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Dietary patterns, oxidative stress, and cognitive decline—A multiple mediation analysis based on structural equation modeling

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Abstract. Objective: To examine the relationship between older adults' diet-and-lifestyle Oxidative Balance Score (OBS) and cognitive function, and to investigate whether oxidative stress mediates that relationship. Methods: A total of 1,044 adults aged 60 years and older were included from the 2011-2014 National Health and Nutrition Examination Survey (NHANES). Cognitive function was assessed by four tests: the Immediate Recall Test (IRT), Delayed Recall Test (DIR), Animal Fluency Test (AFT), and the Digit Symbol Substitution Test (DSST). Weighted multivariable linear regression and Restricted Cubic Spline (RCS) analyses evaluated the associations between OBS and cognitive outcomes. Mediation analysis using Structural Equation Modeling (SEM) tested the indirect effects of oxidative-stress biomarkers on these associations. Results: OBS was positively associated with IRT, DIR, AFT, DSST, and overall cognitive function; the β estimates (95% CI) were 5.83 (5.10-6.56), 0.38 (0.17-0.59), 15.37 (13.64-17.09), 45.22 (40.97-49.46), and 66.79 (61.48-72.11), respectively. RCS analyses revealed approximately linear dose–response relationships between OBS and IRT, DSST, and overall cognitive function. The 75th percentile and the highest quartile of scores on these three measures were also significantly associated with OBS. OBS directly and positively predicted overall cognitive ability, and was positively correlated with serum albumin and vitamin D levels while negatively correlated with uric acid. OBS may indirectly influence memory performance by modulating albumin, uric acid, and serum 25-hydroxyvitamin D (25(OH)D) levels. Conclusions: We propose a four-dimensional regulatory model — "diet → lifestyle → oxidative microenvironment → cognitive function" — and provide evidence that multifactorial, synergistic antioxidant interventions have cumulative protective effects on cognition in older adults via a biomarker-network mediation mechanism. These findings support the development of personalized, oxidative-balance-based cognitive interventions and underscore the public-health value of whole-diet pattern adjustment combined with lifestyle optimization for preventing cognitive decline.

Keywords: Oxidative Balance Score, structural equation modeling, oxidative stress pathways, NHANES, cognitive function

1. Introduction

With the intensification of global population aging, cognitive decline has become a major public health challenge. In 2023, more than 55 million individuals worldwide were living with Alzheimer's disease, a number projected to rise to 78 million by 2030 and to 139 million by 2050 [1, 2]. In recent years, research on diet-cognition relationships has shifted from focusing on single nutrients to evaluating overall dietary patterns. Within this context, dietary antioxidant capacity, a key indicator of diet quality, has been proposed to exert neuroprotective effects against neurodegenerative disorders through the modulation of oxidative-stress pathways [3-5]. However, the mechanisms by which antioxidant capacity influences cognition remain incompletely understood, and the mediating role of biomarkers is still a matter of debate [6].

A growing body of evidence shows that dietary antioxidant capacity is inversely associated with chronic-disease risk. Plant-based dietary patterns, such as the Mediterranean and DASH diets [7], are abundant in polyphenols, vitamins C and E, and carotenoids, which markedly enhance Total Antioxidant Capacity (TAC) and reduce the risk of metabolic syndrome, cardiovascular disease, and Type 2 Diabetes Mellitus (T2DM) [3, 4]. For example, Li et al. reported that each 1-standard-deviation increase in the Dietary Antioxidant Quality Score (DAQS) was associated with a 15% reduction in T2DM risk among rural Chinese populations [8]. At the same time, assessment methods have been refined. Composite indices such as Oxygen Radical Absorbance Capacity (ORAC) and the Oxidative Balance Score (OBS) are now widely used to quantify the oxidative-antioxidative balance of diets [9, 10]. Importantly, the OBS integrates pro-oxidant factors (e.g., iron, polyunsaturated fatty acids) and antioxidant factors (e.g., selenium, vitamin C), providing a more comprehensive picture of individual oxidative-stress status

[10]. Yet, the associations between OBS and specific biomarkers (e.g., IL-6, C-reactive protein) vary across populations, sometimes yielding contradictory results in patients with chronic diseases [10], which underscores its complexity as a mediating variable.

Oxidative stress damages cognitive function via multiple mechanisms: direct neuronal DNA and mitochondrial injury that reduces synaptic plasticity [11, 12]; activation of inflammatory pathways that accelerate neurodegeneration [3, 13]; and disruption of calcium homeostasis and neurotransmitter release, thereby impairing hippocampus-dependent memory [6]. Animal studies demonstrate that antioxidants such as resveratrol and hydroxytyrosol enhance neuroprotection through activation of the Nrf2 pathway [14]. In population studies, NHANES data reveal that each 5-point increase in Mediterranean diet adherence is associated with a 0.21-standard-deviation improvement in CERAD word-learning test scores among older adults [15]. Adequate intake of vitamin B2 and magnesium has also been positively associated with cognitive performance [16, 17]. Notably, the neuroprotective effects of antioxidants exhibit dose dependency and synergism; for instance, combined supplementation of vitamin E and β-carotene improves executive function more effectively than either component alone [18], underscoring the need to assess antioxidant capacity from an overall dietary-pattern perspective.

Accordingly, this study incorporated six potential biomarkers of oxidative-stress status—serum albumin (g/dL), Creatine Phosphokinase (CPK, IU/L), γ-Glutamyl Transferase (GGT, IU/L), total bilirubin (mg/dL), uric acid (mg/dL), and 25-hydroxyvitamin D [25(OH)D, nmol/L]—to examine their possible mediating roles in the association between OBS and cognitive function.

2. Method

2.1. Study population

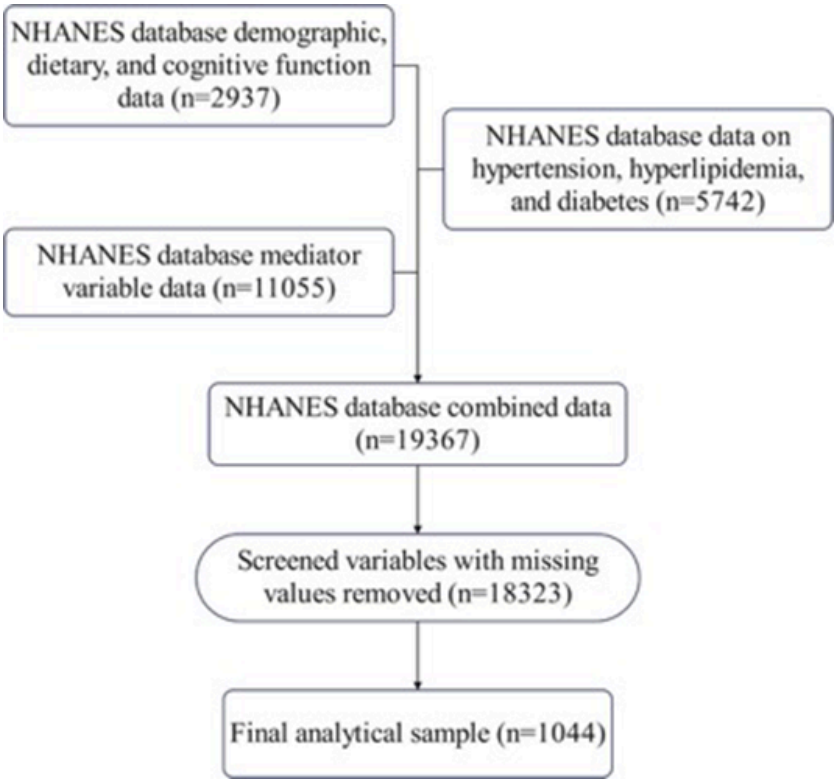

Figure 1. Flowchart of participant inclusion and exclusion

This study utilized data from two cycles of the National Health and Nutrition Examination Survey (NHANES), 2011-2012 and 2013-2014, which included four cognitive function tests for individuals aged 60 years and older. Participants who completed all cognitive assessments were initially included (n = 2,937). Those with missing information on any OBS component or dietary energy intake were excluded (n = 2,588). Individuals with missing data on oxidative-stress biomarkers or covariates were further excluded (n = 1,544). Ultimately, 1,044 participants were included in the final analysis (Figure 1).

2.2. Data collection

The Oxidative Balance Score (OBS) comprised two components: dietary intake and lifestyle factors. In NHANES, dietary data were collected through two 24-Hour Dietary Recall Interviews (24HRs). The first recall was conducted in the Mobile Examination Center (MEC), and the second was conducted by telephone 3-10 days later. Information on dietary supplement use was also collected during both interviews. In this study, both dietary intake and supplement use were included. The lifestyle component included alcohol consumption, smoking status, Body Mass Index (BMI), and physical activity, consistent with previous studies [6]. Alcohol intake and physical activity were assessed using standardized questionnaires. Serum cotinine, the primary metabolite of nicotine with a substantially longer half-life, was used to evaluate active smoking and environmental tobacco exposure. Serum cotinine was measured using Isotope-dilution High-performance Liquid Chromatography coupled with Atmospheric-pressure Chemical Ionization Tandem Mass Spectrometry (ID HPLC-APCI MS/MS). Anthropometric measurements were conducted by trained health technicians, and BMI was calculated as weight divided by height squared (kg/m^2). Physical activity data were obtained from a validated questionnaire adapted from the Global Physical Activity Questionnaire (GPAQ) using a computer-assisted personal interview system. Cognitive tests were administered by trained interviewers during private face-to-face interviews at the end of the MEC examination.

2.3. Oxidative Balance Score (OBS)

The OBS was constructed to reflect the overall balance between antioxidant and pro-oxidant exposures, with higher scores indicating greater predominance of antioxidants and, consequently, lower oxidative-stress risk (Table 1). The score was used to examine the relationship between diet, lifestyle, and oxidative damage.

The OBS comprised 20 components (16 nutrients and 4 lifestyle factors), divided into two categories: antioxidants (15 components) and pro-oxidants (5 components). Higher scores for antioxidants indicated stronger antioxidative effects, while higher scores for pro-oxidants indicated weaker pro-oxidative effects. Based on recent literature, six additional nutrients were included: riboflavin, niacin, vitamin B6, vitamin B12, magnesium, and copper. Smoking was assessed using serum cotinine as a biomarker of tobacco exposure.

Scoring was performed as follows. For alcohol consumption, non-drinkers were assigned 2 points, non-heavy drinkers ($\leq$ 15 g/day for women, $\leq$ 30 g/day for men) 1 point, and heavy drinkers (> 15 g/day for women, > 30 g/day for men) 0 points. For all other components, sex-specific tertiles of intake were created. For antioxidant exposures, the lowest tertile received 0 points, the middle tertile 1 point, and the highest tertile 2 points. For pro-oxidant exposures, scoring was reversed (lowest tertile = 2 points, middle = 1 point, highest = 0 points).

The total OBS ranged from 0 to 40 (20 components × maximum 2 points per component). For example, high vitamin C intake was scored as 2 points, whereas high red meat consumption was scored as 0 points [19].

2.4. Cognitive function tests

In NHANES, cognitive function was assessed using four standardized tests: the Immediate Recall Test (IRT), Delayed Recall Test (DRT), Animal Fluency Test (AFT), and Digit Symbol Substitution Test (DSST). The IRT and DRT were derived from the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery and served as indicators of immediate and delayed verbal learning, respectively. The IRT consisted of three sequential learning trials. In each trial, participants were asked to read aloud 10 unrelated words, immediately followed by recalling as many words as possible. Word order varied across trials. The IRT score was calculated as the sum of correctly recalled words across three trials (range: 0-30). The AFT required participants to name as many animals as possible within one minute, with one point awarded per unique animal. This task assessed verbal fluency, a component of executive function. The DSST, a subtest of the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III), measured processing speed, sustained attention, and working memory. Participants were asked to copy symbols corresponding to 133 numbers within two minutes, and the score represented the number of correct matches. Finally, after completing the IRT, AFT, and DSST, participants were asked to recall words from the IRT list, which provided the DRT score. For all cognitive tests, higher scores indicated better cognitive performance.

Table 1. Reference scoring criteria for the Oxidative Balance Score (n = 1044)

OBS components	Property	Male			Female		
		0	1	2	0	1	2
Dietary OBS components							
Dietary fiber (g/d)	A	< 12.56	12.56-19.70	≥ 19.70	< 10.10	10.10-16.31	≥ 16.31
Carotene (RE/d)	A	< 98.83	98.83-306.25	≥ 306.25	< 98.08	98.08-383.50	≥ 383.50
Riboflavin (mg/d)	A	< 1.79	1.79-2.69	≥ 2.69	< 1.34	1.34-2.02	≥ 2.02
Niacin (mg/d)	A	< 20.65	20.65-29.75	≥ 29.75	< 14.52	14.52-21.86	≥ 21.86
Vitamin B_6 (mg/d)	A	< 1.59	1.59-2.40	≥ 2.40	< 1.13	1.13-1.77	≥ 1.77
Total folate (mcg/d)	A	< 316.00	316.00-492.00	≥ 492.00	< 251.00	251.00-388.96	≥ 388.96
Vitamin B_{12} (mcg/d)	A	< 3.36	3.36-6.20	≥ 6.20	< 2.22	2.22-4.22	≥ 4.22
Vitamin C (mg/d)	A	< 42.44	42.44-113.21	≥ 113.21	< 38.01	38.01-98.49	≥ 98.49
Vitamin E (ATE) (mg/d)	A	< 5.82	5.82-9.42	≥ 9.42	< 4.53	4.53-7.52	≥ 7.52
Calcium (mg/d)	A	< 646.00	646.00-1,072.00	≥ 1,072.00	< 499.24	499.24-849.00	≥ 849.00
Magnesium (mg/d)	A	< 257.00	257.00-361.28	≥ 361.28	< 187.00	187.00-283.43	≥ 283.43
Zinc (mg/d)	A	< 9.75	9.75-15.10	≥ 15.10	< 6.73	6.73-10.75	≥ 10.75
Copper (mg/d)	A	< 1.12	1.12-1.57	≥ 1.57	< 0.85	0.85-1.28	≥ 1.28
Selenium (mcg/d)	A	< 94.94	94.94-141.80	≥ 141.80	< 67.79	67.79-99.50	≥ 99.50
Total fat (g/d)	P	≥ 69.83	69.83-107.43	< 107.43	≥ 50.98	50.98-75.79	< 75.79
Iron (mg/d)	P	≥ 12.88	12.88-19.17	< 19.17	≥ 9.65	9.65-14.32	< 14.32
Lifestyle OBS components							
Physical activity (MET-minute/week)	A	< 417.86	417.86-1,135.71	≥ 1,135.71	< 270.00	270.00-845.71	≥ 845.71
Alcohol (g/d)	P	≥ 30	0-30	None	≥ 15	0-15	None
Body mass index (kg/m^2)	P	≥ 25.54	25.54-29.17	< 29.17	≥ 23.74	23.74-28.64	< 28.64
Cotinine (ng/mL)	P	≥ 0.038	0.038-1.13	< 1.13	≥ 0.035	0.035-0.172	< 0.172

2.5. Covariates

Covariates included sex, age, race/ethnicity, educational attainment, the ratio of family income to the poverty threshold, and disease status (hypertension, hyperlipidemia, diabetes). Age was grouped into 5-year intervals: 60-65, 66-70, 71-75, and 76-80 years. Sex was categorized as male or female. Race/ethnicity was classified into four categories: non-Hispanic White, non-Hispanic Black, Mexican American, and other races. Demographic and socioeconomic data were collected through standardized household interview questionnaires. Dietary energy intake was averaged from two 24-Hour Dietary Recalls (24HR). Educational attainment was categorized as: below 9th grade, 9th-11th grade (including non-graduated 12th grade), high school graduate or GED equivalent, some college or associate degree, bachelor's degree or above, and refusal to answer. The Poverty-Income Ratio (PIR) was calculated as the ratio of total household income to the federal poverty threshold, reflecting economic status. Following analytic standards, PIR was divided into ≤ 1.3 (deep poverty), 1.3-3.5 (low-to-middle income), and > 3.5 (higher income) [1].

Disease status was recorded as binary variables (yes/no). Diabetes was defined as Hemoglobin A1c (HbA1c) ≥ 6.5%, use of insulin or hypoglycemic agents, fasting plasma glucose ≥ 7.0 mmol/L, random plasma glucose ≥ 11.1 mmol/L, or Oral Glucose Tolerance Test (OGTT) ≥ 11.1 mmol/L. Hyperlipidemia was defined as total cholesterol < 200 mg/dL, triglycerides < 150 mg/dL, LDL cholesterol < 130 mg/dL, and HDL cholesterol < 40 mg/dL. Hypertension was defined as the average of three blood pressure measurements showing systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg.

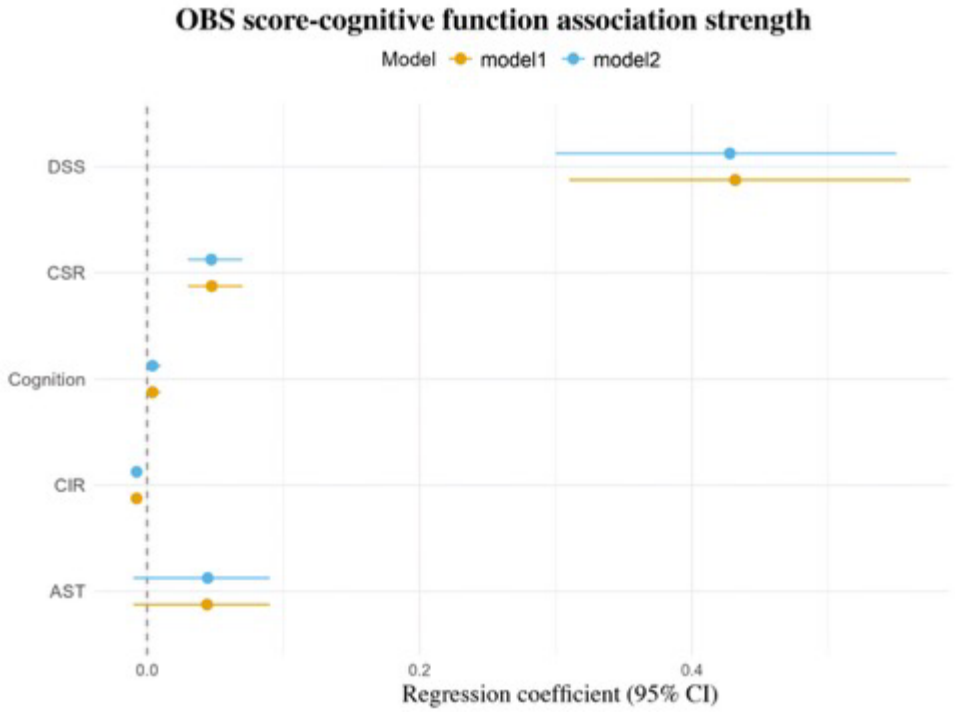

Figure 2. Comparison of group effects across different cognitive test models

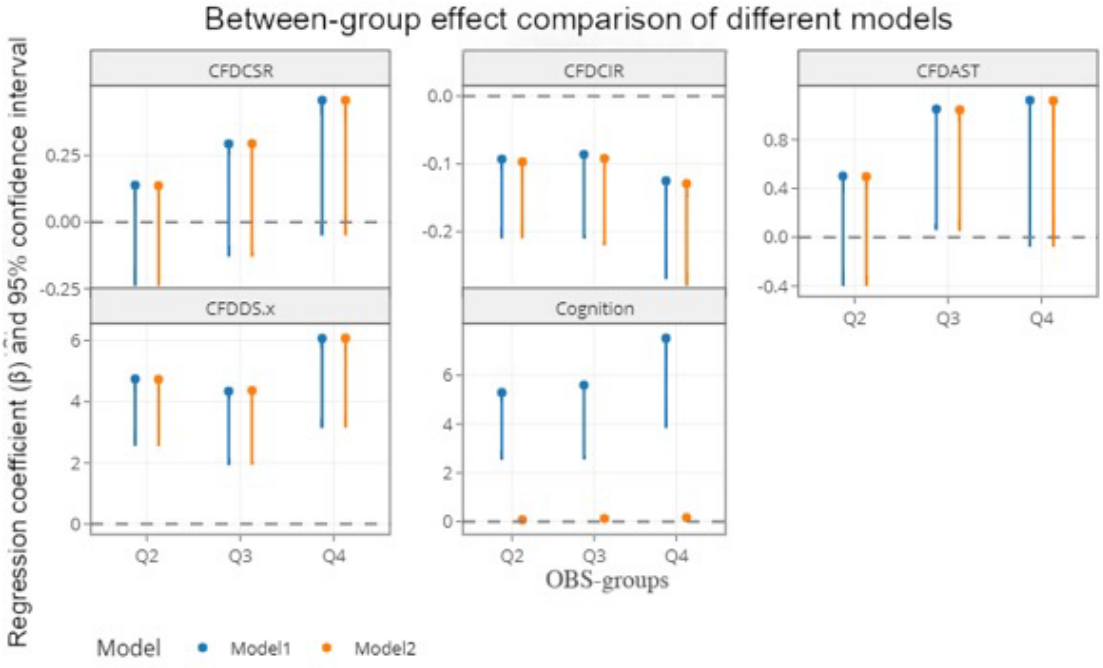

Figure 3. Strength of the associations between OBS and cognitive function

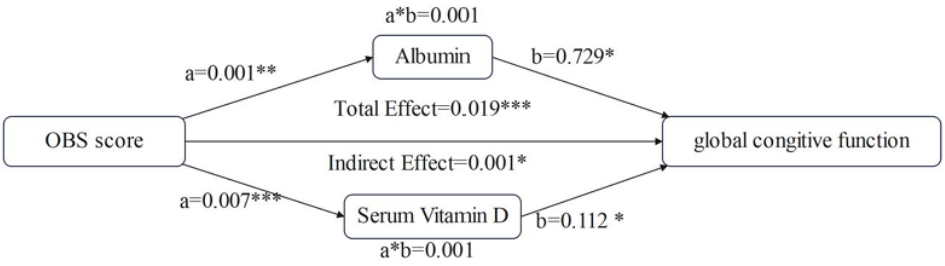

Figure 4. Indirect effects of OBS on global cognitive function in the mediation analysis (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$)

Table 2. Baseline characteristics of participants and cognitive function test results (n = 1044)

Characteristics	Overall (%)	IRT	p	DRT	p	AST	p	DSST	p
		M		M		M		M	
	(N = 1,044)	(P25-P75)		(P25-P75)		(P25-P75)		(P25-P75)	
RIAGENDR.x (%)	1,044								
male	503 (48.2)	6 (4-7)	< 0.001***	0 (0-0)	0.93	16 (13-21)	0.327	43 (34-55)	< 0.001***
female	541 (51.8)	7 (5-8)		0 (0-0)		17 (13-20)		50 (38-62)	
RIDAGEYR.x (%)									
60-65	380 (36.4)	7 (5-8)	< 0.001***	0 (0-0)	0.504	18 (14-22)	< 0.001***	54 (43-65)	< 0.001***
66-70	234 (22.4)	7 (5-8)		0 (0-0)		17 (13.25-21)		48 (35-58)	
71-75	166 (15.9)	6 (5-8)		0 (0-0)		16 (12-20)		44 (33.25-54)	
76-80	264 (25.3)	5 (4-7)		0 (0-0)		16 (12-19)		39 (29-49)	
RIDRETH1.x (%)									
Mexican American	94 (9.0)	6 (4-7)	< 0.001***	0 (0-0)	< 0.001***	16 (12.25-20)	< 0.001***	38.5 (28.25-52.75)	< 0.001***
Other Hispanic	90 (8.6)	6 (4-7)		0 (0-1)		16 (13-19)		36 (25.5-48.75)	
Non-Hispanic White	570 (54.6)	6 (5-8)		0 (0-0)		18 (15-22)		51 (40-62)	
Non-Hispanic Black	206 (19.7)	6 (5-7)		0 (0-1)		15 (11.25-18)		40.5 (29-51)	
Other Race (Including Multi-Racial)	84 (8.0)	7 (6-8)		0 (0-0)		15 (12.75-18)		51.5 (44-63)	
DMDEDUC2.x (%)									
Less than 9th grade	99 (9.5)	5 (4-7)	< 0.001***	0 (0-1)	< 0.05*	15 (11.5-16)	< 0.001***	26 (20.5-33)	< 0.001***
9-11th grade (Includes 12th grade with no diploma)	141 (13.5)	5 (4-7)		0 (0-0)		15 (11-17)		37 (30-46)	
High school graduate/GED or equivalent	244 (23.4)	6 (4-8)		0 (0-0)		16 (12-20)		44 (34-55)	
Some college or AA degree	306 (29.3)	7 (6-8)		0 (0-0)		17 (14-21)		50 (42-61)	
College graduate or above	252 (24.1)	7 (5-8)		0 (0-0)		19 (16-24)		57 (48-66)	
Refused/Don't Know	2 (0.2)	3 (2-4)		0.5 (0.25-0.75)		9 (8-10)		26.5 (23.25-29.75)	

Table 2. Continued

INDFMPIR.x (%)									
PIR < 1.3	282 (27.0)	6 (4-7)	< 0.001***	0 (0-0)	0.686	15 (12-19)	< 0.001***	36.5 (26-48)	< 0.001***
1.3 ≤ PIR < 3.5	417 (39.9)	6 (5-8)		0 (0-0)		16 (13-20)		47 (37-56)	
PIR ≥ 3.5	345 (33.0)	7 (5-8)		0 (0-0)		19 (15-23)		56 (45-66)	
Diabetes (%)									
Yes	304 (29.1)	6 (4-7)	< 0.001***	0 (0-0)	< 0.05*	16 (13-19)	< 0.01**	43 (29-53)	< 0.001***
No	740 (70.9)	7 (5-8)		0 (0-0)		17 (14-21)		49 (37-61.25)	
Hyperlipidemia (%)									
Yes	328 (31.4)	6 (5-8)	0.975	0 (0-0)	<0.05*	16.5 (14-20)	0.709	47 (35-58)	0.813
No	716 (68.6)	6 (5-8)		0 (0-0)		16 (13-20)		47 (35-59)	
Hypertension (%)									
Yes	287 (27.5)	6 (4-8)	< 0.01**	0 (0-0)	0.455	16 (12.5-19)	< 0.01**	42 (30-55.5)	< 0.001***
No	757 (72.5)	6 (5-8)		0 (0-0)		17 (14-21)		49 (37-60)	

2.6. Oxidative stress biomarkers

Based on the potential relevance of oxidative stress, six biomarkers were included in the analysis: albumin (g/dL), Creatine Phosphokinase (CPK; IU/L), γ-Glutamyl Transferase (GGT; IU/L), total bilirubin (mg/dL), uric acid (mg/dL), and 25(OH)D (nmol/L). In this study, the sum of 25-hydroxyvitamin D2 and 25-hydroxyvitamin D3 concentrations was used to estimate serum 25(OH)D levels. Albumin, CPK, GGT, bilirubin, and uric acid were measured using the Beckman Coulter UniCel DxC 800 system (Beckman Coulter). GGT activity was determined using an enzymatic rate method. Albumin concentration was measured using a bichromatic digital endpoint method. Total bilirubin was quantified using the timed endpoint diazo method (Jendrassik-Grof), while uric acid was assessed using a timed endpoint assay. Serum 25(OH)D levels were quantified using ultra-high performance liquid chromatography coupled with tandem mass spectrometry (UHPLC-MS/MS; Thermo Electron Corp).

2.7. Statistical analysis

Continuous variables were expressed as weighted means with standard deviations (mean ± SD) or as medians with interquartile ranges (M, IQR), while categorical variables were presented as counts (*n*) and percentages (%). To examine differences in cognitive function tests across covariates, Rao–Scott chi-square tests were applied to categorical variables, and univariate linear regression was used for normally distributed continuous variables. To enhance comparability, standardized z-scores were created for each cognitive test by subtracting the observed score of any participant and dividing by the standard deviation of the cognitive score. Global cognitive function was calculated by integrating standardized scores from the Consortium to Establish a Registry for Alzheimer's Disease Word Learning test (CERAD-WL), the Animal Fluency Test (AFT), and the Digit Symbol Substitution Test (DSST), generating a composite cognitive score [20]:

$$Z_{cognition} = 0.4 \times Z_{CERAD} + 0.3 \times Z_{AFT} + 0.3 \times Z_{DSST} \quad (1)$$

Oxidative stress biomarkers were log-transformed to normalize their distributions.

Multivariate linear regression models were used to assess the associations between OBS and the four cognitive function tests as well as global cognition. Model 1 was adjusted for demographic variables (age, sex, race/ethnicity, education level, and PIR), dietary energy intake, and caffeine intake. Model 2 was further adjusted for disease status, including hypertension, hyperlipidemia, and diabetes. In this study, OBS was analyzed both as a continuous variable and as a categorical variable based on quartiles.

To explore the potential mediating role of oxidative stress in the association between OBS and cognitive function, we analyzed the effects of OBS on global cognition as well as the effects of oxidative stress biomarkers on cognition. Among the six oxidative stress biomarkers, simple mediation analyses were first performed; those showing significant mediation effects ($p <$

0.05) were subsequently included in a multivariable model to identify key mediators driving the OBS-cognition relationship. The mediation model was adjusted for overall covariates. Following the recommendations of Preacher and Hayes, bootstrapping procedures were used to calculate bias-corrected 95% Confidence Intervals (CIs) for indirect effects; if the CI did not include zero, the mediation effect was considered statistically significant [21].

All statistical analyses were conducted using R software (version 4.3.3). A two-tailed p-value < 0.05 was considered statistically significant.

2.8. Model description

2.8.1. Structural Equation Modeling (SEM)

Structural Equation Modeling (SEM) is a multivariate statistical method that integrates factor analysis and path analysis to examine complex relationships among observed variables, latent variables, and their interconnections. Its framework consists of two core components: the measurement model (describing relationships between latent variables and their observed indicators) and the structural model (depicting causal pathways among variables). Together, these allow for holistic validation and refinement of theoretical models. The measurement model specifies how observed variables—measured directly through instruments such as questionnaires or scales—reflect latent constructs. For instance, a latent variable may be represented by multiple observed items collectively capturing a particular trait or concept. The structural model describes causal relationships among latent variables, including path coefficients that quantify both direct and indirect effects (Appendix Figure 1).

SEM is a confirmatory analytic approach, requiring model construction based on theoretical assumptions, followed by empirical validation. It accommodates simultaneous examination of multiple variable relationships, explicitly models measurement error, and thereby enhances the accuracy of analysis. General operational steps of SEM are illustrated in Appendix Figure 2.

3. Results

3.1. Baseline characteristics of the study population

A total of 1,044 adults (aged ≥ 60 years) were included in this study. The mean age was 69.52 ± 6.77 years, and 48.2% were male. The mean OBS score was 20.01 ± 8.23. The median values of IRT, DRT, AFT, and DSST were 6 (0-10), 0 (0-5), 16 (3-36), and 47 (4-105), respectively. The median levels of albumin (g/dL), Creatine Phosphokinase (CPK, IU/L), γ-Glutamyl Transferase (GGT, IU/L), total bilirubin (mg/dL), uric acid (mg/dL), and 25(OH)D (nmol/L) were 4.2 (3.00-5.20), 97 (21.00-862.00), 19 (6.00-423.00), 0.70 (0.20-2.20), 5.6 (1.10-11.20), and 74.85 (10.8-210.00), respectively. Table 2 summarizes the characteristics of the participants included in the study. In univariate analysis, lower overall cognitive performance was associated with older age and higher caloric intake, as well as lower income and educational attainment (p < .01). Significant differences in the four cognitive tests were observed across racial groups (p < .01). Male participants scored significantly lower on CSR, DSST, and total cognitive performance compared to females (p < .01).

3.2. Association between OBS and cognitive function

Table 3 presents the associations between OBS and cognitive function tests using multivariable linear regression models. When OBS was treated as a continuous variable (Figure 2), it was positively associated with CSR (β = 0.05), AST (β = 0.12), DSST (β = 0.53), and overall cognitive function (β = 0.02), and negatively associated with CIR (β = –0.01). These associations remained significant after full adjustment, with estimated β values of 5.86, 0.38, 15.33, 45.49, and 67.07, respectively. In Model 1, when OBS was treated as a categorical variable (Figure 3), significant associations were observed for AST in Q3 (Model 1 Q3: 1.051 [0.06, 2.04]); for DSST in Q2, Q3, and Q4 (Model 1 Q2: 4.743 [2.55, 6.93]; Q3: 4.339 [1.92, 6.76]; Q4: 6.067 [3.14, 8.99]); and for overall cognitive function in Q2, Q3, and Q4 (Model 1 Q2: 5.29 [2.53, 8.04]; Q3: 5.597 [2.55, 8.65]; Q4: 7.523 [3.84, 11.21]*). In the fully adjusted Model 2, the associations between OBS and AST (Q3), DSST (Q2, Q3, and Q4), and overall cognitive function (Q4) remained significant.

Table 3. Weighted multivariable linear regression analysis of OBS and cognitive function (n = 1044)

OBS		Cognitive function tests β CI				
		CSR	CIR	AST	DSST	Global cognitive function
Continuous variable						
	model 1	5.81 (5.09-6.52)***	0.39 (0.18-0.60)***	15.36 (13.67-17.05)***	44.72 (40.58-48.86)***	66.28 (61.08-71.48)***
	model 2	5.86 (5.13-6.59)***	0.38 (0.17-0.60)***	15.33 (13.61-17.05)***	45.49 (41.28-49.70)***	67.07 (61.78-72.36)***
Classified variable						
Q1 (Reference)						
Q2						
	model 1	0.139 (-0.24, 0.52)	-0.093 (-0.21, 0.02)	0.501 (-0.40, 1.40)	4.743 (2.55, 6.93)***	5.29 (2.53, 8.04)***
	model 2	0.137 (-0.24, 0.52)	-0.097 (-0.21, 0.01)	0.497 (-0.40, 1.40)	4.727 (2.54, 6.92)***	0.072 (-0.05, 0.19)
Q3						
	model 1	0.294 (-0.13, 0.72)	-0.086 (-0.21, 0.04)	1.051 (0.06, 2.04)*	4.339 (1.92, 6.76)***	5.597 (2.55, 8.65)***
	model 2	0.295 (-0.13, 0.72)	-0.092 (-0.22, 0.03)	1.044 (0.05, 2.04)*	4.364 (1.94, 6.79)***	0.127 (-0.01, 0.26)
Q4						
	model 1	0.458 (-0.05, 0.97)	-0.125 (-0.27, 0.02)	1.123 (-0.08, 2.32)	6.067 (3.14, 8.99)***	7.523 (3.84, 11.21)***
	model 2	0.458 (-0.05, 0.97)	-0.129 (-0.28, 0.02)	1.119 (-0.08, 2.32)	6.075 (3.15, 9.00)***	0.166 (0.00, 0.33)*

3.3. Mediating role of oxidative stress

The mediating effects of oxidative stress on the association between OBS and overall cognitive function are presented in Table 4. When individual mediators were entered into the model with OBS and overall cognitive function, albumin (0.001; 95% CI: 0.000, 0.000) and serum 25(OH)D (0.001; 95% CI: 0.000, 0.000) were identified as significant mediators, accounting for 2.0% and 2.1% of the mediation effect, respectively (Table 4). When these key mediators were combined in a multivariable model, the overall mediating effect was significant, with 5.26% of the effect of OBS on overall cognitive function mediated through albumin and serum 25(OH)D (Table 4, Figure 4).

4. Conclusion

The results of this study demonstrate that the dietary Oxidative Balance Score (OBS), when treated as a continuous variable, was positively associated with multiple cognitive test outcomes (CSR, AST, DSST, and overall cognitive performance; β range: 0.02-0.53), and negatively associated with the pro-inflammatory indicator CIR (β = –0.01). These findings suggest that OBS may exert a protective effect on cognitive function through the regulation of oxidative stress and inflammatory pathways. OBS integrates 16 dietary antioxidant/pro-oxidant components (e.g., vitamins C, E, B vitamins, calcium, magnesium) and four lifestyle factors (e.g., smoking status, BMI, physical activity). A higher OBS reflects stronger antioxidant capacity [22]. Antioxidant nutrients can neutralize free radicals, reduce DNA damage and lipid peroxidation, and suppress neuroinflammatory responses (e.g., NF-κB pathway activation), thereby protecting neuronal function [23].

OBS shares similarities with dietary patterns such as the Mediterranean Diet (MD) and the MIND diet, both of which emphasize antioxidant-rich foods (e.g., leafy greens, nuts) [24]. However, the unique advantage of OBS lies in its inclusion of lifestyle factors (e.g., BMI, smoking), providing a more comprehensive reflection of oxidative balance [25]. Although the MIND diet has been shown to reduce Alzheimer's disease risk, its cognitive protective effects may be limited among smokers because it does not incorporate lifestyle scoring [26]. Our findings support the use of OBS as a tool for personalized nutritional

interventions, especially in older adults. Dietary adjustments (e.g., increasing vitamin C intake) combined with behavioral interventions (e.g., promoting physical activity) may work synergistically to enhance cognitive health [27].

Higher OBS scores may improve cognitive function through two key pathways: Direct reduction of neuroinflammatory responses—by suppressing microglial activation and pro-inflammatory cytokine release. And indirect protection of cerebrovascular endothelial function—as animal studies have shown that oxidative stress exacerbates blood–brain barrier permeability. This study further found that the protective effect of dietary OBS on cognitive function was moderated by SIRI (systemic inflammation response index; P for interaction < .001), suggesting that anti-inflammatory pathways may play a key role. Although this cross-sectional analysis revealed a cascading association between OBS, SIRI, and cognitive function [28], it cannot establish causality. Future studies should employ longitudinal cohorts to track dynamic changes in OBS and their long-term effects on inflammatory markers [29], as well as experimental models to test whether specific dietary components (e.g., vitamin E, polyphenols) regulate cognitive function via the NLRP3 inflammasome–SIRI pathway. We also examined six oxidative stress–related biomarkers (albumin, Creatine Phosphokinase [CPK], γ-Glutamyl Transferase [GGT], total bilirubin, uric acid, and 25(OH)D) as potential mediators. Among these, albumin and 25(OH)D were identified as significant mediators, suggesting that future research may explore the relationships between biochemical indicators and cognitive function, and whether improving these biomarkers can help prevent cognitive decline.

Oxidative stress results from excessive free radical (e.g., ROS) production, leading to cell membrane damage, protein denaturation, and lipid peroxidation. These changes impair neuronal function, promote apoptosis, and cause synaptic dysfunction, ultimately leading to cognitive impairment. In Alzheimer's Disease (AD), oxidative stress accelerates brain aging and cognitive decline by promoting β-amyloid deposition and tau hyperphosphorylation [30]. Similarly, in vascular parkinsonism, imbalances in oxidative stress markers such as SOD and MDA further exacerbate cognitive impairment [31]. Going forward, incorporating the dietary inflammation index alongside OBS may allow researchers to investigate the combined influence of dietary oxidative/antioxidative capacity and inflammatory/anti-inflammatory potential on cognitive function.

Table 4. Single and multiple mediation analyses of OBS and overall cognitive function (n = 1044)

	a Estimate (95% CI)	*b* Estimate (95% CI)	Direct effect (*c*') Estimate (95% CI)	Indirect effect (*a*b*) Estimate (95% CI)	Proportion Mediated
Separate mediators					
Albumin	-1.060 (-1.528, 0.818)**	1.410 (0.001,1.410)***	0.018 (0.012,0.02)***	0.001 (0.000,0.000)*	2.00%
CPK	-0.083 (-0.083,0.019)	4.56 (0.003,3.109)***	0.019 (0.0139,0.020)***	-0.0002 (-0.0008,0.000)	NA
GGT	-0.433 (-0.433,0.019)**	3.109 (-0.003,2.331)***	0.019 (0.013,0.02)***	0.000 (-0.000,0.000)	NA
Bilirubin	-0.388 (-0.388,0.019)***	-0.427 (-0.427,0.001)***	0.019 (0.013,0.02)***	-0.000 (-0.000,0.000)	NA
Uric acid	-0.434 (-0.434,0.034)*	1.791 (-0.004,1.791)***	0.0189 (0.013,0.02)***	-0.000 (-0.001,0.000)	NA
25(OH)D	-0.900 (-0.900,0.128)***	4.121 (-2.311,2.659)***	0.018 (0.012,0.02)***	0.001 (0.000,0.000)*	2.10%
Multiple mediators			0.602 (0.553,0.650)***		5.26%
Albumin	0.001 (0.000, 0.001)**	0.729 (0.044,1.438)*	0.005 (0.005, 0.006)***	0.001 (0.000,0.001)	5.26%
25(OH)D	0.007 (0.003,0.010)***	0.112 (0.005,0.220)*	0.186 (0.168,0.204)***	0.001 (0.000,0.002)	5.26%

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As this statistical modeling competition draws to a close, I have gained profound insights. In the process of striving to complete the project, I not only improved my literature review and rapid learning skills but also developed a more comprehensive understanding of data collection and utilization. My theoretical learning and derivation abilities have also been strengthened. More importantly, I have come to appreciate the crucial role of both quality and presentation in academic work. These experiences will continue to inspire me to keep progressing and to embrace future challenges with confidence.

This competition has also highlighted for me the importance of teamwork and revealed the close connection between theoretical knowledge and practical application. By engaging deeply with data and modeling, I learned how to apply theory flexibly to real-world problems and continuously refine my approach through practice. This growth not only benefits my development in mathematical modeling but also lays a solid foundation for my future academic and professional pursuits.

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