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ORIGINAL RESEARCH

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Higher serum albumin levels as a potential indicator for reduced risk of erectile dysfunction: evidence from NHANES study

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Abstract

Background: While blood albumin levels indicate organ function, their relationship to erectile dysfunction (ED) is unclear. The purpose of this study is to look at the association between serum albumin levels and ED in the general population. **Methods**: This cross-sectional research involved subjects from the National Health and Nutrition Examination Survey (NHANES) conducted between 2001 and 2004. The study employed weighted multivariable regression, performed subgroup analyses and applied restricted cubic spline (RCS) analyses. **Results**: Of the 3413 adults involved in this study, 868 (25.45%) indicated experiencing ED. A weighted multivariable logistic regression model indicated a negative association between serum albumin levels and ED (odds ratio (OR), 0.92; 95% confidence interval (CI), 0.88–0.96). Serum albumin and ED were consistently associated across subgroups. Sensitivity analyses, which excluded individuals with albumin levels below 35 g/L, also indicated a connection between serum albumin and ED (OR, 0.82; 95% CI, 0.79–0.85). Similarly, a stricter definition of ED yielded an association (OR, 0.92; 95% CI, 0.86–0.97), even after additional adjustments for sex hormones. **Conclusions**: Higher serum albumin levels are significantly associated with a reduced risk of ED, suggesting that serum albumin may serve as a potential biomarker for assessing ED risk.

Keywords

Serum albumin; Erectile dysfunction; Sexual dysfunction; NHANES

1. Introduction

Erectile dysfunction (ED) is a common concern among men, especially those dealing with chronic health problems like diabetes [1], heart disease [2], liver cirrhosis [3] and chronic inflammatory disorders of the intestine [4, 5]. This condition is marked by difficulties in achieving or sustaining an erection that is adequate for fulfilling sexual activity, thereby significantly affecting an individual's overall life quality and emotional health [6]. The development of ED is multifaceted, involving a range of factors including vascular, neurogenic, endocrine and psychological aspects [6–9]. Among the various physiological markers, serum albumin has emerged as a potential indicator of ED risk.

Serum albumin, constituting a significant portion of plasma proteins in humans, is essential for preserving osmotic balance and acts as a transporter for a variety of substances that are naturally occurring in the body, as well as those introduced from external sources [10–12]. It has been well-documented that hypoalbuminemia, or low levels of serum albumin, is associated with poor health outcomes in various diseases, including liver cirrhosis, chronic kidney disease and cardiovascular disorders [13, 14]. Recent studies have suggested that serum albumin levels may also be linked to ED, particularly in patients with chronic illnesses [15].

Several studies have explored the association between serum albumin and ED. For instance, a study [16] on patients with liver cirrhosis found that low serum albumin levels were significantly associated with the prevalence of ED. Similarly, research [17] on patients with chronic kidney disease has indicated that hypoalbuminemia is a predictor of ED, highlighting the role of albumin as a marker of overall health status and its potential impact on erectile function. Another study demonstrated that the C-reactive protein-to-albumin ratio could serve as an indicator of inflammation in diagnosing ED, further supporting the link between serum albumin and ED [18].

Despite these findings, the association between serum albumin levels and ED remains underexplored, particularly in the context of large, representative populations. Previous studies [19, 20] based on the National Health and Nutrition Examination Survey (NHANES) data have successfully identified various health determinants and their associations with chronic conditions, making it an ideal dataset for examining the link between serum albumin and ED. This study aims to examine the possible relationship between serum albumin levels and the prevalence of ED, utilizing a comprehensive

dataset from the NHANES conducted between 2001 and 2004. Understanding the role of serum albumin in ED could have significant clinical implications. If a strong association is confirmed, serum albumin could be used as a simple and cost-effective biomarker for identifying individuals at higher risk of ED, particularly among those with chronic diseases. This could facilitate early interventions and improve management strategies aimed at enhancing erectile function and overall quality of life in affected individuals.

2. Methods

2.1 Data sources and study population

The NHANES survey is meticulously designed to provide a sample that accurately reflects the entire U.S. population, ensuring broad demographic and geographic inclusivity. It employs an advanced, stratified, multistage probability cluster sampling technique, which guarantees a diverse cross-section of participants. This method is crucial for capturing a representative view of the population's health status. The study protocol received clearance from the National Center for Health Statistics' (NCHS) research ethics review board, affirming its scientific merit and adherence to ethical standards. Prior to their participation, all subjects gave informed consent, thereby guaranteeing that the study adhered to the principles of voluntary participation and individual autonomy.

Data from the NHANES survey conducted between 2001–2002 and 2003–2004 was used in this study, chosen specifically for the availability of information pertinent to ED. From a total of 4661 individuals with available ED data in the NHANES database during this period, several exclusion criteria were put into effect: (1) Absence of ED information (n = 545). (2) Unavailability of serum albumin information (n = 160). (3) Individuals diagnosed with prostate cancer (n = 107) or rectal cancer (n = 2). (4) Lack of poverty information (n = 201). (5) Missing body mass index (BMI) information (n = 86). (6) Absence of aspartate aminotransferase (AST) information (n = 4). (7) Absence of alcohol intake information (n = 5). (8) Absence of smoking status information (n = 2). (9) Unavailability of marital status information (n = 2). (10) Absence of educational information (n = 2). (11) Absence of cardiovascular disease (CVD) information (n = 1). (12) Absence of moderate activity information (n = 1) and inability to perform activity (n = 127). (13) After enforcing these exclusion criteria, the final analysis comprised a total of 3413 participants.

2.2 Data collection and definition

2.2.1 Evaluation of erectile dysfunction and albumin

In the NHANES survey, interviews with participants were carried out in secluded areas of the Mobile Examination Center (MEC) to maintain privacy and comfort. The assessment of ED is similar to a question from the Massachusetts Male Aging Study [21], which confirmed that this single inquiry has a very high concordance with the International Index of Erectile Function-5 (IIEF-5) diagnosis of ED. The question is as follows: how would you rate your ability to obtain and maintain an erection sufficient for satisfactory sexual intercourse? Participants who reported occasionally or never being able to maintain an erection were classified as having ED. In contrast, the non-ED group included those who were able to maintain an erection always or usually [22].

In this study, albumin was referred to as serum albumin. The measurement of albumin concentration in the NHANES survey utilized bromocresol purple dye. These protocols ensure that the laboratory procedures and practices meet the necessary quality standards for measuring albumin levels. By adhering to these regulations, the NHANES survey maintains the integrity and validity of the collected data.

2.2.2 Other covariates of interest

In this research, we took into account various variables, including: baseline characteristics like age, race, family income to poverty ratio (FIR), body mass index (BMI), marriage and educational attainment; lifestyle factors such as alcohol intake, smoking behaviors, and levels of physical activity; comorbid conditions including diabetes mellitus (DM), hypertension, and cardiovascular disease (CVD); as well as biochemical markers like C-reactive protein (CRP), estimated glomerular filtration rate (eGFR), along with serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

Marital status categories include "cohabitation" for individuals who are either married or living with a partner, while all others are classified as "Solitude". Current smokers are defined as those who are actively smoking and have smoked more than 100 cigarettes in their lifetime. Former smokers are individuals who do not currently smoke but have a history of smoking more than 100 cigarettes, whereas non-smokers are defined as individuals who have smoked no more than 100 cigarettes throughout their lives. Drinkers are characterized as individuals who have consumed alcoholic beverages at least 12 times either in their lifetime or within any given year, and who have also consumed alcohol at least once in the past 12 months; all others are classified as non-drinkers. The diabetes population includes individuals diagnosed by healthcare providers, defined by fasting plasma glucose levels of $\geq$7 mmol/L, hemoglobin A1c (HbA1c) levels of $\geq$6.5%, random blood glucose levels of $\geq$11.1 mmol/L or two-hour oral glucose tolerance test (OGTT) blood glucose levels of $\geq$11.1 mmol/L, as well as participants who are currently using diabetes medications or insulin. Hypertension is defined as individuals who are taking antihypertensive medications or who have a systolic blood pressure of $\geq$140 mmHg or a diastolic blood pressure of $\geq$90 mmHg. Cardiovascular disease (CVD) includes myocardial infarction, or congestive heart failure, or angina or coronary artery disease. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration Equation (CKD-EPI equation) [23].

2.3 Statistical analysis

Our analysis followed the analytical guidelines set by NHANES, incorporating appropriate sampling weights throughout the process. For continuous variables, we

calculated weighted mean ± SE (Standard Error), with corresponding *p*-values obtained from weighted survey linear regression. For categorical variables, we employed counts represented by weighted proportions, and relevant *p*-values were determined through weighted survey chi-square tests. The independent relationship of serum albumin with ED was assessed through a weighted multivariable logistic regression model. Additionally, restricted cubic splines were utilized to investigate the non-linear associations between serum albumin and ED.

This study employed three distinct models: Model 1 adjusted for variables such as age, race, marital status, FIR, BMI and education level; Model 2 incorporated further adjustments for factors like alcohol intake, smoking habits, vigorous exercise and moderate physical activity; Model 3 additionally adjusted for conditions including DM, CVD, hypertension, eGFR, CRP, AST and ALT. In the course of this research, we encountered minimal missing data, which led us to exclude any records that contained incomplete information.

Several sensitivity analyses were conducted. First, serum albumin levels were categorized into quartiles (Q1 to Q4). Second, we performed stratified analyses to segment the data by various subgroups. Interaction tests were utilized in Model 3 to assess the heterogeneity of associations across these various subgroups. Third, we adopted a more stringent definition of ED, classifying participants who reported never being able to achieve and maintain an erection as having ED. Additionally, we carried out a subgroup analysis focused on individuals with serum albumin levels exceeding 35 g/L to further explore the relationship between albumin and ED. Finally, to assess potential confounding effects of sex hormones, we employed an additional adjusted model (Model 3 + each sex hormone) incorporating these hormonal variables.

Statistical evaluations were performed utilizing R version 4.2.0, in conjunction with the "survey" package and the statistical software version 1.9 from the Free Software Foundation. All analyses were executed at a significance threshold of $p < 0.05$ (two-sided) in order to ascertain statistical significance.

3. Results

3.1 Participant characteristics

After excluding participants with incomplete data, our study comprised a comprehensive sample of 3413 individuals aged between 20 and 85 years. Among this demographic, 868 individuals, representing 25.45% of the study population, were identified as experiencing ED, while 2545 individuals, accounting for 74.55% of the sample, did not report ED, as illustrated in Fig. 1.

In the ED group, 76 participants (11.36%) were under the age of 40, whereas the majority, which consisted of 792 participants (88.64%), were over 40 years old. Several notable

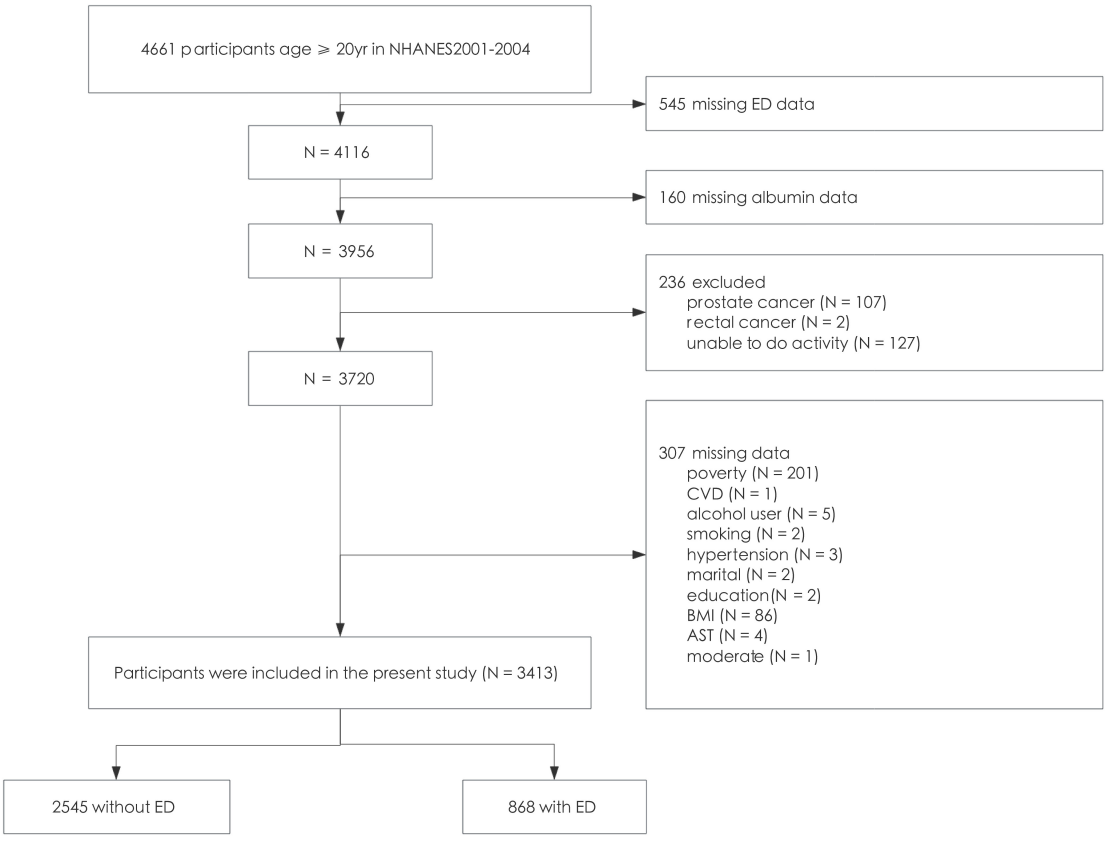


FIGURE 1. Flow Diagram of the screening and enrollment of study participants. ED: erectile dysfunction; CVD: cardiovascular disease; BMI: body mass index; AST: aspartate aminotransferase; NHANES: National Health and Nutrition Examination Survey.

differences were observed between men with ED and non-ED. Men experiencing ED were older, have lower FIR, lower educational level, lower rates of current smoking, lower alcohol intake, higher BMI, less physical activity, lower serum albumin levels, higher AST levels, lower ALT levels, lower eGFR, higher levels of CRP and a higher prevalence of DM, hypertension, and CVD compared to men without ED. However, no significant racial disparities in the prevalence of ED were observed (Table 1).

3.2 The association between serum albumin and ED

The univariate logistic regression analysis indicated a noteworthy association between serum albumin concentrations and the likelihood of ED (OR: 0.83, 95% CI: 0.80–0.86). In the multivariable logistic analysis, three individual models were implemented. Each model yielded statistically significant outcomes, exhibiting OR and respective 95% CIs as follows: 0.89 (0.85–0.93), 0.90 (0.86–0.93) and 0.92 (0.88–0.96). In Model 3, a rise of one unit in albumin correlated with an 8% decrease in the likelihood of experiencing ED.

To assess reliability, albumin was converted into a categorical variable. Table 2 illustrates a significant and continuous trend of reduced prevalence of ED when albumin levels rose throughout higher quartiles in comparison to the lowest quartile (all p for trend < 0.05). Notably, in Model 3, Q4 participants exhibited a striking 55% reduced risk of ED in comparison to those in Q1, with an odds ratio of 0.45 and a 95% confidence interval of 0.29 to 0.70 (p for trend = 0.004). Additionally, a smooth curve fitting analysis performed with restricted cubic splines demonstrated a negative association between serum albumin levels and the incidence of ED (p for non-linearity: 0.42), as illustrated in Fig. 2.

3.3 Subgroup analysis

The outcomes of the subgroup analysis are summarized in Table 3 and illustrated in Fig. 3. This analysis reveals that the relationship between serum albumin levels and ED remains stable across different subgroups. A significant interaction effect exists (p for interaction = 0.004) among those participating in moderate-intensity physical exercise. Particularly, the effect of albumin on ED is more noticeable for individuals who engage in moderately intense exercise (OR: 0.90, 95% CI: 0.85–0.94) than for those who do not participate in such activities (OR: 0.94, 95% CI: 0.89–0.98).

3.4 Sensitivity analysis

We performed a sample-weighted multivariable regression for sensitivity analysis, the results of which are depicted in Tables 4,5,6. Employing a stricter definition of ED individuals as those who "never" achieved an acceptable erection, we found that the OR were similar in Models 1 and 3, while they increased in Model 2 (Table 4). There was an 8% drop in ED for every unit increase in serum albumin (OR = 0.92, 95% CI: 0.86–0.97) in Model 3. These results remained consistent when we divided albumin into quantiles.

Similarly, we confined our analysis to individuals with albumin levels greater than 35g/L (the normal serum albumin level) and executed three adjusted models (Table 5). The outcomes proved to be consistent even after this limitation. Each unit increase in albumin continued to correlate with a 9% decreased risk of ED in the fully-adjusted model (Model 3), yielding an OR of 0.91 and a 95% CI of 0.87–0.96. In the categorical models, a comparison between Q4 and Q1 albumin levels revealed a 54% risk decrease in ED, showing an OR of 0.46 and a 95% CI of 0.27–0.80.

Furthermore, our analysis was constricted to men with available data on serum sex hormone levels. We only integrated these sex hormones into Model 3 (Table 6). The outcomes suggest a stronger association between albumin and ED (OR = 0.78–0.84, $p < 0.05$). Although the smaller sample size resulted in a notably wider 95% CI, it remained statistically significant.

4. Discussion

The objective of this study was to examine the relationship between serum albumin levels and ED in a representative group of adult men, using data obtained from the NHANES. Our primary finding indicates that lower serum albumin levels are independently associated with an increased risk of ED, even after adjusting for a comprehensive range of potential confounders. This observation supports the hypothesis that hypoalbuminemia may serve as a significant marker for ED, corroborating previous studies that have emphasized the role of albumin in vascular health and endothelial function [14, 24]. The robustness of our results was further validated through multiple sensitivity analyses, which consistently demonstrated that low serum albumin levels correlate with a heightened risk of ED.

Serum albumin is the most abundant protein in plasma, constituting approximately 50% of the total proteins in healthy individuals [25]. It serves not only as an inflammatory and nutritional marker [26], but also plays critical roles in various biochemical functions. Albumin has been implicated in several diseases, including liver disease, kidney disease, depression, cardiovascular disease and sleep disorders [3, 27–30]. In the context of ED research, existing studies have identified albumin as an independent risk factor for ED within chronic disease populations [13, 16, 31, 32]. Nevertheless, there is a significant scarcity of research that specifically investigates the independent relationship between serum albumin levels and ED. In this research, we utilized the benefits of the NHANES database design to examine the independent association between serum albumin levels and ED in a broader population. Notably, our findings suggest an observed decrease in the incidence of ED by 8% for each unit increase in serum albumin. Additionally, stratifying albumin into quartiles revealed that the top quartile had a 55% reduced risk of ED in comparison to the lowest quartile. These findings suggest an inverse relationship between serum albumin levels and ED, reinforcing the notion that albumin concentrations serve as an independent risk factor for ED. In sensitivity analyses, we found that even among individuals with normal serum albumin levels, each additional unit of albumin resulted in an 8% reduction in the risk of ED. This finding remained stable, indicating that the

TABLE 1. Descriptive characteristics of study participants.

Variable	All participants	Non-ED	ED	*p* value
Serum albumin (g/L)	43.90 ± 0.09	44.17 ± 0.09	42.56 ± 0.13	<0.0001
Serum albumin quartile, N (%)				
Q1	822 (18.96)	506 (15.82)	316 (34.13)	<0.0001
Q2	861 (24.29)	623 (23.88)	238 (26.25)	
Q3	896 (27.94)	693 (28.47)	203 (25.37)	
Q4	834 (28.82)	723 (31.82)	111 (14.24)	
Age (yr), N (%)				
<40	1200 (41.05)	1124 (47.18)	76 (11.36)	<0.0001
≥40	2213 (58.95)	1421 (52.82)	792 (88.64)	
BMI (kg/m^2)	28.06 ± 0.10	27.85 ± 0.11	29.09 ± 0.30	<0.001
FIR, N (%)	3.25 ± 0.05	3.30 ± 0.05	3.01 ± 0.08	<0.0001
Race, N (%)				
Non-Hispanic white	1832 (74.02)	1342 (73.76)	490 (75.28)	0.79
Non-Hispanic black	634 (9.48)	500 (9.66)	134 (8.61)	
Mexican American	726 (8.05)	531 (8.14)	195 (7.63)	
Other race	221 (8.45)	172 (8.44)	49 (8.48)	
Marital status, N (%)				
Solitude	1039 (29.57)	823 (30.97)	216 (22.80)	<0.001
Cohabitation	2374 (70.43)	1722 (69.03)	652 (77.20)	
Education level, N (%)				
Less than or high school	1769 (43.25)	1241 (41.32)	528 (52.60)	<0.0001
Above high school	1644 (56.75)	1304 (58.68)	340 (47.40)	
Alcohol intake, N (%)				
No	889 (22.40)	561 (20.14)	328 (33.33)	<0.0001
Yes	2524 (77.60)	1984 (79.86)	540 (66.67)	
Smoking status, N (%)				
Never	1401 (43.46)	1144 (46.03)	257 (31.05)	<0.0001
Former	1069 (28.28)	646 (24.77)	423 (45.28)	
Current	943 (28.26)	755 (29.20)	188 (23.66)	
Vigorous, N (%)				
No	2191 (58.74)	1486 (54.68)	705 (78.43)	<0.0001
Yes	1222 (41.26)	1059 (45.32)	163 (21.57)	
Moderate, N (%)				
No	1676 (42.43)	1195 (40.96)	481 (49.57)	0.002
Yes	1737 (57.57)	1350 (59.04)	387 (50.43)	
DM, N (%)				
No	2948 (90.43)	2338 (94.12)	610 (72.57)	<0.0001
Yes	465 (9.57)	207 (5.88)	258 (27.43)	
CVD, N (%)				
No	3023 (92.10)	2386 (95.08)	637 (77.67)	<0.0001
Yes	390 (7.90)	159 (4.92)	231 (22.33)	
Hypertension, N (%)				
No	2094 (66.76)	1758 (71.53)	336 (43.64)	<0.0001
Yes	1319 (33.24)	787 (28.47)	532 (56.36)	

TABLE 1. Continued.

Variable	All participants	Non-ED	ED	*p* value
eGFR	93.94 ± 0.58	96.38 ± 0.62	82.12 ± 0.95	<0.0001
CRP (mg/dL)	0.33 ± 0.01	0.31 ± 0.01	0.43 ± 0.03	<0.0001
AST (U/L)	27.05 ± 0.30	26.92 ± 0.36	27.63 ± 0.58	0.34
ALT (U/L)	30.38 ± 0.39	30.75 ± 0.45	28.58 ± 0.84	0.04
Testosterone (ng/dL)	525.79 ± 21.19	546.58 ± 24.94	435.36 ± 26.28	0.005
Sex hormone binding globulin (nmol/L)	36.13 ± 1.08	34.00 ± 1.14	45.37 ± 2.09	<0.0001
Estradiol (pg/mL)	35.65 ± 1.42	36.12 ± 1.64	33.60 ± 2.49	0.4
Free testosterone (ng/dL)	11.38 ± 0.76	12.20 ± 0.91	7.81 ± 0.51	<0.001
Bioavailable testosterone (ng/dL)	11.38 ± 0.76	12.20 ± 0.91	7.81 ± 0.51	<0.001

ED: erectile dysfunction; FIR: family income to poverty ratio; BMI: body mass index; DM: diabetes mellitus; CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

TABLE 2. Association between serum albumin with ED.

Variable	Crude model OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Serum albumin	0.83 (0.80–0.86)	0.89 (0.85–0.93)	0.90 (0.86–0.93)	0.92 (0.88–0.96)
Serum albumin quantile				
Q1	ref	ref	ref	ref
Q2	0.51 (0.39–0.67)	0.67 (0.51–0.87)	0.72 (0.57–0.91)	0.77 (0.60–0.99)
Q3	0.41 (0.32–0.54)	0.62 (0.46–0.83)	0.63 (0.47–0.83)	0.73 (0.53–1.00)
Q4	0.21 (0.15–0.28)	0.40 (0.27–0.58)	0.41 (0.28–0.60)	0.45 (0.29–0.70)
p for trend	<0.0001	<0.001	<0.001	0.004

Crude model: no variables were adjusted.
Model 1 adjusted for age, marital status, race, FIR, education levels and BMI.
Model 2 adjusted for Model 1 + alcohol intake, smoking, vigorous and moderate activity.
Model 3 adjusted for Model 2 + DM, hypertension, CVD, eGFR, CRP, ALT and AST.
OR: odds ratio; CI: confidence interval.

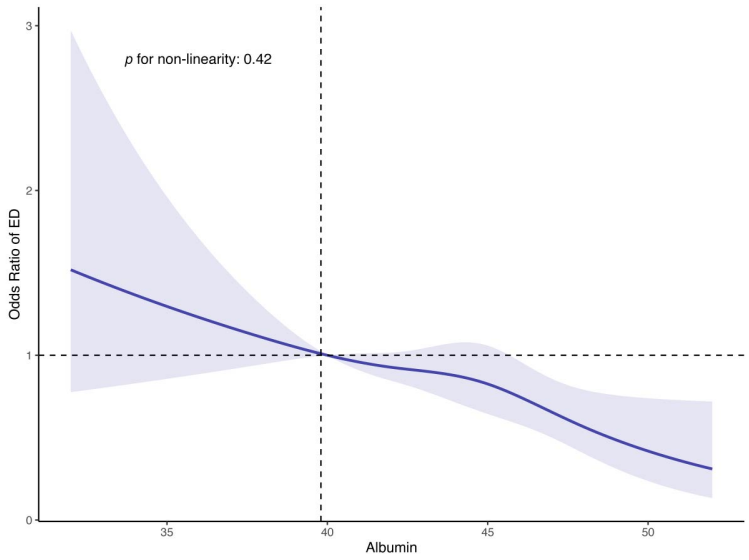
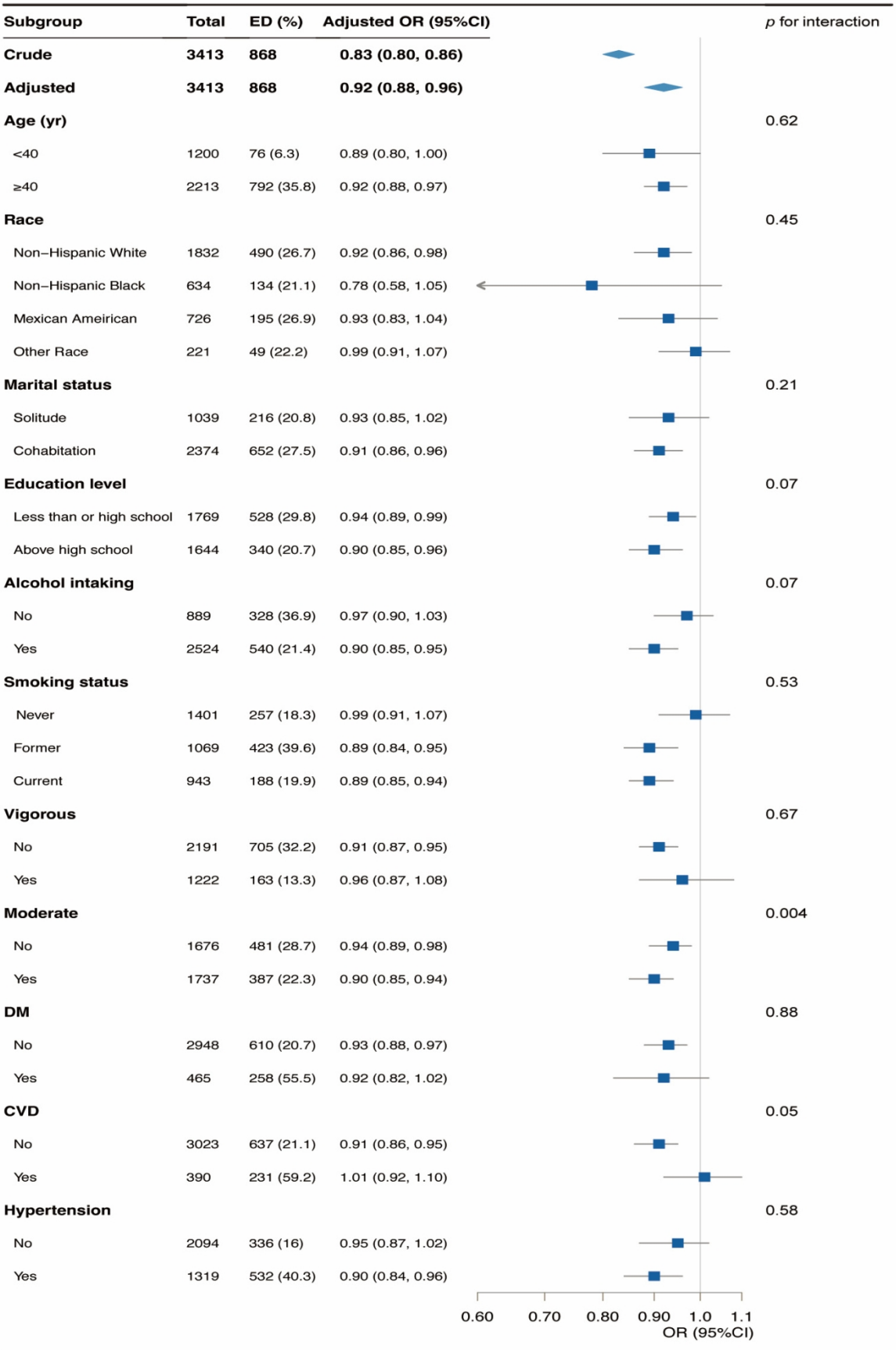


FIGURE 2. Smooth curve fitting for serum albumin and ED. The area between the upper and lower light blue represents the 95% CI. The blue solid line indicates that the negative linear association between albumin and ED is proven by generalized additive model. ED: erectile dysfunction.

TABLE 3. Subgroup analysis for the association between serum albumin and ED.

Variable	Crude model OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	*p* for interaction*
Age (yr)					
<40	0.87 (0.79–0.95)	0.88 (0.79–0.97)	0.89 (0.80–0.98)	0.89 (0.80–1.00)	0.62
≥40	0.88 (0.84–0.91)	0.89 (0.86–0.93)	0.90 (0.86–0.93)	0.92 (0.88–0.97)	
Race					
Non-Hispanic white	0.82 (0.78–0.86)	0.89 (0.84–0.94)	0.89 (0.84–0.94)	0.92 (0.86–0.98)	0.45
Non-Hispanic black	0.76 (0.65–0.90)	0.82 (0.65–1.04)	0.81 (0.64–1.03)	0.78 (0.58–1.05)	
Mexican American	0.83 (0.77–0.90)	0.89 (0.81–0.99)	0.90 (0.82–1.00)	0.93 (0.83–1.04)	
Other race	0.92 (0.86–0.98)	0.95 (0.88–1.02)	0.95 (0.88–1.03)	0.99 (0.91–1.07)	
Marital status					
Solitude	0.84 (0.79–0.90)	0.92 (0.85–0.99)	0.92 (0.85–1.00)	0.93 (0.85–1.02)	0.21
Cohabitation	0.82 (0.78–0.86)	0.88 (0.84–0.93)	0.89 (0.84–0.93)	0.91 (0.86–0.96)	
Education level					
Less than or high school	0.85 (0.81–0.89)	0.91 (0.87–0.96)	0.92 (0.88–0.96)	0.94 (0.89–0.99)	0.07
Above high school	0.81 (0.77–0.86)	0.88 (0.82–0.93)	0.88 (0.83–0.94)	0.90 (0.85–0.96)	
Alcohol intake					
No	0.88 (0.82–0.94)	0.94 (0.87–1.01)	0.94 (0.87–1.01)	0.97 (0.90–1.03)	0.07
Yes	0.82 (0.78–0.85)	0.88 (0.83–0.92)	0.88 (0.84–0.93)	0.90 (0.85–0.95)	
Smoking status					
Never	0.84 (0.78–0.90)	0.95 (0.88–1.03)	0.96 (0.89–1.03)	0.99 (0.91–1.07)	0.53
Former	0.82 (0.78–0.86)	0.86 (0.81–0.90)	0.86 (0.82–0.90)	0.89 (0.84–0.95)	
Current	0.84 (0.80–0.89)	0.90 (0.85–0.95)	0.89 (0.85–0.93)	0.89 (0.85–0.94)	
Vigorous activity					
No	0.84 (0.81–0.88)	0.89 (0.86–0.93)	0.89 (0.86–0.93)	0.91 (0.87–0.95)	0.67
Yes	0.84 (0.77–0.90)	0.92 (0.83–1.01)	0.92 (0.83–1.02)	0.96 (0.87–1.08)	
Moderate activity					
No	0.86 (0.82–0.90)	0.92 (0.88–0.97)	0.92 (0.88–0.97)	0.94 (0.89–0.98)	0.004
Yes	0.80 (0.77–0.83)	0.87 (0.83–0.91)	0.87 (0.83–0.91)	0.90 (0.85–0.94)	
DM					
No	0.84 (0.80–0.88)	0.90 (0.85–0.94)	0.91 (0.86–0.95)	0.93 (0.88–0.97)	0.88
Yes	0.89 (0.82–0.98)	0.92 (0.84–1.00)	0.91 (0.83–1.00)	0.92 (0.82–1.02)	
CVD					
No	0.82 (0.79–0.86)	0.89 (0.85–0.93)	0.89 (0.86–0.93)	0.91 (0.86–0.95)	0.05
Yes	0.94 (0.88–1.02)	0.97 (0.88–1.07)	0.97 (0.89–1.07)	1.01 (0.92–1.10)	
Hypertension					
No	0.84 (0.79–0.88)	0.90 (0.85–0.97)	0.92 (0.86–0.99)	0.95 (0.87–1.02)	0.58
Yes	0.85 (0.80–0.89)	0.88 (0.84–0.93)	0.88 (0.83–0.93)	0.90 (0.84–0.96)	

Crude model: no variables were adjusted.
Model 1 adjusted for age, marital status, race, FIR, education levels and BMI.
Model 2 adjusted for Model 1 + alcohol intake, smoking, vigorous and moderate activity.
Model 3 adjusted for Model 2 + DM, hypertension, CVD, eGFR, CRP, ALT and AST.
**means only in Model 3.*
OR: odds ratio; CI: confidence interval; DM: diabetes mellitus; CVD: cardiovascular disease.



F I G U R E 3. Association between serum albumin and ED. Note: Each stratification was adjusted for age, race, marital status, education, FIR, BMI, DM, CVD, hypertension, eGFR, CRP, ALT and AST, except the stratification factor itself. Squares indicate ORs, with horizontal lines indicating 95% CIs. Diamonds indicate overall ORs, with outer points of the diamonds indicating 95% CIs. ED: erectile dysfunction; OR: odds ratio; CI: confidence interval; DM: diabetes mellitus; CVD: cardiovascular disease.

TABLE 4. Sensitivity analysis of the association between serum albumin and ED*.

Variable	Crude model OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Serum albumin	0.82 (0.79–0.86)	0.89 (0.85–0.93)	0.88 (0.84–0.92)	0.92 (0.86–0.97)
Serum albumin quantile				
Q1	ref	ref	ref	ref
Q2	0.63 (0.43–0.92)	0.86 (0.59–1.26)	0.89 (0.61–1.29)	1.06 (0.69–1.63)
Q3	0.36 (0.26–0.51)	0.58 (0.40–0.84)	0.55 (0.39–0.77)	0.65 (0.41–1.05)
Q4	0.20 (0.14–0.30)	0.43 (0.28–0.66)	0.40 (0.26–0.61)	0.46 (0.27–0.80)
p for trend	<0.0001	<0.0001	<0.0001	0.0040

Crude model: no variables were adjusted.
Model 1 adjusted for age, marital status, race, FIR, education levels and BMI.
Model 2 adjusted for Model 1 + alcohol intake, smoking, vigorous and moderate activity.
Model 3 adjusted for Model 2 + DM, hypertension, CVD, eGFR, CRP, ALT and AST.
**mean ED is defined as never able to keep an erection.*
OR: odds ratio; CI: confidence interval.

TABLE 5. Sensitivity analysis of the association between serum albumin* and ED.

Variable	Crude model OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Serum albumin	0.82 (0.79–0.85)	0.89 (0.85–0.93)	0.89 (0.86–0.93)	0.91 (0.87–0.96)
Serum albumin quantile				
Q1	ref	ref	ref	ref
Q2	0.63 (0.43–0.92)	0.86 (0.59–1.26)	0.89 (0.61–1.29)	1.06 (0.69–1.63)
Q3	0.36 (0.26–0.51)	0.58 (0.40–0.84)	0.55 (0.39–0.77)	0.65 (0.41–1.05)
Q4	0.20 (0.14–0.30)	0.43 (0.28–0.66)	0.40 (0.26–0.61)	0.46 (0.27–0.80)
p for trend	0.004	<0.001	<0.001	0.004

Crude model: no variables were adjusted.
Model 1 adjusted for age, marital status, race, FIR, education levels and BMI.
Model 2 adjusted for Model 1 + alcohol intake, smoking, vigorous and moderate activity.
Model 3 adjusted for Model 2 + DM, hypertension, CVD, eGFR, CRP, ALT and AST.
**mean serum albumin defined as more than or equal to 35g/L.*
OR: odds ratio; CI: confidence interval.

TABLE 6. Sensitivity analysis of the association between serum albumin and ED with adjusted sex hormone.

Adjustment	Number	Event	OR (95% CI)	*p* value
Model 3 + testosterone	559	139	0.78 (0.64–0.94)	0.02
Model 3 + SHBG	558	138	0.84 (0.71–0.99)	0.04
Model 3 + estradiol	559	139	0.80 (0.66–0.97)	0.03
Model 3 + free testosterone	558	138	0.81 (0.68–0.97)	0.03
Model 3 + bio-available testosterone	558	138	0.81 (0.68–0.97)	0.03

Model 3 adjusted for age, marital status, race, FIR, education levels, BMI, alcohol intake, smoking, vigorous, moderate activity, DM, hypertension, CVD, eGFR, CRP, ALT and AST.
OR: odds ratio; CI: confidence interval; SHBG: sex hormone-binding globulin.

association of albumin with ED persists even in populations with normal levels. Previous isolated studies [16, 31–34] have reported similar negative correlations between albumin and ED; however, their study populations primarily consisted of specific groups, such as patients with diabetes, renal insufficiency or liver disease. In contrast, our findings encompass a broader range of individuals, reflecting the general population due to the characteristics of the NHANES database.

In subgroup analyses, we discovered that the impact of serum albumin levels on ED is influenced by moderate-intensity physical activity. Our results indicate that the protective effect of albumin on ED is more pronounced in individuals engaging in moderate physical activity compared to those who do not participate in any physical

activity. Existing literature [16, 31, 32, 35] has previously noted the beneficial effects of moderate or high-intensity physical activity on ED, which aligns with our findings. The underlying mechanisms driving this interaction warrant further investigation and clarification in future research.

The role of albumin in the context of ED may be intricately linked to its interactions with sex hormone binding [36–38]. After adjusting for various sex hormones—including testosterone, sex hormone-binding globulin, estradiol, free testosterone and bioavailable testosterone—in our sensitivity analyses, serum albumin consistently emerged as an independent protective factor. A prior study [37] has indicated that albumin can exert its effects through such hormonal interactions. Beyond potential mediations involving sex hormones, our study suggests that albumin may influence ED through alternative biological pathways. Nevertheless, additional studies are crucial to confirm this hypothesis and clarify the particular mechanisms that play a role in these interactions.

This study contains multiple significant strengths that deserve recognition. The results offer strong support for clinical treatments aimed at adults facing ED. Specifically, they highlight the importance of monitoring and managing low albumin levels as part of a comprehensive approach to maintaining optimal health, particularly among individuals with chronic diseases. Furthermore, this study signifies a groundbreaking attempt to explore the relationship between ED and serum albumin concentrations in adult individuals, since no previous studies addressing this subject have been found. By integrating our findings with existing literature, we underscore the potential of albumin as a clinical immuno-inflammatory predictor in ED, thereby illuminating possible underlying mechanisms. Furthermore, our results raise awareness of a significant public health concern related to the prevalence of ED.

Although our research offers specific benefits, recognizing its limitations is crucial. Initially, the diagnosis of ED relies on the self-reports of participants, which do not provide comprehensive details or objective evaluations regarding the severity of ED. Additionally, due to the cross-sectional nature of this study, a causal relationship between serum albumin levels and ED cannot be confirmed. Future longitudinal research with bigger participant cohorts is necessary to elucidate the impact of albumin on ED, and to examine the enduring nature of the link found in our findings. Besides, the outcomes mainly reflect the U.S. demographic and may not be directly relevant to other racial populations. Lastly, although the data from NHANES has been collected through rigorous standardization and we have conducted various sensitivity analyses to verify the stability of our results, it is important to note that the information regarding ED in NHANES is relatively outdated. Further validation is needed in the future.

5. Conclusions

Our study revealed a notable link between increased serum albumin levels and a lower risk of ED in the broader population. Importantly, this relationship held strong even after accounting for several confounding variables, suggesting that albumin concentrations could serve as an independent and supplementary predictor of ED. These results point to possible clinical significance for tracking albumin levels concerning ED risk and highlight the need for additional studies to investigate the mechanisms behind this association.

AVAILABILITY OF DATA AND MATERIALS

All data analyzed in this study are derived from the National Health and Nutrition Examination Survey (NHANES), a publicly accessible database maintained by the Centers for Disease Control and Prevention (CDC). Further inquiries can be directed to the corresponding authors.

AUTHOR CONTRIBUTIONS

XBC and JWL—conceptualization; data curation; formal analysis; investigation; methodology; software; visualization; funding acquisition and writing original draft. BHL—investigation; resources. LJL and WJ—validation; methodology; supervision and visualization. RYX—project administration; supervision; review and editing.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The NHANES survey protocol was approved annually by the NCHS Research Ethics Review Board, and all participants provided written informed consent. Therefore, human subjects' approval was not necessary nor sought since this was a de-identified data-only study.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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