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Association between Dietary Inflammatory Index and Oxidative Balance Score with Cardiovascular-Kidney-Metabolic Syndrome in US Adults

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Abstract

Background: Inflammation and oxidative stress are key factors in the development of chronic diseases. Diet, a major determinant of these processes, has gained significant attention. This study evaluates the relationship between the Dietary Inflammation Index (DII) and the Dietary Oxidative Balance Score (DOBS) with Cardiovascular-Kidney-Metabolic (CKM) Syndrome. **Methods:** Using database from the National Health and Nutrition Examination Survey (NHANES) 1999-2018, dietary data were meticulously gathered through two 24-h recall assessments to ascertain the DOBS and DII. Multivariate weighted logistic regression, coupled with restricted cubic spline methodologies, were employed to evaluate the correlations between DOBS, DII, and CKM Syndrome. Subgroup analyses and interaction tests examined effects across genders, ages, races, BMI, smoking, and alcohol consumption. **Results:** After adjusting for covariates, elevated DOBS concentrations were markedly correlated with a lower prevalence of CKM Syndrome [Q4: OR = 0.49 (0.35, 0.69)], While elevated DII levels were markedly correlated with a higher odds [Q4: OR = 1.62 (1.14, 2.29)]. Restricted cubic splines showed linear negative and positive correlations for DOBS and DII, respectively. Subgroup analyses revealed that DOBS's protective effect was stronger in females, Whites, and individuals with BMI < 25, whereas DII's adverse effects were more pronounced in Whites, alcohol consumers, and those with BMI < 25. **Conclusion:** Higher DOBS is associated with significantly lower odds, and higher DII with higher odds, of having CKM Syndrome. These findings underscore the position of dietary antioxidants and anti-inflammatory components in preventing multisystem diseases, suggest-

ing that dietary improvements may effectively lower odds of CKM syndrome. This research supports public health policies and clinical interventions and provides directions for future studies.

Keywords

Dietary Inflammation Index, Dietary Oxidative Balance Score, Dietary Intervention, Cardiovascular-Kidney-Metabolic Syndrome, NHANES

1. Introduction

Cardiovascular-Kidney-Metabolic (CKM) syndrome constitutes a complex, multifaceted systemic malady, marked by the intricate physiological interplay between the cardiovascular apparatus, chronic kidney disease (CKD), and metabolic irregularities [1]. The American Heart Association (AHA) recently proposed a comprehensive CKM staging framework that categorizes individuals from stage 0 (no risk factors) to stage 4 (clinical cardiovascular disease with metabolic and/or renal dysfunction). However, in epidemiological research using existing datasets, an alternative operational approach focusing on the coexistence of established cardiometabolic syndrome and CKD may provide a more practical and reproducible phenotype for investigation. In recent years, the prevalence and prevalence of CKM syndrome have significantly increased due to lifestyle changes and an aging population. Studies indicate that from 2011 to 2020, approximately 90% of Americans met the criteria for CKM stage 1 or higher, with about 15% classified as late-stage CKM syndrome (stage 3 or 4) [2]. Consequently, CKM syndrome has become a critical issue in global public health requiring urgent attention.

Within the complex pathophysiological process of CKM syndrome, systemic inflammation is identified as a core mechanism driving its development, permeating multiple pathological aspects of cardiovascular diseases, CKD, and metabolic disorders [3]. Systemic inflammation significantly exacerbates cardiovascular and renal damage by upregulating inflammatory signs (like CRP and IL-6) and activating immune-inflammatory response indices (such as SIRI), and It is linked to a higher odds of all-encompassing and cardiovascular-related mortality [4]. The persistence of an inflammatory condition results in insulin sensitivity impairment, endothelial dysfunction, and the advancement of atherosclerotic disease [5]-[7]. Additionally, altered adipose tissue functionality and persistent mild inflammation (like obesity-related inflammation) are considered major triggers of CKM syndrome, significantly increasing the odds of metabolic disorders and organ function deterioration [8]. Diet, as an important factor in regulating systemic inflammation, has received widespread attention in recent years. Research demonstrates that specific nutrients and food components within the dietary structure can significantly influence inflammation levels in the body. For example, he consump-

tion of high levels of saturated fats and processed sugars has been linked to a rise in pro-inflammatory elements, whereas diets abundant in antioxidants, dietary fiber, and polyunsaturated fatty acids tend to demonstrate anti-inflammatory properties [9] [10]. By adjusting their diet, individuals can partially control inflammatory responses, thereby influencing the development and progression of CKM syndrome.

Oxidative stress plays a crucial role in the pathogenesis of CKM Syndrome, involving a complex array of processes such as the heightened expression of enzymes that generate reactive oxygen species (ROS), an overproduction of ROS, and a reduction in antioxidant defenses [11]. For instance, in animal models of CKM induced by maternal high fructose diets [12], maternal stress [13], nicotine exposure [14], and alcohol exposure [15], significant increases in ROS-generating enzyme expression and ROS levels have been observed. Additionally, Under hyperglycemic conditions, an overabundance of glucose metabolism results in the production of mitochondrial superoxide, thereby intensifying oxidative stress and precipitating tissue damage via the polyol pathways, the formation of advanced glycation end products (AGEs), and persistent inflammation [1] [16]. Diets laden with high levels of fat and sugar are linked to the overproduction of ROS, whereas those abundant in vitamin C, vitamin E, polyphenols, and other antioxidants help to counteract ROS, thus alleviating the tissue damage caused by oxidative stress [17]-[19]. The therapeutic potential of antioxidants has been validated, demonstrating their ability to alleviate the progression of CKM in individuals exposed to early oxidative stress by reducing oxidative damage, inflammation, and metabolic dysregulation [20].

The DII and DOBS, indices reflective of the inflammatory and oxidative responses to nutrient consumption, respectively, serve as tools for assessing the dietary influence on inflammation and oxidative stress [21] [22]. Growing body of research suggests that the DII is potentially linked to a multitude of chronic illnesses, including diabetes [23], cardiovascular diseases [24], and cancer. Higher DII values reflect a greater presence of pro-inflammatory components in the diet, whereas lower DII values indicate a higher presence of anti-inflammatory components. Conversely, DOBS is negatively correlated with multiple diseases, such as metabolic syndrome, respiratory diseases, cardiovascular diseases, and diabetes. Generally, Higher DOBS ratings indicate a pronounced antioxidant effect, whereas lower scores reflect a more pronounced pro-oxidant tendency. The DOBS assessment protocol has gained recognition as a dependable metric for evaluating the antioxidant potential of regular dietary consumption [25]. Prior research has established an inverse correlation between DOBS and the prevalence of various ailments, such as diabetes and cardiovascular disorders [26] [27].

Nevertheless, current literature lacks research into the connection between DOBS and DII in conjunction with CKM syndrome among patient populations. Consequently, the objective of this investigation is to leverage data from the Na-

tional Health and Nutrition Examination Survey to explore the potential correlations between DOBS, DII, and CKM syndrome in the adult population of the US.

2. Subjects and Methods

2.1. Source of Data

The National Health and Nutrition Examination Survey (NHANES), administered by the Centers for Disease Control and Prevention (CDC), employs a sophisticated, multistage probability sampling methodology. This survey is a benchmark of national significance, meticulously designed to gauge the health and nutritional well-being of adults and children across the US. Presently, the National Center for Health Statistics (NCHS), a division of the CDC, systematically gathers and disseminates this invaluable data on a biennial basis, encompassing a wealth of information ranging from demographic and dietary insights to examination, laboratory, and questionnaire findings. The NHANES research protocol has received the nod from the NCHS Ethics Review Board, with all participants providing written informed consent. Within the framework of this cross-sectional investigation, data were meticulously culled from 10 NHANES cycles, covering the period from 1999 to 2018, to serve as the analytical foundation. The study includes participants who are younger than 20 years of age (N = 46,235), those with missing CKM syndrome data (N = 29,858), individuals with missing DOBS and DII data (N = 1534), and participants with missing covariate and weight data (N = 6650) were excluded. After weeding out these participants, a total of 17,039 subjects were incorporated into the research (**Figure 1**).

2.2. Dietary Data

The evaluation of daily dietary consumption was carried out via 24-hour dietary recall interviews, which were conducted on two successive days. The computation of each dietary nutrient, as well as the total dietary energy, adhered to the protocols specified in the USDA's Food and Nutrient Database for Dietary Studies (FNDDS) [28]. Information on the application of dietary supplements was assessed through specialized questionnaires. In addition, nutrient assessment did not encompass a range of dietary components derived from dietary supplements. Across all NHANES cycles from 1999 to 2018, up to two 24-hour dietary recalls were collected per participant. In this study, we used the average of the two recalls when both were available; otherwise, the single recall was used.

2.3. Assessment of DOBS

The assessment of DOBS entailed evaluating the mingling of pro-oxidant and antioxidant nutrients present within the dietary intake [22]. Building on prior understanding of the relationship between specific nutrients and DOBS, a thorough assessment was conducted on 16 nutrients, encompassing 2 pro-oxidants and 14 antioxidants [29]. Dietary supplements were not included in the calculations. For par-

ticipants with two valid 24-hour dietary recalls, nutrient intakes were averaged; for those with only one recall, the single recall was used. The persistent dietary elements were segmented into three equal parts, where antioxidant ratings spanned from 1 to 3, and pro-oxidant ratings were inversely assigned. The consumption level of each participant was ascertained by aggregating the scores allotted to each dietary constituent. Detailed setting of DDOBS components is provided in Supplementary Table A1.

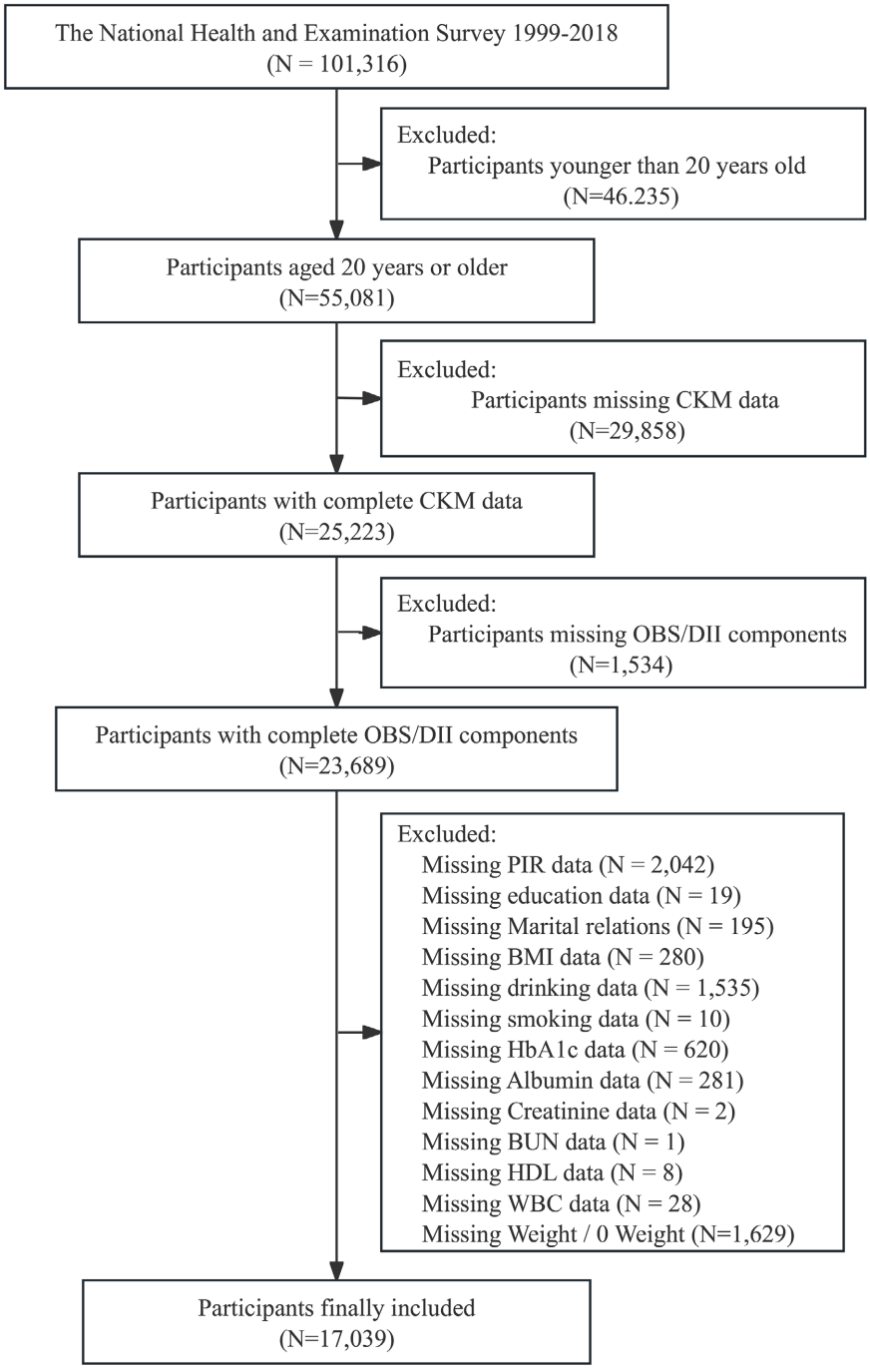

Figure 1. Flowchart of the selection strategy.

2.4. Assessment of DII

DII serves as a criterion for assessing the inflammatory potential of a person's dietary intake. It involves 45 dietary components sourced from scientific literature, which are determined based on their effects on inflammatory indicators, involving CRP, IL-6, and TNF-α. The complete list of components included in this study (based on NHANES availability) is provided in Supplementary **Table A2**. Dietary supplements were not included, and intakes from two 24-hour recalls were averaged as described above. Scoring scale for each component ranges from -1 (anti-inflammatory) to +1 (pro-inflammatory) [30]. The FFQ or 24-h dietary review was applied for assessing participants' nutritional consumption, and considering these differences in energy intake, the intake was standardized to per 1000 kcal. Subsequently, The adjustment of the intake was accomplished by applying the formula: [(daily intake—mean daily global intake)/standard deviation of the mean daily global intake], followed by multiplying the adjusted intake by the cumulative inflammatory response score pertaining to the dietary constituents. Each participant's total DII score was calculated, with a greater score implying a outstanding consumption for pro-inflammatory foods.

2.5. Diagnosis of Cardiovascular-Kidney-Metabolic Syndrome

At present, no conclusive diagnostic standards exist for CKM syndrome. This investigation operationalized CKM syndrome as the concurrent presence of cardiometabolic syndrome (CMS) and CKD, rather than the American Heart Association (AHA) CKM staging framework. This definition captures the clinical overlap between metabolic dysfunction and kidney impairment, representing a distinct phenotype from the stage-based CKM classification proposed by the AHA. The definition of CMS is derived from the guidelines set forth in the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) report [31], where a diagnosis is established upon an individual fulfilling at least three out of the five specified criteria: central obesity, as evidenced by a waist circumference exceeding 102 cm in males or surpassing 88 cm in females; hypertriglyceridemia, characterized by serum TG levels that reach or exceed 150 mg/dL; reduced HDL-C, with levels falling short of 40 mg/dL in males or below 50 mg/dL in females; hypertension, marked by a SBP of 130 mmHg or higher, or a DBP of 85 mmHg or higher, or the ongoing use of antihypertensive medications; and hyperglycemia, discernible by fasting blood glucose levels of 100 mg/dL or higher, or the current reliance on hypoglycemic medication. During physical examinations, waist circumference, weight, and height are collected using standard procedures, while SBP and DBP are calculated as the arithmetic mean of up to four repeated measurements for each participant. The levels of TG and HDL-C are determined in serum samples, while fasting blood glucose concentrations are assayed in plasma. CKD is characterized by eGFR below 60 mL/min/1.73 m^2 or a urine albumin-to-creatinine ratio exceeding 30 mg/g [32].

The eGFR is determined utilizing CKD Epidemiology Collaboration (CKD-EPI) creatinine formula, which was established in 2009 [33].

2.6. Covariate Assessment

In this investigation, a comprehensive set of covariates was taken into account, encompassing gender, age, ethnicity, poverty income ratio (PIR), tobacco use, alcohol intake, BMI, educational attainment, marital status, glycated hemoglobin (HbA1c) levels, albumin (Alb), creatinine (Cr), blood urea nitrogen (BUN), high-density lipoprotein cholesterol (HDL), red blood cell count (RBC), white blood cell count (WBC), hemoglobin (HB) concentration, and red blood cell distribution width (RDW). The selection of these variables was informed by the findings of earlier studies. Demographic information was gathered via in-depth household interviews, wherein racial classification was divided into non-Hispanic white, non-Hispanic black, Mexican American, and an 'other' category. Marital status was delineated into categories such as married, unmarried, separated, widowed, divorced, and cohabitating with a partner. The smoking status was determined based on whether participants had smoked a minimum of 100 cigarettes throughout their lives, while alcohol consumption was identified by whether individuals had ingested at least 12 alcoholic beverages. BMI was computed by dividing the weight by the square of the height (kg/m^2). Educational attainment was classified into four tiers: those without completion of the 9th grade, those completing grades 9 through 11, high school graduates or their equivalents, and those with a college degree or higher. The PIR, a measure indicative of economic status, was determined by dividing the total household income by the poverty threshold and was segmented into three categories: ≤1.3, 1.3 - 3.5, and >3.5, in adherence with established guidelines [34].

While HbA1c, HDL, creatinine, and BUN are related to components of the CKM outcome definition (hyperglycemia, low HDL, and kidney function), we included them as continuous covariates for the following reasons. First, HbA1c captures long-term glycemic control beyond a single fasting glucose measurement, thereby adjusting for residual glycemic variability not fully accounted for by the metabolic syndrome criteria. Second, adjusting for HDL and creatinine/BUN as continuous variables allows us to test whether DII and DOBS are associated with CKM independent of these specific biomarkers, which is a more conservative approach. Third, we conducted sensitivity analyses using propensity score matching without conditioning on these variables, and the results remained consistent, suggesting that our findings are not driven by overadjustment.

2.7. Statistical Analysis

All analytical procedures performed in the course of this research strictly conformed to NHANES dataset's analytical protocols. The main sampling units, pseudo variances, and masked variances in sampling weights were adopted in multi-stage sampling designs, and obtaining nationally representative estimates was ensured. To ac-

count for the complex, multistage probability sampling design of NHANES and to obtain nationally representative estimates for the combined 1999-2018 cycles, we constructed a pooled 10-year dietary weight variable. Specifically, for participants from the 1999-2002 cycles, we used the 4-year dietary day 1 weight variable (WTDR4YR) and divided it by 2.5 (representing the 2.5 two-year cycles within the 4-year period). For participants from the 2003-2018 cycles (each covering a 2-year period), we used the 2-year dietary day 1 weight variable (WTDR2D) and divided it by 5 (the total number of 2-year cycles from 1999–2018). The final analytic weight was calculated as: For 1999-2002: final_weight = WTDR4YR/2.5, For 2003-2018: final_weight = WTDR2D/5. Median values were used to represent continuous variables (P25, P75), whereas categorical variables were depicted using numbers (percentages). In this investigation, the researchers utilized Pearson's chi-square test to compare categorical variables across different groups. Given that the continuous variables examined in this study did not conform to a normal distribution as indicated by the Kolmogorov-Smirnov test, the team resorted to non-parametric testing methods to evaluate the differences between groups.

DII and DOBS were each stratified into four quartiles for the purposes of statistical evaluation, with the first quartile (Q1) designated as the baseline comparator. In the initial phase, both univariate and multivariate weighted logistic regression analyses, complemented by RCS, were conducted to determine the odds ratios (ORs) and their corresponding 95% confidence intervals (CIs), aiming to evaluate the correlations between DOBS and DII in relation to CKM syndrome. Adjustments were made for variables including gender, age, race, educational attainment, marital status, smoking habits, alcohol intake, PIR, BMI, HbA1c, Alb, Cr, BUN, HDL, WBC, RBC, HB, and RDW. Subsequently, subgroup researches were administered to examine potential modifying affects of key demographic and clinical variables on the relationships between DOBS, DII, and CKM syndrome, with all covariates (excluding those used for stratification) adjusted in the models. These analyses were stratified by genders (male/female), age (<60/> = 60), race (Black/White/Mexican American/Other), BMI (<25/> = 25), smoking status (yes/no), and alcohol consumption (yes/no). The logistic regression models incorporated interaction terms between DOBS/DII and the aforementioned variables, to ascertain whether the relationship between dietary scores and the prevalence of CKM syndrome varied among different subgroups. The significance of interactions was tested using analysis of variance (ANOVA). Propensity score matching (PSM) was utilized for reducing potential choice bias and confounding. Because PSM alters the original sample structure and is not inherently designed for complex survey data, we performed matching without survey weights to avoid distorting the propensity score estimation. Propensity scores were calculated through logistic regression analyses (without incorporating survey weights), incorporating pertinent covariates to ensure accuracy. Participants were meticulously paired in a 1:2 proportion through the nearest-neighbor matching technique, utilizing the propensity scores as the basis for pairing. Post-matching equilibrium was evaluated by analyzing the standardized mean differences (SMD) in the covariates across the paired

groups, where an SMD below 0.1 was deemed indicative of an acceptable equilibrium. Following this, the matched sample no longer represents the original complex survey design. Therefore, we refrained from applying the original NHANES survey weights in the post-matching analysis. Instead, weighted multivariable logistic regression analyses (unweighted for survey design) were conducted to ascertain the correlations between DII, DOBS, and CKM syndrome as a sensitivity analysis to complement the primary weighted survey analysis. All statistical computations were executed with R version 4.4.1 (courtesy of the R Foundation for Statistical Computing, based in Vienna, Austria). Statistical significance was determined at the p-value threshold of less than 0.05.

3. Results

3.1. Baseline Characteristics

The fundamental attributes of the subjects involved in the study are delineated in Table 1. The participants, numbering 17,039, had a median age of 49 years, with a female composition of 51% and a predominant white demographic. When contrasted with individuals in the lowest quartile of DOBS, those in the highest quartile exhibited a greater propensity to be female, to be of a younger age, to have a lower Body Mass Index (BMI), to be married, to identify as white, to have achieved a higher level of education, and to enjoy a higher income bracket. Supplementary Table A3 details the clinical baseline features of players with and without CKM Syndrome, while Supplementary Table A4 outlines the clinical baseline characteristics categorized by quartiles of the Dietary Inflammation Index (DII).

3.2. Association of DOBS and DII with CKM Syndrome

The correlation between DOBS and CKM syndrome was assessed through sophisticated multivariate logistic regression analyses (Table 2). In the initial model (Model 1), a notable increase in DOBS levels was found to be significantly linked to lower odds of having CKM syndrome (OR = 0.94, 95% CI: 0.93 - 0.96, P < 0.001). Participants within the highest quartile of DOBS (Q4) demonstrated a remarkable 64% lower odds of CKM syndrome compared to those in the lowest quartile (Q1), with a OR of 0.36 (95% CI: 0.28 - 0.45, P for trend<0.0001). Upon adjusting for variables such as gender, age, race, education level, marital status, personal income ratio, and body mass index in the second model, it was observed that for every unit increase in DOBS, there was a 4% decrease in the likelihood of developing CKM syndrome (OR = 0.97, 95% CI: 0.95 - 0.98, P-value < 0.001). In this particular model, individuals belonging to the DOBS Q4 cohort experienced a 55% reduction in the likelihood of developing CKM syndrome when contrasted with those in the Q1 cohort (OR = 0.45, 95% CI: 0.33 - 0.63, P for trend < 0.0001). In the comprehensive Model 3, a single unit increase in DOBS corresponded to a 3% reduction in the likelihood of developing CKM syndrome (OR = 0.97, 95% CI: 0.95 - 0.98, P < 0.001), and those in the top quartile of DOBS experienced a 51% decrease in odds in comparison to those in the bottom quartile (OR = 0.49, 95% CI: 0.35 - 0.69, P for trend<0.001).

Table 1. Baseline characteristics of the participants.

Variables	Total (n = 17,039)	Q1 (n = 4477)	Q2 (n = 4360)	Q3 (n = 4577)	Q4 (n = 3625)	Statistic	*P*
Gender, n (%)						χ^2 = 28.732	<0.001
female	8818 (51.752)	2184 (48.783)	2239 (51.353)	2424 (52.960)	1971 (54.372)		
male	8221 (48.248)	2293 (51.217)	2121 (48.647)	2153 (47.040)	1654 (45.628)		
Age, M (Q_1, Q_3)	49.000 (34.000, 64.000)	52.000 (36.000, 67.000)	50.000 (35.000, 65.000)	48.000 (34.000, 63.000)	46.000 (33.000, 61.000)	χ^2 = 125.438#	<0.001
Race, n (%)						χ^2 = 392.242	<0.001
Black	3236 (18.992)	1236 (27.608)	859 (19.702)	726 (15.862)	415 (11.448)		
Mexican American	2947 (17.296)	734 (16.395)	773 (17.729)	811 (17.719)	629 (17.352)		
Other	2555 (14.995)	572 (12.776)	644 (14.771)	726 (15.862)	613 (16.910)		
White	8301 (48.718)	1935 (43.221)	2084 (47.798)	2314 (50.557)	1968 (54.290)		
PIR, n (%)						χ^2 = 522.313	<0.001
<=1.0	3187 (18.704)	1103 (24.637)	827 (18.968)	736 (16.080)	521 (14.372)		
>3.0	6698 (39.310)	1236 (27.608)	1626 (37.294)	2002 (43.740)	1834 (50.593)		
1.0 - 3.0	7154 (41.986)	2138 (47.755)	1907 (43.739)	1839 (40.179)	1270 (35.034)		
Education, n (%)						χ^2 = 825.863	<0.001
9 - 11th grade	2428 (14.250)	861 (19.232)	619 (14.197)	594 (12.978)	354 (9.766)		
college graduate or above	8900 (52.233)	1708 (38.151)	2135 (48.968)	2614 (57.112)	2443 (67.393)		
high school graduate/equivalent	3928 (23.053)	1206 (26.938)	1080 (24.771)	1021 (22.307)	621 (17.131)		
less than 9th grade	1783 (10.464)	702 (15.680)	526 (12.064)	348 (7.603)	207 (5.710)		
Alcohol, n (%)						χ^2 = 6.442	0.092
no	2299 (13.493)	650 (14.519)	589 (13.509)	586 (12.803)	474 (13.076)		
yes	14740 (86.507)	3827 (85.481)	3771 (86.491)	3991 (87.197)	3151 (86.924)		
Smoke, n (%)						χ^2 = 276.486	<0.001
no	9117 (53.507)	2007 (44.829)	2266 (51.972)	2570 (56.150)	2274 (62.731)		
yes	7922 (46.493)	2470 (55.171)	2094 (48.028)	2007 (43.850)	1351 (37.269)		
Marital relations, n (%)						χ^2 = 133.439	<0.001
divorced	1748 (10.259)	525 (11.727)	479 (10.986)	435 (9.504)	309 (8.524)		
living with partner	1282 (7.524)	346 (7.728)	316 (7.248)	360 (7.865)	260 (7.172)		
married	9369 (54.986)	2227 (49.743)	2379 (54.564)	2599 (56.784)	2164 (59.697)		
never married	2751 (16.145)	767 (17.132)	683 (15.665)	701 (15.316)	600 (16.552)		
separated	502 (2.946)	155 (3.462)	145 (3.326)	125 (2.731)	77 (2.124)		
widowed	1387 (8.140)	457 (10.208)	358 (8.211)	357 (7.800)	215 (5.931)		

Continued

BMI, M (Q_1, Q_3)	27.910 (24.400, 32.310)	28.900 (25.160, 33.200)	28.500 (24.940, 32.900)	27.900 (24.390, 32.150)	26.300 (23.240, 30.280)	χ^2 = 369.436#	<0.001
HbA1c, M (Q_1, Q_3)	5.500 (5.200, 5.800)	5.500 (5.200, 5.900)	5.500 (5.200, 5.900)	5.500 (5.200, 5.800)	5.400 (5.100, 5.700)	χ^2 = 214.468#	<0.001
Creatinine, M (Q_1, Q_3)	0.830 (0.700, 1.000)	0.860 (0.700, 1.020)	0.850 (0.700, 1.000)	0.810 (0.700, 0.990)	0.810 (0.690, 0.960)	χ^2 = 141.707#	<0.001
BUN, M (Q_1, Q_3)	13.000 (10.000, 16.000)	12.000 (10.000, 16.000)	13.000 (10.000, 16.000)	13.000 (10.000, 16.000)	13.000 (10.000, 16.000)	χ^2 = 19.148#	<0.001
HDL, M (Q_1, Q_3)	51.000 (42.000, 62.000)	48.000 (41.000, 60.000)	50.000 (42.000, 61.000)	52.000 (43.000, 63.000)	55.000 (45.000, 67.000)	χ^2 = 287.934#	<0.001
WBC, M (Q_1, Q_3)	6.600 (5.500, 7.900)	6.800 (5.600, 8.200)	6.600 (5.500, 7.900)	6.500 (5.500, 7.900)	6.300 (5.200, 7.500)	χ^2 = 143.296#	<0.001
RBC, M (Q_1, Q_3)	4.700 (4.360, 5.050)	4.710 (4.360, 5.070)	4.710 (4.360, 5.060)	4.710 (4.360, 5.050)	4.660 (4.340, 5.010)	χ^2 = 17.602#	<0.001
HB, M (Q_1, Q_3)	14.300 (13.300, 15.300)	14.200 (13.100, 15.300)	14.300 (13.200, 15.300)	14.300 (13.300, 15.300)	14.300 (13.300, 15.300)	χ^2 = 3.216#	0.36
RDW, M (Q_1, Q_3)	12.900 (12.300, 13.600)	13.000 (12.400, 13.800)	12.900 (12.400, 13.600)	12.900 (12.300, 13.500)	12.700 (12.200, 13.400)	χ^2 = 185.642#	<0.001

#: Kruskal-waills test, χ^2: Chi-square test, M: Median, Q_1: 1st Quartile, Q_3: 3st Quartile, Abbreviation: PIR, poverty income ratio; BMI, body mass index; HbA1c, glycated hemoglobin; BUN, blood urea nitrogen; HDL, high-density lipoprotein cholesterol; WBC, white blood cell count; RBC, red blood cell count; HB, hemoglobin; RDW, red blood cell distribution width.

Table 2 delineates the logistic regression analyses examining the correlation between DII and the occurrence of CKM syndrome. The crude model (Model 1) indicates a notable association between a higher DII and an elevated risk for developing CKM syndrome (OR = 1.09, 95% CI: 1.04 - 1.13, P < 0.001). In contrast to individuals within the lowest DII quartile (Q1), those belonging to the highest quartile (Q4) exhibited a 54% higher odds of having CKM syndrome (OR = 1.54, 95% CI: 1.24 - 1.90, P for trend<0.001). After accounting for gender, age, racial background, educational level, marital status, personal income ratio, and body mass index in the second model, it was observed that for every unit increment in DII, there was a corresponding 10% higher odds of having CKM syndrome (OR = 1.10, 95% CI: 1.04 - 1.17, P = 0.002). According to this model, the DII Q4 group participants were found to have an 81% increased odds of developing CKM syndrome, as opposed to those in the Q1 group. (OR = 1.81, 95% CI: 1.30 - 2.51, P for trend = 0.004). Upon examination of the fully adjusted model (Model 3), it was observed that a single unit increase in DII correlates with an 8% heightened odds of CKM syndrome (OR = 1.08, 95% CI: 1.01 - 1.15, P = 0.02), and those situated in the highest quartile of DII experienced a 62% increased odds relative to those in the lowest quartile (OR = 1.62, 95% CI: 1.14 - 2.29, P for trend = 0.032).

Table 2. Correlation of OBS and DII with CKM. The data were represented by weighted OR estimates and 95% CIs.

Variable	Model 1			Model 2			Model 3		
	OR (95% CI)	P	P for trend	OR (95% CI)	P	P for trend	OR (95% CI)	P	P for trend
OBS continuous	0.94 (0.93, 0.96)	<0.001		0.96 (0.95, 0.98)	<0.001		0.97 (0.95, 0.98)	<0.001	
OBS quartile			<0.0001			<0.0001			<0.001
Q1	ref	-		ref	-		ref	-	
Q2	0.65 (0.51, 0.83)	<0.001		0.54 (0.39, 0.75)	<0.001		0.57 (0.41, 0.80)	<0.001	
Q3	0.50 (0.40, 0.63)	<0.001		0.49 (0.36, 0.68)	<0.001		0.53 (0.38, 0.73)	<0.001	
Q4	0.36 (0.28, 0.45)	<0.001		0.45 (0.33, 0.63)	<0.001		0.49 (0.35, 0.69)	<0.001	
DII continuous	1.09 (1.04, 1.13)	<0.001		1.10 (1.04, 1.17)	0.002		1.08 (1.01, 1.15)	0.02	
DII quartile			<0.001			0.004			0.032
Q1	ref	-		ref	-		ref	-	
Q2	1.14 (0.91, 1.42)	0.3		1.05 (0.80, 1.39)	0.7		1.00 (0.75, 1.32)	0.9	
Q3	1.20 (0.95, 1.53)	0.13		1.22 (0.89, 1.66)	0.2		1.16 (0.84, 1.58)	0.4	
Q4	1.54 (1.24, 1.90)	<0.001		1.81 (1.30, 2.51)	<0.001		1.62 (1.14, 2.29)	0.008	

Model 1: No covariates were adjusted; Model 2: Gender, age, race, education, marital relation, PIR, BMI were adjusted; Model 3: Gender, age, race, education, marital relation, PIR, BMI, smoking, drinking, HbA1c, albumin, creatinine, BUN, HDL, WBC, RBC, RDW, HB were adjusted.

3.3. Analysis of Restricted Cubic Spline Regression

Multivariable-adjusted restricted cubic spline (RCS) analyses revealed nonlinear trends between DOBS and DII with CKM syndrome. As illustrated in **Figure 2(A)**, a direct negative correlation was noted between DOBS and CKM syndrome (P for nonlinearity = 0.072). Similarly, **Figure 2(B)** demonstrates a linear positive association between DII and CKM syndrome (P for nonlinearity = 0.145).

3.4. Subgroup Analysis

To determine whether substantial associations exist between DOBS and DII with CKM syndrome within specific subgroups, subgroup analyses were conducted in this study. Participants were initially categorized by gender, age, race, BMI, smoking level, and alcohol expenditure. Subsequently, another round of logistic regression models was performed on these subgroups. All covariates, except those used for stratification, were adjusted in the models. As illustrated in **Figure 3**, elevated concentrations of DOBS (Q4) were markedly correlated with a diminished prev-

alence of CKM syndrome in female subjects (OR = 0.60, 95% CI: 0.40 - 0.90), Whites (OR = 0.51, 95% CI: 0.34 - 0.78), individuals of other races (OR = 0.51, 95% CI: 0.28 - 0.93), and those having BMI <25 (OR = 0.58, 95% CI: 0.42 - 0.80). In subgroups stratified by age, smoking status, and alcohol consumption, high level of DOBS (Q4) was considerably negatively linked to CKM syndrome. As shown in Figure 4, high levels of DII (Q4) were relatively positively affiliated with CKM syndrome among Whites (OR = 1.56, 95% CI: 1.04 - 2.32), individuals with a BMI <25 (OR = 1.41, 95% CI: 1.03 - 1.93), and alcohol consumers (OR = 1.42, 95% CI: 1.02 - 1.99). Interaction p-values indicated that there were no significant interactions between DOBS and DII traversing the tiered variables (P-interaction > 0.05).

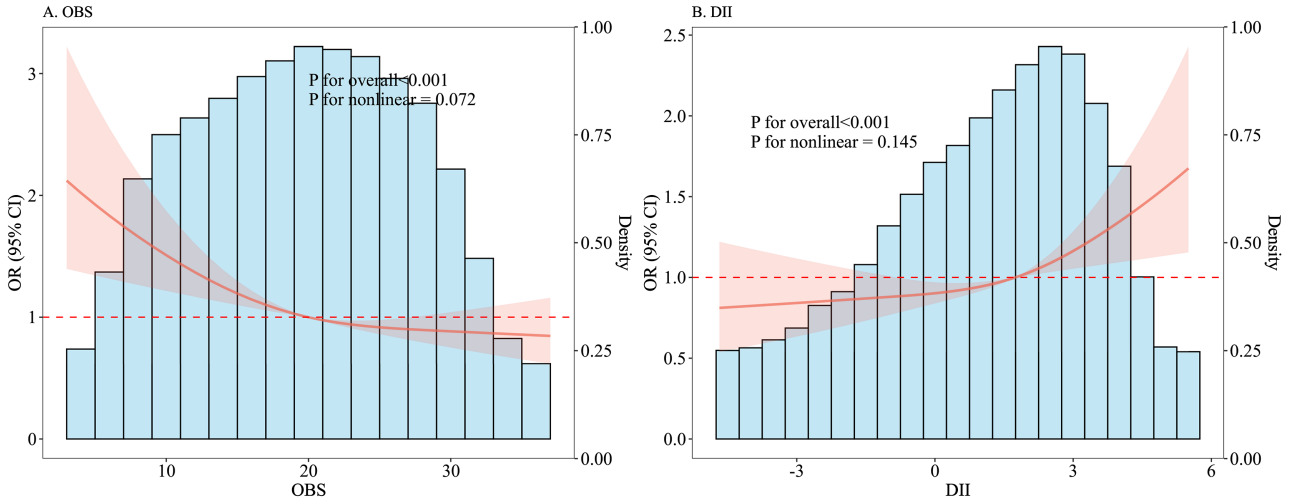

Figure 2. Correlation of OBS and DII with CKM syndrome. Adjustments were based on gender, age, race, BMI, educational level, marital relations, smoking, drinking, PIR, HbA1c, albumin, creatinine, BUN, HDL, WBC, RBC, RDW and HB. The central estimate was represented by a black solid line, and the red shaded area indicated the 95% CI.

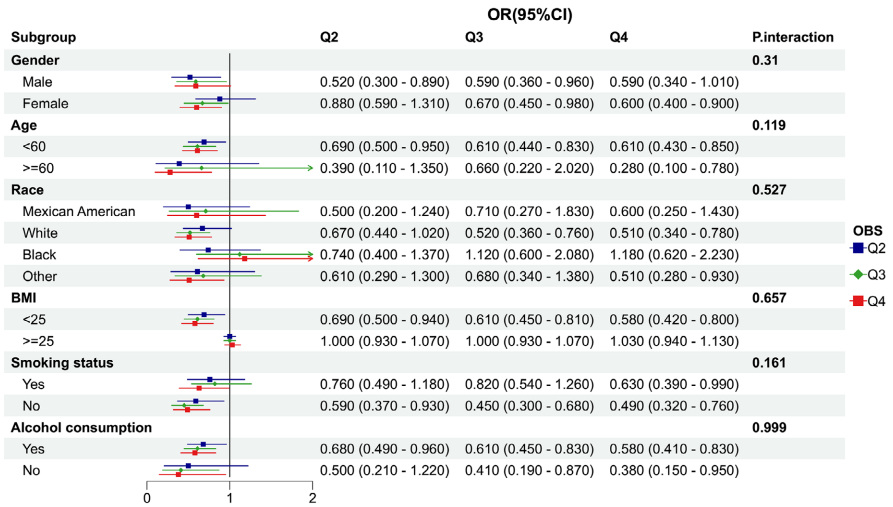

Figure 3. The subgroup analysis of OBS and CKM syndrome. The adjustment factors included gender, age, race, BMI, educational level, marital relations, smoking, drinking, PIR, HbA1c, albumin, creatinine, BUN, HDL, WBC, RBC, RDW and HB.

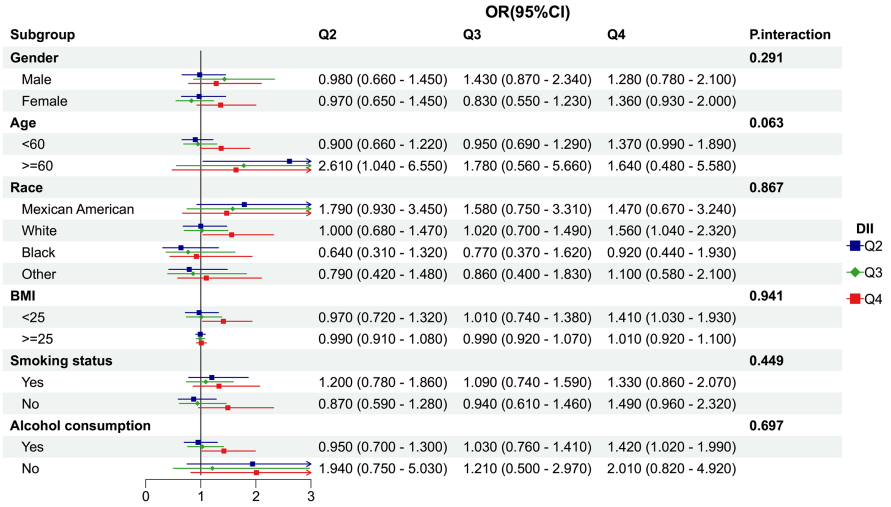

Figure 4. The subgroup analysis of DII and CKM syndrome. The adjustment factors included gender, age, race, BMI, educational level, marital relations, smoking, drinking, PIR, HbA1c, albumin, creatinine, BUN, HDL, WBC, RBC, RDW and HB.

3.5. Sensitivity Analysis

To control for confounding factors, propensity score matching (PSM) analysis was conducted using multivariate logistic regression models, meticulously adjusting for a multitude of potential confounders within the original, unpaired cohort. The results were consistent with these main estimates reported. After matching, as shown in Supplementary Table A5, participants in the highest quarter of DOBS (Q4) displayed 46% diminished odds of CKM syndrome in contrast to individuals in the lowest quartile (Q1) [OR = 0.54, 95% CI: 0.39 - 0.75]. Conversely, participants in the greatest quartile of DII (Q4) demonstrated 55% increased odds of CKM syndrome than those in Q1 [OR = 1.55, 95% CI: 1.10 - 2.20].

4. Discussion

By incorporating 45 dietary components related to inflammatory potential and 16 specific pro-inflammatory and antioxidant nutrients, two scores were constructed to examine individual dietary pro-inflammatory and antioxidant levels. The findings of the study reveal a notable correlation between elevated DOBS values and a reduced prevalence of CKM syndrome. On the other hand, elevated values of the DII correlate substantially with an augmented odds of developing CKM syndrome. A direct linear negative correlation was noted between DOBS and CKM syndrome, while a linear positive correlation was found between DII and CKM syndrome. These correlations persisted even after accounting for potential confounding variables. These findings provide important evidence for the roles of DOBS and DII within cardiovascular, renal, and metabolic dysregulation and indicate fresh guidance for future research.

Oxidative stress plays a crucial role as a pathogenic factor in the pathophysiological mechanisms underlying CKM Syndrome, serving as a crucial bridge in interactions among the cardiovascular, renal, and metabolic systems [13] [35] [36].

The core characteristics of CKM syndrome include metabolic disorders, impaired cardiovascular function, and CKD, with oxidative stress promoting dysfunction in these systems through multiple mechanisms [37]. The overproduction of ROS plays a pivotal role in the impairment of endothelial function and the progression of atherosclerosis. ROS interact with NO to built peroxynitrite (ONOO-), significantly reducing the bioavailability of NO, thereby diminishing its roles in maintaining vascular dilation, inhibiting platelet aggregation, and protecting endothelial cell function [38]-[40]. Concurrently, ROS induce lipid peroxidation and protein oxidation, disrupting cell membrane structure and function, and exacerbating endothelial damage. Uncoupling of endothelial nitric oxide synthase (eNOS) further increases ROS production, forging a detrimental cycle of oxidative stress [41]. These mechanisms collectively lead to the disruption of the endothelial barrier function and accelerate the early stages of atherosclerosis, such as endothelial cell apoptosis and smooth muscle cell migration, thereby laying the foundation for the onset and progression of CKM syndrome [42]. Additionally, Oxidative stress not only activates pro-inflammatory signaling pathways, like NF-κB and JNK, but also triggers the secretion of pro-inflammatory cytokines, thereby intensifying systemic inflammatory responses. This escalation consequently leads to augmented harm to both the renal and cardiovascular systems [43]. Moreover, within the complex metabolic environment of CKM syndrome, oxidative stress disrupts mitochondrial function, increases the risk of tubular cell apoptosis and fibrosis, and thereby promotes the progression of CKD [44].

DOBS, as a comprehensive indicator reflecting individual dietary antioxidant and pro-oxidant exposures, fulfills a crucial function in the complex pathological mechanisms of CKM Syndrome across multiple systems. This investigation revealed a substantial inverse relationship between DOBS concentrations and the prevalence of CKM, suggesting that increased dietary antioxidant exposure contributes to mitigating the multisystem pathological alterations associated with CKM. High DOBS levels are typically associated with elevated intake of dietary antioxidant components, like vitamin C, vitamin E, polyphenols, magnesium, and selenium. These components exert protective effects across various pathological pathways via neutralizing ROS, curbing lipid peroxidation, and stabilizing mitochondrial function [45]. For instance, vitamin E and polyphenols not only inhibit the production of pro-inflammatory factors but also decrease the oxidation of low-density lipoprotein (LDL), suppress endothelial cell dysfunction, regulate smooth muscle cell migration and proliferation, help maintain vascular wall structural integrity, and delay the progression of atherosclerosis [46]-[48]. Additionally, magnesium and selenium contribute to reducing renal oxidative damage and maintaining tubular function by activating antioxidant enzymes, like glutathione peroxidase and superoxide dismutase [49] [50]. Importantly, DOBS not only enhances dietary antioxidant capacity but also reduces pro-oxidant components, including saturated fatty acids, alcohol, and iron, thereby decreasing ROS production and further alleviating the inflammatory and oxidative stress states of CKM

syndrome. These findings suggest that dietary pattern modifications aimed at increasing antioxidant exposure and reducing pro-oxidant exposure may serve as effective strategies for intervening in CKM syndrome. The integrative nature of DOBS makes it an effective tool for investigating the impact of diet on CKM syndrome, as it captures the combined effects of dietary antioxidants and pro-oxidants, thereby elucidating the inherent connections between dietary patterns and the pathogenesis of CKM.

The correlation between DII and CKM Syndrome underscores the pivotal role of dietary inflammatory potential in the underlying pathophysiological processes of CKM syndrome. The DII functions as an all-encompassing instrument for assessing the influence of dietary intake on systemic inflammation, by measuring the influence of 45 distinct dietary elements on both pro-inflammatory and anti-inflammatory biomarkers, including CRP, IL-6, and TNF-α. This work demonstrates that higher DII levels, indicating a greater proportion of pro-inflammatory components in the diet, are significantly linked to a heightened likelihood of CKM manifestation. This link is likely mediated through multiple interwoven pathophysiological pathways. Firstly, a high-DII diet, characterized by high saturated fatty acids, high refined sugars, and low fiber, activates pro-inflammatory signaling pathways like NF-κB and JAK/STAT, thereby increasing the levels of inflammatory cytokines [51] [52]. These cytokines not only directly promote endothelial dysfunction but also reduce the bioactivity of nitric oxide (NO), inducing early atherosclerotic events including endothelial cell apoptosis, smooth muscle cell migration, and lipid deposition [53]. These processes further exacerbate insulin resistance, creating a vicious cycle of "pro-inflammatory-metabolic disorder-endothelial damage," thereby driving the bidirectional deterioration of cardiovascular and metabolic functions [54]. Additionally, the persistent activation of inflammatory cytokines accelerates glomerulosclerosis and tubulointerstitial fibrosis through fibrotic pathways such as the TGF-β/Smad signaling pathway, leading to these progressions of CKD [55] [56]. Secondly, DII is closely related to gut microbiota dysbiosis [57]. A high-DII dietary pattern, lacking in dietary fiber and antioxidant components, reduces the diversity of the gut microbiota while enhancing intestinal barrier permeability. In this state, endotoxins (such as lipopolysaccharide [LPS]) enter the systemic circulation, triggering the immune system and activating the Toll-like receptor 4 (TLR4) signaling pathway in macrophages, thereby further sustaining systemic inflammation [58]. Moreover, an increase in pro-inflammatory SCFAs fabricated by gut microbiology metabolism may exacerbate metabolic abnormalities of CKM syndrome by affecting energy metabolism and insulin sensitivity [59]. A high-DII diet may also promote the onset and progression of CKM syndrome through the synergistic effects of oxidative stress and inflammation. A pro-inflammatory diet induces mitochondrial dysfunction and excessive generation of ROS, exacerbating lipid peroxidation and DNA damage, being not only key mechanisms of metabolic disorders but may also compromise the integrity of renal tubular cells and induce renal fibrosis, thereby accelerating

the onset of CKD. It is noteworthy that a positive feedback loop exists between ROS and pro-inflammatory cytokines; for example, ROS can oxidatively regulate the activation of NF-κB, further exacerbating the inflammatory response [60]. This mechanism may explain the cumulative effects of high-DII diets on multi-system damage. In contrast, low-DII diets, such as those abundant for polyunsaturated fatty acids, dietary fiber, and plant polyphenols, exhibit significant anti-inflammatory effects. Low-DII diets demonstrate considerable potential in cardiovascular and renal protection by downregulating levels of inflammatory cytokines and enhancing antioxidant defense mechanisms [61]. These findings suggest that dietary pattern interventions, such as reducing the intake of saturated fatty acids and refined sugars while increasing the intake of dietary fiber, dark vegetables, and antioxidant components, may serve as core strategies for the comprehensive management of CKM syndrome.

Subgroup analyses indicate that the associations between DOBS and DII with CKM syndrome are more pronounced in specific populations, potentially due to individual physiological and behavioral characteristics as well as genetic backgrounds. For instance, Elevated DOBS levels exhibit a notable negative correlation with women, Caucasians, and individuals who have a BMI below 25, suggesting that these groups may derive greater benefits from antioxidant-rich dietary patterns. However, interaction tests were not statistically significant (all P-interaction > 0.05), indicating that these observed numerical differences do not represent confirmed effect modification. This observation may partially reflect female-specific biological mechanisms, such as anti-inflammatory and antioxidant reflects of estrogen, which collaborate with dietary antioxidants to alleviate the damage inflicted by inflammation and oxidative stress, thus showcasing enhanced protective benefits [62]. In individuals with a BMI below 25, elevated DOBS levels may more effectively alleviate the pathological processes of CKM syndrome by reducing oxidative stress and metabolic load. This finding aligns with studies demonstrating that high DII levels exert significant pro-inflammatory effects in individuals with lower BMI, indicating that populations with lower BMI may be more sensitive to dietary components and thus represent important targets for dietary antioxidant optimization. Additionally, the significant response of White populations to high DOBS diets may be associated with genetic backgrounds, dietary habits, or cultural differences. Research suggests that genetic backgrounds may amplify the effects of dietary anti-inflammatory or pro-inflammatory components through interactions with dietary behaviors. Conversely, elevated DII levels are substantially and positively correlated with an increased odds of CKM syndrome in Whites, alcohol consumers, and individuals with a BMI below 25, which may reveal that pro-inflammatory dietary patterns have more pronounced negative impacts on these groups. Specifically, in individuals with lower BMI, high DII diets may directly exacerbate inflammation and oxidative stress states. These individuals, having lower metabolic reserves, may find it more challenging to alleviate the metabolic burden imposed by pro-inflammatory diets [63]. Furthermore, alcohol consumption may synergize with dietary pro-inflammatory components to further

activate pro-inflammatory signaling pathways, thereby exacerbating the multisystem pathological changes associated with CKM syndrome [64]. For example, alcohol metabolism may enhance the adverse effects of pro-inflammatory components, such as saturated fatty acids and refined sugars, on inflammatory markers like CRP and IL-6, thereby amplifying inflammatory responses. In White populations, the significant negative impact of high DII diets may be related to interactions between genetic backgrounds and dietary behaviors, where genetic susceptibility may render Whites more vulnerable to the effects of pro-inflammatory dietary components, thereby accelerating the maintenance of pro-inflammatory states. Overall, the results of subgroup analyses emphasize the importance of individualized dietary interventions across different populations. The distinct responsiveness of certain populations to the anti-inflammatory or pro-inflammatory impacts of nutrition implies that tailoring dietary regimens to individual traits is crucial for optimal health consequences such as gender, race, BMI, and dietary behaviors. This personalized dietary adjustment strategy not only effectively reduces the odds of CKM syndrome but also provides more precise intervention methods by alleviating its multisystem pathological mechanisms. Thus, the associations between DOBS/DII and CKM syndrome appear to be generally consistent across all subgroups examined, and the apparent subgroup differences should be interpreted with caution.

This investigation boasts a number of notable merits. Foremost among them is its foundation on a sample that is both nationally representative and sourced from the NHANES dataset, encompassing a large sample size and multiple survey cycles, which confer high statistical power and broad generalizability to the findings. Secondly, this research is the first to concurrently utilize the DOBS and the DII to evaluate the friendship among oxidative stress, inflammation, and CKM Syndrome, thereby offering a novel perspective on the interactions between dietary patterns and multisystem diseases. However, certain limitations are acknowledged. Primarily, due to constraints inherent in the NHANES database, not all dietary components that may influence oxidative stress and inflammation, such as specific phytochemicals, could be comprehensively included, potentially impacting the precise evaluation of DOBS and DII. Additionally, the study did not separately investigate the staging of CKM Syndrome or its specific components (e.g., cardiovascular disease, kidney disease, or metabolic disorders), which may conceal heterogeneity among these components. It is important to note that our operational definition of CKM syndrome as the co-occurrence of CMS and CKD differs from the AHA CKM staging framework. While the AHA approach provides a comprehensive life-course perspective on cardiovascular-kidney-metabolic health, our definition focuses on identifying individuals with established metabolic and renal dysfunction, representing a clinically relevant high-risk population. Future studies incorporating the full AHA staging criteria may provide additional insights into the dietary influences across the CKM spectrum. Future research should explore the differential impacts of dietary patterns across various stages or components of CKM Syndrome. Lastly, this study's cross-sectional design inhibits the

establishment of causative links between DOBS and DII in conjunction with CKM Syndrome., necessitating further validation through prospective studies.

5. Conclusion

This study systematically examined the associations between the DOBS and DII with CKM Syndrome. The findings revealed that elevated DOBS concentrations were markedly correlated with a diminished likelihood of contracting CKM syndrome, whereas increased DII levels were distinctly linked to a heightened susceptibility to the ailment. These results imply that modifying diet to increase antioxidant intake and decrease pro-inflammatory substances may be associated with a lower prevalence of CKM syndrome. However, causal inference cannot be drawn from this cross-sectional design, and prospective studies are needed. This investigation furnishes compelling insights into the correlation between eating habits and multisystem illnesses, albeit additional research is necessary to substantiate the intrinsic mechanisms and to ascertain the efficacy of potential interventions.

Ethics Approval and Consent to Participate

The NHANES obtained approval from the National Centre for Health Statistics Research Ethics Review Board and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Each participant gave written informed consent agreement when they were enrolled in the NHANES, and the National Center for Health Statistics' ethics review board approved the study.

Data Availability Statement

The data supporting this article have been included as part of the Supplementary Information.

Author Contributions

All authors contributed to the study conception and design. Writing—original draft preparation: [Tong Wang]; Writing—review and editing: [Tong Wang]; Conceptualization: [Tong Wang]; Methodology: [Tong Wang]; Formal analysis and investigation: [Tong Wang]; Resources: [Lin Li]; Supervision: [Lin Li], and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare that they have no conflict interest.

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Appendix

Table A1. Allocation scheme for oxidative balance score.

OBS components	Property	Scoring assignment		
		0	1	2
Dietary components				
Dietary fiber (g/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Carotene (RE/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Riboflavin (mg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Niacin (mg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Vitamin B6 (mg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Total folate (mcg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Vitamin B12 (mcg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Vitamin C (mg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Vitamin E (ATE) (mg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Calcium (mg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Magnesium (mg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Zinc (mg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Copper (mg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Selenium (mcg/d)	Antioxidant	Tertile 1	Tertile 2	Tertile 3
Total fat (g/d)	Pro-oxidant	Tertile 3	Tertile 2	Tertile 1
Iron (mg/d)	Pro-oxidant	Tertile 3	Tertile 2	Tertile 1

Table A2. Dietary composition parameters involved in DII, inflammatory effect scores, and intake values from the global composite data setc.

Dietary composition parameter	Overall inflammatory effect score[b]	Global daily mean intake (units/d)	Standard deviation of the global daily intake
Alcohol (g)	−0.278	13.98	3.72
Vitamin B12 (μg)	0.106	5.15	2.7
Vitamin B6 (mg)	−0.365	1.47	0.74
β-Carotene (μg)	−0.584	3718	1720
Caffeine (g)	−0.11	8.05	6.67
Carbohydrate (g)	0.097	272.2	40
Cholesterol (mg)	0.11	279.4	51.2

Continued

Energy (kcal)	0.18	2056	338
Total fat (g)	0.298	71.4	19.4
Fiber (g)	−0.663	18.8	4.9
Folic acid (μg)	−0.19	273	70.7
Iron (mg)	0.032	13.35	3.71
Magnesium (mg)	−0.484	310.1	139.4
MUFA[d](g)	−0.009	27	6.1
Niacin (mg)	−0.246	25.9	11.77
Protein (g)	0.021	79.4	13.9
PUFA[e](g)	−0.337	13.88	3.76
Vitamin B2 (mg)	−0.068	1.7	0.79
Saturated fat (g)	0.373	28.6	8
Selenium (μg)	−0.191	67	25.1
Vitamin B1 (mg)	−0.098	1.7	0.66
Vitamin A (RE [a])	−0.401	983.9	518.6
Vitamin C (mg)	−0.424	118.2	43.46
Vitamin D (μg)	−0.446	6.26	2.21
Vitamin E (mg)	−0.419	8.73	1.49
Zinc (mg)	−0.313	9.84	2.19

[a]Retinol equivalents. [b]Dietary composition parameter-specific overall inflammatory effect score. [c]DII of a certain dietary component = (Daily intake of the dietary component—Global daily mean intake of the dietary component)/Standard deviation of the global daily intake for the dietary component *Overall inflammatory effect score of the dietary component. The DII for each participant was obtained by summing the DII of the 26 dietary components selected in this study. [d]Monounsaturated fatty acids. [e]Polyunsaturated fatty acids.

Table A3. Baseline information from the Non-CKM and CKM groups. Continuous variables were represented by weighted mean (SE). Categorical variables were expressed in the form of counts (weighted percentages).

Characteristic	N[1]	Overall	Non-CKM	CKM	p-value[3]
		N = 17,039[2]	N = 1,521[2]	N = 15,518[2]	
Gender	17,039				<0.001
female		8818 (51%)	977 (65%)	7841 (50%)	
male		8221 (49%)	544 (35%)	7677 (50%)	
Age	17,039	47 (33, 60)	33 (25, 43)	49 (35, 62)	<0.001
Race	17,039				<0.001
Black		3236 (10%)	225 (7.9%)	3011 (10%)	

Continued

Mexican American		2947 (7.5%)	206 (5.6%)	2741 (7.7%)	
Other		2555 (11%)	254 (10%)	2301 (11%)	
White		8301 (71%)	836 (76%)	7465 (71%)	
Education	17,039				<0.001
9-11th grade		2428 (11%)	149 (7.5%)	2279 (11%)	
college graduate or above		8900 (60%)	998 (69%)	7902 (59%)	
high school graduate/equivalent		3928 (24%)	302 (21%)	3626 (24%)	
less than 9th grade		1783 (5.2%)	72 (2.5%)	1711 (5.5%)	
Marital_relations	17,039				<0.001
divorced		1748 (10%)	100 (7.4%)	1648 (11%)	
living with partner		1282 (7.7%)	153 (11%)	1129 (7.3%)	
married		9369 (57%)	709 (47%)	8660 (58%)	
never married		2751 (17%)	511 (32%)	2240 (15%)	
separated		502 (2.1%)	29 (1.4%)	473 (2.2%)	
widowed		1387 (6.0%)	19 (1.0%)	1368 (6.6%)	
PIR	17,039				0.007
<=1.0		3187 (13%)	261 (14%)	2926 (13%)	
>3.0		6698 (50%)	688 (55%)	6010 (50%)	
1.0 - 3.0		7154 (36%)	572 (32%)	6582 (37%)	
BMI	17,039	28 (24, 32)	22 (20, 24)	28 (25, 33)	<0.001
Alcohol	17,039	14740 (89%)	1321 (90%)	13419 (89%)	0.521
smoke	17,039	7922 (47%)	550 (38%)	7372 (48%)	<0.001
HbA1c	17,039	5.40 (5.10, 5.70)	5.10 (4.90, 5.30)	5.40 (5.20, 5.70)	<0.001
Albumin	17,039	4.30 (4.00, 4.50)	4.40 (4.20, 4.60)	4.30 (4.00, 4.50)	<0.001
Creatinine	17,039	0.84 (0.70, 1.00)	0.80 (0.70, 0.90)	0.85 (0.71, 1.00)	<0.001
BUN	17,039	13 (10, 16)	11 (9, 14)	13 (10, 16)	<0.001
HDL	17,039	51 (42, 62)	61 (50, 71)	50 (41, 61)	<0.001
WBC	17,039	6.50 (5.50, 7.90)	5.90 (4.90, 7.10)	6.60 (5.50, 8.00)	<0.001
RBC	17,039	4.73 (4.40, 5.07)	4.56 (4.30, 4.92)	4.75 (4.43, 5.09)	<0.001
HB	17,039	14.40 (13.50, 15.40)	14.10 (13.30, 15.10)	14.50 (13.50, 15.50)	<0.001
RDW	17,039	12.80 (12.30, 13.50)	12.50 (12.10, 13.00)	12.80 (12.30, 13.50)	<0.001

[1]N not Missing (unweighted); [2]n (unweighted) (%); Median(Q_1, Q_3); [3]Pearson's X^2: Rao & Scott adjustment; Design-based KruskalWallis test. Abbreviation: PIR, poverty income ratio; BMI, body mass index; HbA1c, glycated hemoglobin; BUN, blood urea nitrogen; HDL, high-density lipoprotein cholesterol; WBC, white blood cell count; RBC, red blood cell count; HB, hemoglobin; RDW, red blood cell distribution width.

Table A4. Baseline characteristics categorized by DII quartiles.

Variables	Total (n = 17,039)	Q1 (n = 4261)	Q2 (n = 4260)	Q3 (n = 4259)	Q4 (n = 4259)	Statistic	P
Gender, n (%)						χ^2 = 549.326	<0.001
female	8818 (51.752)	1683 (39.498)	2047 (48.052)	2377 (55.811)	2711 (63.653)		
male	8221 (48.248)	2578 (60.502)	2213 (51.948)	1882 (44.189)	1548 (36.347)		
Age, M (Q_1, Q_3)	49.000 (34.000, 64.000)	48.000 (34.000, 63.000)	50.000 (35.000, 64.000)	49.000 (34.000, 64.000)	50.000 (34.000, 65.000)	χ^2 = 4.160#	0.245
Race, n (%)						χ^2 = 165.740	<0.001
Black	3236 (18.992)	602 (14.128)	720 (16.901)	897 (21.061)	1017 (23.879)		
Mexican American	2947 (17.296)	805 (18.892)	771 (18.099)	734 (17.234)	637 (14.957)		
Other	2555 (14.995)	677 (15.888)	673 (15.798)	587 (13.783)	618 (14.510)		
White	8301 (48.718)	2177 (51.091)	2096 (49.202)	2041 (47.922)	1987 (46.654)		
PIR, n(%)						χ^2 = 396.564	<0.001
<=1.0	3187 (18.704)	646 (15.161)	706 (16.573)	803 (18.854)	1032 (24.231)		
>3.0	6698 (39.310)	2087 (48.979)	1779 (41.761)	1592 (37.380)	1240 (29.115)		
1.0 - 3.0	7154 (41.986)	1528 (35.860)	1775 (41.667)	1864 (43.766)	1987 (46.654)		
Education, n (%)						χ^2 = 339.290	<0.001
9 - 11th grade	2428 (14.250)	463 (10.866)	554 (13.005)	653 (15.332)	758 (17.798)		
college graduate or above	8900 (52.233)	2624 (61.582)	2347 (55.094)	2115 (49.660)	1814 (42.592)		
high school graduate/equivalent	3928 (23.053)	820 (19.244)	920 (21.596)	1034 (24.278)	1154 (27.096)		
less than 9th grade	1783 (10.464)	354 (8.308)	439 (10.305)	457 (10.730)	533 (12.515)		
Alcohol, n (%)						χ^2 = 67.924	<0.001
no	2299 (13.493)	463 (10.866)	549 (12.887)	569 (13.360)	718 (16.858)		
yes	14740 (86.507)	3798 (89.134)	3711 (87.113)	3690 (86.640)	3541 (83.142)		
Smoke, n (%)						χ^2 = 18.210	<0.001
no	9117 (53.507)	2362 (55.433)	2318 (54.413)	2262 (53.111)	2175 (51.068)		
yes	7922 (46.493)	1899 (44.567)	1942 (45.587)	1997 (46.889)	2084 (48.932)		
Marital relations, n (%)						χ^2 = 177.257	<0.001
divorced	1748 (10.259)	375 (8.801)	416 (9.765)	434 (10.190)	523 (12.280)		
living with partner	1282 (7.524)	321 (7.533)	325 (7.629)	289 (6.786)	347 (8.147)		
married	9369 (54.986)	2559 (60.056)	2469 (57.958)	2262 (53.111)	2079 (48.814)		
never married	2751 (16.145)	662 (15.536)	619 (14.531)	739 (17.351)	731 (17.164)		

Continued

separated	502 (2.946)	91 (2.136)	114 (2.676)	148 (3.475)	149 (3.498)		
widowed	1387 (8.140)	253 (5.938)	317 (7.441)	387 (9.087)	430 (10.096)		
BMI, M (Q_1, Q_3)	27.910 (24.400, 32.310)	27.200 (24.100, 31.200)	27.900 (24.370, 32.100)	28.160 (24.650, 32.610)	28.580 (24.595, 33.350)	χ^2 = 93.133#	<0.001
HbA1c, M (Q_1, Q_3)	5.500 (5.200, 5.800)	5.400 (5.200, 5.700)	5.500 (5.200, 5.800)	5.500 (5.200, 5.800)	5.500 (5.200, 5.900)	χ^2 = 60.120#	<0.001
Albumin, M (Q_1, Q_3)	4.200 (4.000, 4.400)	4.300 (4.100, 4.500)	4.200 (4.000, 4.500)	4.200 (4.000, 4.400)	4.200 (3.900, 4.400)	χ^2 = 282.263#	<0.001
Creatinine, M (Q_1, Q_3)	0.830 (0.700, 1.000)	0.860 (0.700, 1.000)	0.820 (0.700, 1.000)	0.820 (0.700, 1.000)	0.810 (0.700, 1.000)	χ^2 = 11.554#	0.009
BUN, M (Q_1, Q_3)	13.000 (10.000, 16.000)	13.000 (10.000, 16.000)	13.000 (10.000, 16.000)	13.000 (10.000, 16.000)	12.000 (9.000, 16.000)	χ^2 = 76.469#	<0.001
HDL, M (Q_1, Q_3)	51.000 (42.000, 62.000)	51.000 (42.000, 63.000)	51.000 (42.000, 63.000)	51.000 (42.000, 63.000)	50.000 (42.000, 62.000)	χ^2 = 11.368#	0.01
WBC, M (Q_1, Q_3)	6.600 (5.500, 7.900)	6.300 (5.300, 7.600)	6.500 (5.500, 7.800)	6.600 (5.500, 8.050)	6.700 (5.600, 8.100)	χ^2 = 126.290#	<0.001
RBC, M (Q_1, Q_3)	4.700 (4.360, 5.050)	4.770 (4.410, 5.100)	4.740 (4.390, 5.070)	4.680 (4.340, 5.030)	4.630 (4.300, 4.975)	χ^2 = 141.045#	<0.001
HB, M (Q_1, Q_3)	14.300 (13.300, 15.300)	14.600 (13.500, 15.600)	14.400 (13.300, 15.400)	14.200 (13.200, 15.200)	13.900 (12.900, 15.000)	χ^2 = 328.837#	<0.001
RDW, M (Q_1, Q_3)	12.900 (12.300, 13.600)	12.700 (12.300, 13.400)	12.800 (12.300, 13.500)	12.900 (12.300, 13.600)	13.100 (12.500, 13.800)	χ^2 = 221.348#	<0.001

#: Kruskal-wailles test, χ^2: Chi-square test. M: Median, Q_1: 1st Quartile, Q_3: 3st Quartile. Abbreviation: PIR, poverty income ratio; BMI, body mass index; HbA1c, glycated hemoglobin; BUN, blood urea nitrogen; HDL, high-density lipoprotein cholesterol; WBC, white blood cell count; RBC, red blood cell count; HB, hemoglobin; RDW, red blood cell distribution width.

Table A5. The association between OBS and DII and CKM after sensitivity analysis.

Variable	Model	
	OR (95% CI)	P
OBS continuous	0.97 (0.96, 0.99)	0.001
OBS quartile		
Q1	ref	-
Q2	0.59 (0.43, 0.82)	0.002
Q3	0.54 (0.39, 0.75)	<0.001
Q4	0.54 (0.39, 0.75)	<0.001
DII continuous	1.07 (1.00, 1.14)	0.057
DII quartile		
Q1	ref	-
Q2	1.01 (0.75, 1.37)	0.9
Q3	1.14 (0.84, 1.55)	0.4
Q4	1.55 (1.10, 2.20)	0.014