated with anemia risk (OR: 0.88, 95% CI 0.79–0.98, $P = 0.0249$), whereas above it, a positive association emerged (OR: 1.21, 95% CI 1.18–1.25, $P < 0.0001$). A log-likelihood ratio test affirmed the superior fit of the two-piecewise model over the standard model ($P < 0.001$), validating its utility in detecting threshold effects.

### Subgroup analyses

Subgroup analysis showed consistent NPAR-anemia associations across diverse demographic and clinical characteristics (Table 5). Notably, the association was stronger among diabetic individuals (OR 1.22, 95% CI 1.18–1.27) compared to non-diabetic participants (OR 1.14, 95% CI 1.11–1.17; p for interaction = 0.0010). Significant interactions were also observed for gender ($p = 0.0004$), race ($p = 0.0348$), and marital status ($p = 0.0052$). Interestingly, the association remained robust across age groups, education levels, and body mass index categories, suggesting a pervasive relationship between NPAR and anemia risk.

Smooth curve fits and generalized additive models illustrated in Figs. 3, 4 and 5 demonstrate a non-linear, inverted U-shaped NPAR-anemia association. This pattern is particularly evident in men, Non-Hispanic White individuals, and those without diabetes, suggesting a nuanced interaction across these populations.

Table 4 indicates a significant positive association between NPAR and anemia within the male subgroup, identified by the standard linear model (OR = 1.13; 95% CI 1.08–1.17; $P < 0.0001$). Piecewise regression revealed an NPAR threshold of 13.57, with a significant inverse relationship below (OR: 0.88, 95% CI 0.80–0.96, $P = 0.0043$) and a positive association above (OR: 1.26, 95% CI 1.20–1.33, $P < 0.0001$). The log-likelihood ratio test showed that the piecewise model significantly outperformed the standard linear model ($P < 0.001$), indicating a threshold effect. Similar trends are observed in Non-Hispanic Whites, with an inflection at 11.96 (reduction in anemia risk below threshold by 22%, $P = 0.0012$, and increase above by 24%, $P < 0.0001$). In subgroups without diabetes, thresholds of 12.05, show a 13% risk decrease below and 20% increase above these points, with all likelihood ratio tests confirming significant model differences ($P < 0.001$).

| | Non-anemia | Anemia | *p*-value |
|---|---|---|---|
| Age (year) | 46.00 (33.00 ,59.00) | 51.00 (40.00 ,69.00) | < 0.0001 |
| Gender (%) | | | < 0.0001 |
| Male | 52.69 | 33.62 | |
| Female | 47.31 | 66.38 | |
| Race/Ethnicity (%) | | | < 0.0001 |
| Mexican American | 7.76 | 7.32 | |
| Other Hispanic | 4.84 | 5.71 | |
| Non-Hispanic White | 72.59 | 52.55 | |
| Non-Hispanic Black | 8.42 | 28.73 | |
| Other Race | 6.39 | 5.69 | |
| Education level (%) | | | < 0.0001 |
| Less than high school | 3.87 | 6.91 | |
| High school | 32.74 | 36.11 | |
| More than high school | 63.39 | 56.98 | |
| Marital status (%) | | | < 0.0001 |
| Married/living with partner | 64.77 | 58.40 | |
| Widowed/divorced/separated | 17.93 | 26.31 | |
| Never married | 17.30 | 15.29 | |
| Income to poverty ratio | 3.26 (1.65 ,5.00) | 2.37 (1.23 ,4.34) | < 0.0001 |
| BMI (kg/m2) | 27.90 (24.26 ,32.50) | 28.30 (23.97 ,34.00) | 0.0054 |
| Smoking status (%) | | | < 0.0001 |
| Current | 22.37 | 14.12 | |
| Former | 27.20 | 29.51 | |
| Never | 50.43 | 56.37 | |
| Drinking status (%) | | | 0.0160 |
| Yes | 11.65 | 8.93 | |
| No | 88.35 | 91.07 | |
| Diabetes (%) | | | < 0.0001 |
| Yes | 8.34 | 20.03 | |
| No | 89.62 | 76.78 | |
| Borderline | 2.05 | 3.19 | |
| Hypertension (%) | | | < 0.0001 |
| Yes | 30.72 | 47.42 | |
| No | 69.28 | 52.58 | |
| Kidney disease (%) | | | < 0.0001 |
| Yes | 1.85 | 7.92 | |
| No | 98.15 | 92.08 | |
| Congestive heart failure (%) | | | < 0.0001 |
| Yes | 2.00 | 6.91 | |
| No | 98.00 | 93.09 | |
| Stroke (%) | | | < 0.0001 |
| Yes | 2.39 | 7.05 | |
| No | 97.61 | 92.95 | |
| Thyroid disease (%) | | | < 0.0001 |
| Yes | 10.36 | 14.40 | |
| No | 89.64 | 85.60 | |
| Cancer (%) | | | < 0.0001 |
| Yes | 9.81 | 15.13 | |
| No | 90.19 | 84.87 | |
| Continued | | | |

| | Non-anemia | Anemia | *p*-value |
|---|---|---|---|
| WBC ($10^3$ cells/uL) | 7.00 (5.80 ,8.40) | 6.70 (5.40 ,8.10) | 0.2311 |
| RBC ($10^3$ cells/uL) | 4.73 (4.43 ,5.05) | 4.07 (3.79 ,4.42) | < 0.0001 |
| PLT ($10^3$ cells/uL) | 240.00 (205.00 ,283.00) | 256.00 (204.00 ,314.00) | < 0.0001 |
| Albumin(g/dL) | 4.30 (4.10 ,4.50) | 4.00 (3.80 ,4.20) | < 0.0001 |
| NPAR | 13.62 (12.09 ,15.21) | 14.71 (12.79 ,16.46) | < 0.0001 |

**Table 1**. Weighted characteristics of the study population based on anemia. Median (Q1, Q3) for continuous variables: the P-value was calculated by the weighted linear regression model. (%) for categorical variables: the P-value was calculated by the weighted chi-square test. BMI, body mass index; WBC, white blood cell; RBC, red blood cell; PLT, platelet; NPAR, neutrophil percentage-to-albumin ratio.

## Discussion

In this large population-based study utilizing NHANES data from 2005 to 2018 ($n = 24{,}938$), we investigated the association between NPAR and anemia risk. Generalized additive models revealed a significant nonlinear relationship between NPAR and anemia risk. Using a recursive algorithm, we identified an inflection point at NPAR = 11.96. Above this threshold, NPAR was positively associated with increased anemia risk (OR = 1.21; 95% CI 1.18–1.25, $P < 0.0001$), while below it, an inverse relationship was observed (OR = 0.88; 95% CI 0.79–0.98, $P = 0.0249$).

This study is the first to investigate the relationship between NPAR and anemia risk, representing a novel contribution to the field. While no previous studies have directly examined this specific association, there is substantial evidence linking inflammatory markers to anemia development in various contexts.

Recent research has established important connections between inflammatory indicators and anemia. For instance, Alshuweishi et al. demonstrated a significant association between NLR and anemia in the Saudi population[16]. Similarly, Chen et al.'s analysis of population-based data revealed that the systemic immune-inflammation index (SII) has a significant relationship with anemia risk[17]. These findings align with our understanding of the complex interplay between inflammation and anemia, particularly through mechanisms involving hepcidin regulation and iron metabolism[9,18].

Our study innovatively introduces NPAR as a novel inflammatory marker for anemia risk assessment, with an identified threshold of 11.96. This finding is particularly significant because NPAR combines two clinically relevant parameters: neutrophil percentage, which reflects inflammatory status[19], and albumin, which serves as an indicator of nutritional status and overall health[20,21]. This dual-component nature of NPAR potentially offers a more comprehensive assessment of inflammatory burden compared to single or combined peripheral blood indicators.

The clinical utility of NPAR has been previously demonstrated in various conditions. Studies by Cui et al.[11]and Wang et al.[12]have shown NPAR's effectiveness in predicting outcomes in cardiovascular patients. Additional research has validated NPAR's predictive value in various clinical contexts, including peritoneal dialysis[13]and bladder cancer[14], supporting its potential as a robust inflammatory marker.

This integration of inflammatory and nutritional status markers is particularly relevant in anemia assessment, as both inflammation and malnutrition are known contributors to anemia development[15,22]. The relationship between inflammation and anemia is well-documented[23,24], and our findings suggest that NPAR could serve as a valuable tool for early identification of anemia risk in clinical practice.

Our findings have significant clinical implications. First, NPAR, as an easily accessible and cost-effective biomarker, can assist clinicians in better assessing anemia risk. Particularly, the identified threshold of 11.96 provides a concrete reference point for clinical practice. When NPAR exceeds this threshold, physicians should consider more detailed anemia screening and preventive interventions. Second, the varying associations between NPAR and anemia risk across different populations have important implications for personalized medicine. For instance, the stronger correlation observed in diabetic patients (OR = 1.22, 95% CI 1.18–1.27, $P < 0.0001$)) suggests that these individuals may require closer monitoring. Furthermore, our analysis based on large-scale population data provides crucial scientific evidence for developing anemia prevention strategies.

Several important limitations warrant consideration in this study. First, the cross-sectional design only allows us to assess associations rather than establish causality between NPAR and anemia. Second, our analysis relied on single measurements of hemoglobin and cell counts, which may not adequately capture individual longitudinal hematological variations. Third, although we adjusted for multiple known confounders, unmeasured factors (such as iron supplementation and dietary habits) might influence result interpretation. Additionally, due to limitations in the data source, we were unable to classify different types of anemia, which may affect the specificity of our findings. Based on these limitations, we recommend: (1) conducting prospective cohort studies with continuous monitoring of NPAR and hemoglobin levels to establish causality; (2) exploring the molecular mechanisms by which NPAR influences anemia development, particularly the interaction between inflammatory factors and iron metabolism; and (3) designing future studies with comprehensive hematological profiling to differentiate between various anemia subtypes.

## Conclusion

This study identifies a significant positive association between NPAR and anemia risk, with a critical threshold at 11.96, beyond which the risk escalates. Stratified analyses revealed that the associations were more pronounced

| NPAR Quartiles | | | | | |
|---|---|---|---|---|---|
| | Quartile1 (0.182–12.064) | Quartile2 (12.064–13.687) | Quartile3 (13.687–15.359) | Quartile4 (15.359–36.100) | p-value |
| Age(years) | 43.00 (29.00 ,56.00) | 45.00 (32.00 ,58.00) | 48.00 (36.00 ,60.00) | 50.00 (38.00 ,64.00) | < 0.0001 |
| Gender (%) | | | | | < 0.0001 |
| Male | 60.64 | 54.28 | 49.12 | 42.12 | |
| Female | 39.36 | 45.72 | 50.88 | 57.88 | |
| Race/Ethnicity (%) | | | | | < 0.0001 |
| Mexican American | 7.31 | 8.36 | 8.20 | 6.98 | |
| Other Hispanic | 5.09 | 5.46 | 4.46 | 4.51 | |
| Non-Hispanic White | 65.33 | 71.61 | 73.81 | 74.73 | |
| Non-Hispanic Black | 14.86 | 7.81 | 7.63 | 8.47 | |
| Other Race | 7.41 | 6.76 | 5.91 | 5.32 | |
| Education level (%) | | | | | < 0.0001 |
| Less than high school | 3.97 | 3.94 | 4.26 | 4.03 | |
| High school | 30.90 | 31.89 | 33.13 | 35.91 | |
| More than high school | 65.13 | 64.17 | 62.62 | 60.06 | |
| Marital status (%) | | | | | < 0.0001 |
| Married/living with partner | 64.11 | 65.89 | 65.81 | 61.57 | |
| Widowed/divorced/separated | 14.12 | 16.99 | 19.28 | 23.38 | |
| Never married | 21.77 | 17.12 | 14.91 | 15.05 | |
| Income to poverty ratio | 3.25 (1.64 ,5.00) | 3.33 (1.68 ,5.00) | 3.26 (1.64 ,5.00) | 2.92 (1.50 ,5.00) | 0.0003 |
| BMI (kg/m2) | 26.60 (23.51 ,30.60) | 27.40 (23.90 ,31.55) | 28.50 (24.70 ,33.10) | 29.72 (25.20 ,35.60) | < 0.0001 |
| Smoking status (%) | | | | | < 0.0001 |
| Current | 20.38 | 20.50 | 22.13 | 24.63 | |
| Former | 26.96 | 25.84 | 27.52 | 29.14 | |
| Never | 52.66 | 53.66 | 50.35 | 46.23 | |
| Drinking status (%) | | | | | 0.0437 |
| Yes | 11.02 | 11.31 | 10.69 | 13.00 | |
| No | 88.98 | 88.69 | 89.31 | 87.00 | |
| Diabetes (%) | | | | | < 0.0001 |
| Yes | 5.73 | 6.60 | 9.38 | 14.58 | |
| No | 92.29 | 91.50 | 88.48 | 82.96 | |
| Borderline | 1.98 | 1.89 | 2.14 | 2.46 | |
| Hypertension (%) | | | | | < 0.0001 |
| Yes | 26.66 | 28.86 | 32.78 | 38.71 | |
| No | 73.34 | 71.14 | 67.22 | 61.29 | |
| Kidney disease (%) | | | | | < 0.0001 |
| Yes | 1.33 | 1.75 | 2.03 | 3.78 | |
| No | 98.67 | 98.25 | 97.97 | 96.22 | |
| Congestive heart failure (%) | | | | | < 0.0001 |
| Yes | 1.10 | 1.36 | 2.20 | 4.59 | |
| No | 98.90 | 98.64 | 97.80 | 95.41 | |
| Stroke (%) | | | | | < 0.0001 |
| Yes | 1.56 | 2.14 | 2.58 | 4.44 | |
| No | 98.44 | 97.86 | 97.42 | 95.56 | |
| Thyroid disease (%) | | | | | < 0.0001 |
| Yes | 8.76 | 8.48 | 11.36 | 13.94 | |
| No | 91.24 | 91.52 | 88.64 | 86.06 | |
| Cancer (%) | | | | | < 0.0001 |
| Yes | 7.74 | 9.20 | 10.23 | 13.39 | |
| No | 92.26 | 90.80 | 89.77 | 86.61 | |
| WBC ($10^3$ cells/uL) | 6.10 (5.10 ,7.40) | 6.60 (5.60 ,8.00) | 7.20 (6.10 ,8.60) | 8.00 (6.60 ,9.70) | < 0.0001 |
| RBC ($10^3$ cells/uL) | 4.77 (4.43 ,5.08) | 4.74 (4.41 ,5.07) | 4.70 (4.39 ,5.03) | 4.64 (4.32 ,4.95) | < 0.0001 |
| PLT ($10^3$ cells/uL) | 235.00 (202.00 ,274.00) | 239.00 (205.00 ,280.00) | 245.00 (208.00 ,288.00) | 248.00 (206.00 ,297.00) | < 0.0001 |
| Albumin(g/dL) | 4.40 (4.20 ,4.60) | 4.40 (4.20 ,4.60) | 4.30 (4.10 ,4.40) | 4.00 (3.80 ,4.20) | < 0.0001 |
| Hb(g/dL) | 14.60 (13.60 ,15.40) | 14.50 (13.60 ,15.50) | 14.40 (13.40 ,15.30) | 14.00 (13.10 ,15.00) | < 0.0001 |
| Continued | | | | | |

| NPAR Quartiles | | | | | |
|---|---|---|---|---|---|
| Anemia (%) | | | | | < 0.0001 |
| Yes | 4.24 | 3.94 | 5.40 | 10.20 | |
| No | 95.76 | 96.06 | 94.60 | 89.80 | |

**Table 2**. Weighted characteristics of the study population based on NPAR quartiles. Median (Q1, Q3) for continuous variables: the *P*-value was calculated by the weighted linear regression model. (%) for categorical variables: the *P*-value was calculated by the weighted chi-square test. BMI, body mass index; WBC, white blood cell; RBC, red blood cell; PLT, platelet; Hb, hemoglobin; NPAR, neutrophil percentage-to-albumin Ratio.

| | OR (95%CI), *P*-Value | | |
|---|---|---|---|
| | Model 1 | Model 2 | Model 3 |
| NPAR | 1.18 (1.15, 1.21) < 0.0001 | 1.16 (1.13, 1.19) < 0.0001 | 1.16 (1.13, 1.18) < 0.0001 |
| NPAR Quartile | | | |
| Q1 | Reference | Reference | Reference |
| Q2 | 0.93 (0.78, 1.10) 0.3938 | 1.04 (0.88, 1.24) 0.6410 | 1.03 (0.86, 1.23) 0.7838 |
| Q3 | 1.29 (1.09, 1.52) 0.0036 | 1.38 (1.16, 1.64) 0.0003 | 1.39 (1.17, 1.65) 0.0003 |
| Q4 | 2.57 (2.16, 3.05) < 0.0001 | 2.54 (2.12, 3.03) < 0.0001 | 2.50 (2.09, 2.98) < 0.0001 |
| P for Trend | 1.43 (1.35, 1.52) < 0.0001 | 1.40 (1.32, 1.49) < 0.0001 | 1.40 (1.32, 1.48) < 0.0001 |

**Table 3**. The odds ratio (95% confidence intervals) for the association between NPAR and anemia in different models. Model 1: No covariates were adjusted. Model 2: Age, gender, race were adjusted. Model 3: Age, gender, race, education level, marital status, income to poverty ratio, body mass index, drinking status, smoking status, diabetes, hypertension, chronic diseases (kidney disease, congestive heart failure, stroke, thyroid disease and cancer) were adjusted. OR, odds ratio; 95% CI, 95% confidence interval; NPAR, neutrophil percentage-to-albumin ratio.

in specific subgroups, including males, non-Hispanic Whites, cohabiting or married individuals, and patients with diabetes. These findings suggest that NPAR is a promising biomarker for anemia risk assessment, offering potential for targeted screening and intervention in clinical practice. However, further prospective studies are needed to validate these results and explore underlying mechanisms.

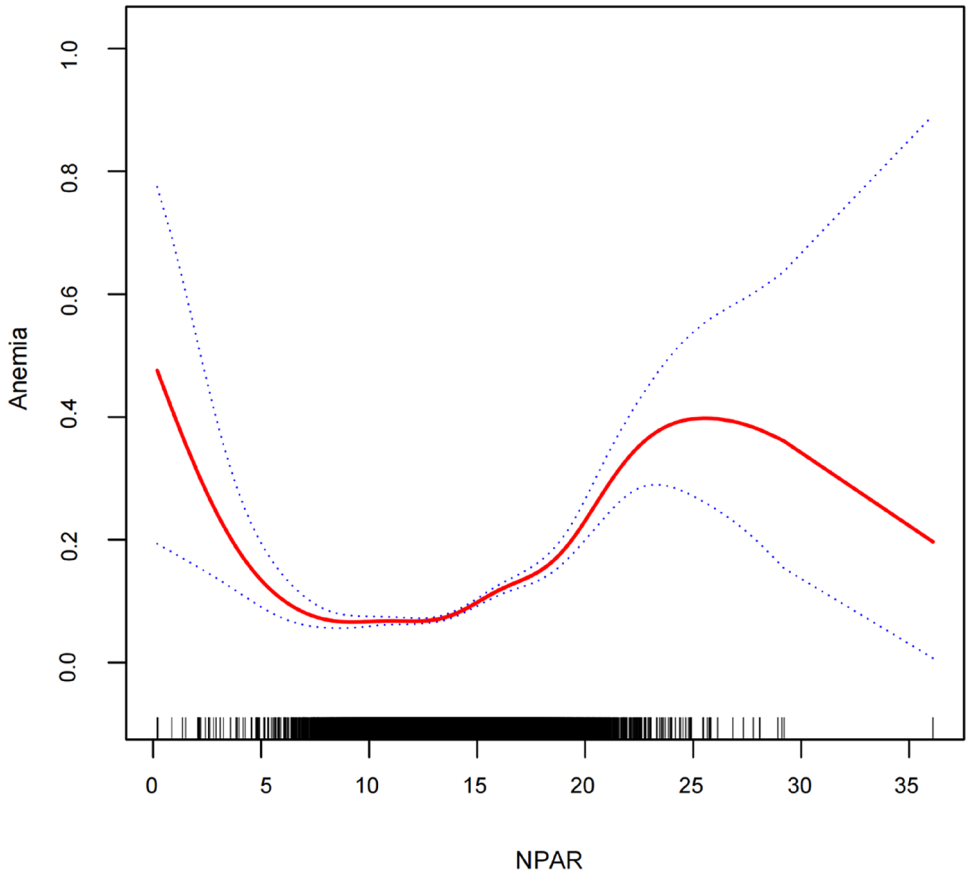


**Fig. 2**. The association between NPAR and anemia. Solid red line represents the smooth curve fit between variables. Blue bands represent the 95% of confidence interval from the fit. Age, gender, race, education level, marital status, income to poverty ratio, body mass index, drinking status, smoking status, diabetes, hypertension, chronic diseases (kidney disease, congestive heart failure, stroke, thyroid disease and cancer) were adjusted.

| NPAR | Adjusted OR (95%CI), *P*-value |
|---|---|
| Total | |
| Fitting by the standard linear model | 1.16 (1.13, 1.18) < 0.0001 |
| Fitting by the two-piecewise linear model | |
| Inflection point | 11.96 |
| NPAR < 11.96 | 0.88 (0.79, 0.98) 0.0249 |
| NPAR ≥ 11.96 | 1.21 (1.18, 1.25) < 0.0001 |
| Log likelihood ratio | < 0.001 |
| Male | |
| Fitting by the standard linear model | 1.13 (1.08, 1.17) < 0.0001 |
| Fitting by the two-piecewise linear model | |
| Inflection point | 13.57 |
| NPAR < 13.57 | 0.88 (0.80, 0.96) 0.0043 |
| NPAR ≥ 13.57 | 1.26 (1.20, 1.33) < 0.0001 |
| Log likelihood ratio | < 0.001 |
| Non-Hispanic White | |
| Fitting by the standard linear model | 1.18 (1.13, 1.23) < 0.0001 |
| Fitting by the standard linear model | |
| Inflection point | 11.96 |
| NPAR < 11.96 | 0.78 (0.67, 0.90) 0.0012 |
| NPAR ≥ 11.96 | 1.24 (1.19, 1.29) < 0.0001 |
| Log likelihood ratio | < 0.001 |
| Non-diabetes | |
| Fitting by the standard linear model | 1.14 (1.11, 1.17) < 0.0001 |
| Fitting by the two-piecewise linear model | |
| Inflection point | 12.05 |
| NPAR < 12.05 | 0.87 (0.78, 0.98) 0.0267 |
| NPAR ≥ 12.05 | 1.20 (1.16, 1.25) < 0.0001 |
| Log likelihood ratio | < 0.001 |

**Table 4**. Threshold effect analysis of NPAR on risk of anemia using the two-piecewise linear regression model. Age, gender, race, education level, marital status, income to poverty ratio, body mass index, drinking status, smoking status, diabetes, hypertension, chronic diseases (kidney disease, congestive heart failure, stroke, thyroid disease and cancer) were adjusted. Each stratification adjusted for the above factors except the stratification factor itself.

| | OR (95%CI) *p*-value | *p* for interaction |
|---|---|---|
| Age(years) | | 0.4800 |
| <60 | 1.15 (1.11, 1.19) < 0.0001 | |
| ≥ 60 | 1.17 (1.13, 1.22) < 0.0001 | |
| Gender | | 0.0004 |
| Male | 1.22 (1.18, 1.26) < 0.0001 | |
| Female | 1.12 (1.08, 1.16) < 0.0001 | |
| Race | | 0.0348 |
| Mexican American | 1.16 (1.08, 1.25) 0.0001 | |
| Other Hispanic | 1.18 (1.11, 1.25) < 0.0001 | |
| Non-Hispanic White | 1.19 (1.14, 1.24) < 0.0001 | |
| Non-Hispanic Black | 1.10 (1.06, 1.13) < 0.0001 | |
| Other Race | 1.17 (1.06, 1.29) 0.0031 | |
| Education level | | 0.6444 |
| Less than high school | 1.18 (1.08, 1.29) 0.0004 | |
| High school | 1.17 (1.12, 1.21) < 0.0001 | |
| More than high school | 1.14 (1.11, 1.18) < 0.0001 | |
| Marital status | | 0.0052 |
| Married/living with partner | 1.19 (1.15, 1.23) < 0.0001 | |
| Widowed/divorced/separated | 1.12 (1.07, 1.17) < 0.0001 | |
| Never married | 1.09 (1.04, 1.15) 0.0009 | |
| Income to poverty ratio | | 0.9554 |
| ≤ 1 | 1.15 (1.09, 1.22) < 0.0001 | |
| > 1 | 1.16 (1.13, 1.19) < 0.0001 | |
| BMI(kg/m2) | | 0.5471 |
| < 25 | 1.13 (1.08, 1.18) < 0.0001 | |
| 25 ≤ BMI < 30 | 1.15 (1.10, 1.20) < 0.0001 | |
| ≥ 30 | 1.17 (1.13, 1.20) < 0.0001 | |
| Smoking status | | 0.6386 |
| Never | 1.16 (1.12, 1.20) < 0.0001 | |
| Former | 1.17 (1.12, 1.21) < 0.0001 | |
| Current | 1.12 (1.05, 1.20) 0.0007 | |
| Drinking status | | 0.3052 |
| No | 1.15 (1.12, 1.18) < 0.0001 | |
| Yes | 1.19 (1.12, 1.27) < 0.0001 | |
| Diabetes | | 0.0010 |
| No | 1.14 (1.11, 1.17) < 0.0001 | |
| Yes | 1.22 (1.18, 1.27) < 0.0001 | |
| Hypertension | | 0.3802 |
| No | 1.14 (1.10, 1.19) < 0.0001 | |
| Yes | 1.17 (1.13, 1.20) < 0.0001 | |
| Kidney disease | | 0.3502 |
| No | 1.15 (1.12, 1.18) < 0.0001 | |
| Yes | 1.21 (1.10, 1.32) 0.0001 | |
| Congestive heart failure | | 0.8986 |
| No | 1.16 (1.12, 1.19) < 0.0001 | |
| Yes | 1.15 (1.06, 1.25) 0.0019 | |
| Stroke | | 0.2728 |
| No | 1.15 (1.12, 1.18) < 0.0001 | |
| Yes | 1.22 (1.10, 1.36) 0.0003 | |
| Thyroid disease | | 0.3392 |
| Continued | | |

| | OR (95%CI) *p*-value | *p* for interaction |
|---|---|---|
| No | 1.16 (1.13, 1.19) < 0.0001 | |
| Yes | 1.12 (1.06, 1.19) 0.0002 | |
| Cancer | | 0.5591 |
| No | 1.16 (1.13, 1.19) < 0.0001 | |
| Yes | 1.13 (1.04, 1.23) 0.0047 | |

**Table 5**. Subgroup analysis of the association between NPAR with anemia. Age, gender, race, education level, marital status, income to poverty ratio, BMI, drinking status, smoking status, diabetes, hypertension, chronic diseases (kidney disease, congestive heart failure, stroke, thyroid disease and cancer) were adjusted. Each stratification adjusted for the above factors except the stratification factor itself. BMI, body mass index.

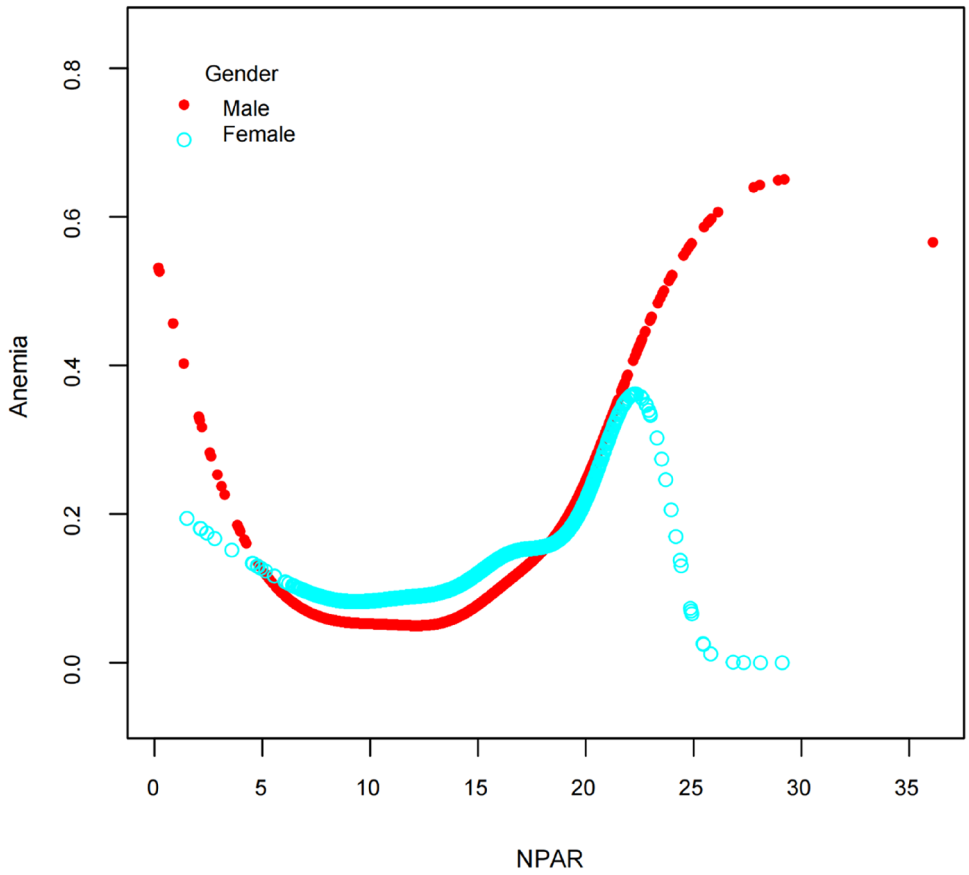


**Fig. 3**. The association between NPAR and anemia stratified by gender. Age, race, education level, marital status, income to poverty ratio, body mass index, drinking status, smoking status, diabetes, hypertension, chronic diseases (kidney disease, congestive heart failure, stroke, thyroid disease and cancer) were adjusted.

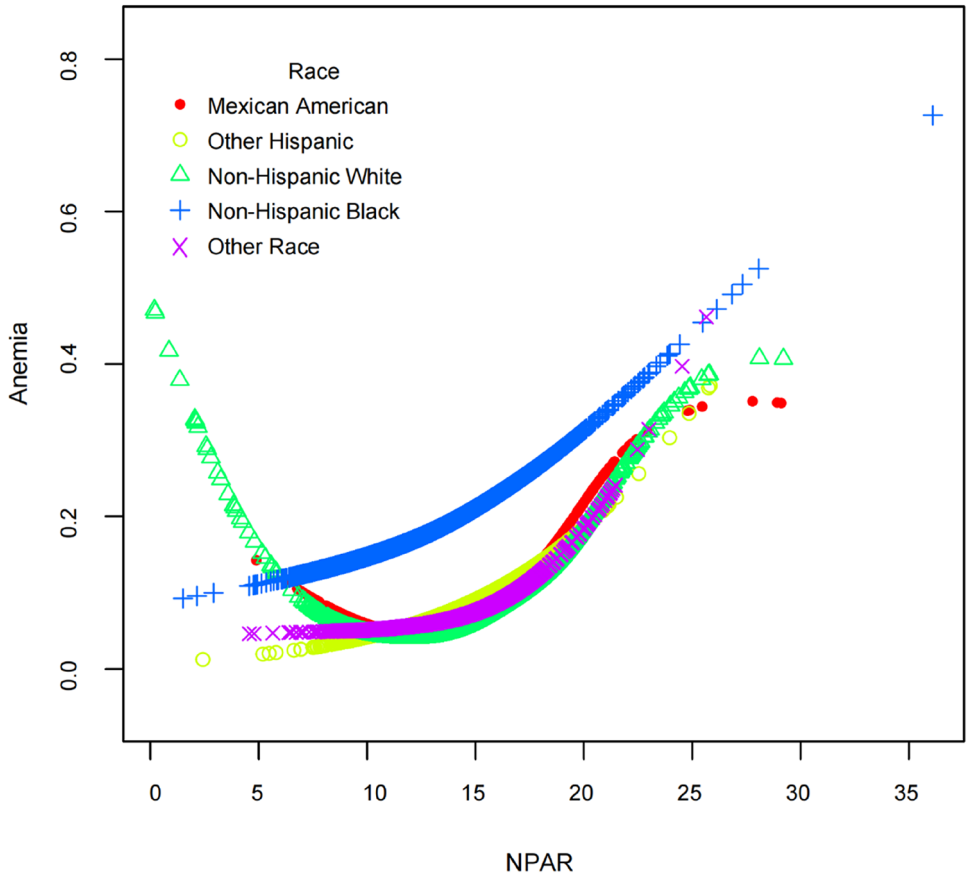


**Fig. 4**. The association between NPAR and anemia stratified by race/ethnicity. Age, gender, education level, marital status, income to poverty ratio, body mass index, drinking status, smoking status, diabetes, hypertension, chronic diseases (kidney disease, congestive heart failure, stroke, thyroid disease and cancer) were adjusted.

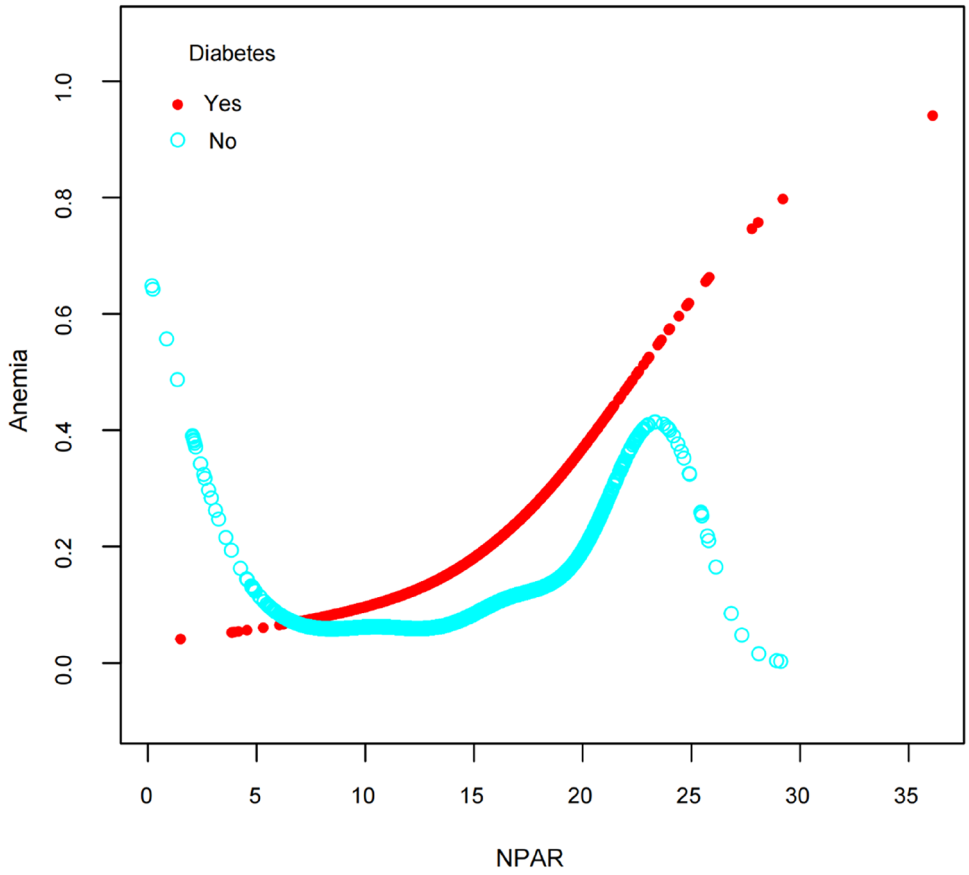


**Fig. 5**. The association between NPAR and anemia stratified by the existence of diabetes. Age, gender, race, education level, marital status, income to poverty ratio, body mass index, drinking status, smoking status, hypertension, chronic diseases (kidney disease, congestive heart failure, stroke, thyroid disease and cancer) were adjusted.

## Data availability

The data used in this study are publicly available from the National Health and Nutrition Examination Survey (NHANES) database (https://www.cdc.gov/nchs/nhanes/index.htm).

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## Author contributions

S.G and Y.H conceptualized and designed the study. S.G and F.Y analyzed and interpreted the data. Y.H evaluated the analyses and drafted the manuscript. S.G and F.Y critically revised the content. All authors approved the final version and agreed to be accountable for all aspects of the work.

## Declarations

## Competing interests

The authors declare no competing interests.

## Additional information

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