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Association between dietary inflammatory index and cardiovascular–kidney–metabolic syndrome risk: a cross-sectional study

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Abstract

Background Dietary inflammation has been linked to various diseases. The dietary inflammatory index (DII) is a tool used to assess the inflammatory potential of a diet. The aim of this study was to explore the relationship between the DII and the risk of developing cardiovascular–kidney–metabolic syndrome (CKMS) in a U.S. population.

Methods Cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) from 2001 to 2020, which included 24,071 participants, were analyzed. CKMS was defined as the coexistence of cardiometabolic syndrome (CMS) and chronic kidney disease (CKD). The DII was calculated on the basis of the anti-inflammatory and pro-inflammatory scores of foods and nutrients. Weighted multivariable logistic regression models were used to estimate the associations between the DII and the risk of developing CKMS. Restricted cubic spline (RCS) regression was conducted to test nonlinear relationships. Subgroup analyses were performed by sex, age, race, smoking status, and alcohol consumption status.

Results After adjusting for confounders, compared with those of the lowest quartile of the DII, the adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for higher DII quartiles were 1.17 (0.93–1.47), 1.43 (1.13–1.81), and 1.76 (1.42–2.18), respectively. Each one-unit increase in the DII was associated with a 12% greater risk of developing CKMS (OR: 1.12, 95% CI: [1.08, 1.18]). RCS regression indicated a significant nonlinear positive association between the DII and the risk of developing CKMS.

Conclusions This study revealed a nonlinear positive association between the DII and the risk of developing CKMS in the U.S. population. Further longitudinal studies are needed to establish causality and explore the underlying biological mechanisms involved.

Keywords Dietary inflammatory index, Cardiovascular–kidney–metabolic syndrome, Cross-sectional study, NHANES

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Introduction

Cardiovascular–kidney–metabolic Syndrome (CKMS) is a complex condition characterized by the interplay of cardiovascular diseases, chronic kidney disease (CKD), and metabolic disorders, which leads to significant morbidity and mortality [1]. CKMS status is closely associated with significantly increased risks of cardiovascular events, kidney failure, and premature death [2, 3]. Diet plays a crucial role in the management of CKMS, as specific dietary patterns can significantly influence inflammation, metabolic health, and overall disease progression [4, 5]. Therefore, understanding the impact of diet on the risk of developing CKMS is key to developing more effective preventive and therapeutic interventions that can alleviate the disease burden and improve long-term patient outcomes.

The dietary inflammatory index (DII) is a tool designed to assess the inflammatory potential of an individual's diet. It is based on the effects of various dietary components on inflammatory biomarkers, such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) [6, 7]. A higher DII score indicates a proinflammatory diet, whereas a lower score suggests an anti-inflammatory diet. The DII scores range from − 8.87 (anti-inflammatory diet) to + 7.98 (proinflammatory diet), with higher scores indicating greater proinflammatory potential [8]. The DII has been used in numerous studies to examine the relationships between diet and various health outcomes [9]. Previous studies have shown significant associations between high dietary inflammatory index (DII) scores and an increased risk of metabolic syndrome and renal insufficiency. For example, diets high in refined sugars, trans fats, and processed foods are associated with higher DII scores, leading to more severe inflammation that contributes to the development and progression of metabolic syndrome [10]. In addition, high DII scores are linked to increased visceral fat (a key indicator of obesity) and elevated blood pressure, both of which are core elements of the pathophysiology of metabolic syndrome [11, 12]. Furthermore, the DII has been shown to influence kidney function, with higher DII scores associated with an increased risk of chronic kidney disease (CKD) and renal insufficiency. Proinflammatory diets reflected by high DII scores may exacerbate kidney damage through inflammatory pathways, thereby increasing the risk of kidney decline [13, 14].

Although numerous epidemiological studies have explored the relationship between the DII and the risk of developing various chronic diseases, evidence regarding the association between the DII and the risk of developing CKMS remains limited. Most studies focus on the associations between the DII and the risk of developing individual CKMS components, such as cardiovascular disease or diabetes, whereas the combined effects of CKMS—where cardiovascular, kidney, and metabolic disorders interact—have not been fully explored. The objective of this study was to assess the association between the DII and the risk of developing CKMS using data from the NHANES cohort.

Methods and materials

Study population

The NHANES is a comprehensive nationwide survey that assesses the health and nutritional status of the U.S. population. Conducted by the National Center for Health Statistics, a component of the U.S. Centers for Disease Control and Prevention, the NHANES investigators collect data biennially and makes them available as a public resource throughout the United States [15].

For cross-sectional analysis, we utilized data spanning from 2001 to 2020, which included 106,911 participants. Individuals lacking information on DII, cardiometabolic syndrome (CMS), or CKD were excluded from the final cohort. Consequently, the final assessment included 24,071 participants from the 2001–2020 NHANES cohort (Fig. 1). On the day of the examination, all participants completed questionnaires, underwent necessary physical exams, and provided blood and urine samples. Trained personnel collected data on demographic characteristics, employment history, personal and family medical histories, and lifestyle behaviors, including smoking and alcohol consumption status, using standardized questionnaires. The NHANES protocol was approved by the Institutional Review Board (IRB) of the National Center for Health Statistics (NCHS), and informed consent was obtained from all participants.

Assessment of dietary information

The DII is an evaluative tool designed to quantify the inflammatory potential of dietary intake. This index incorporates 45 food parameters, with each assigned a specific DII score on the basis of its impact on six key inflammatory biomarkers: IL-1β, IL-4, IL-6, IL-10, TNF-α, and CRP [8]. In the NHANES study, the calculation of the DII relies primarily on 24-hour dietary recall, which requires participants to recall and report the types, quantities, and consumption times of all foods and beverages from the previous day [16]. The food intake data collected through this method are then compared with the food composition data in the global standard database to standardize the intake of each food or nutrient. The standardized data are converted into percentile scores to reduce the impact of skewness in dietary data. The percentile score of each food component is subsequently weighted according to its inflammatory effect score, which reflects the proinflammatory or anti-inflammatory potential of a particular food or nutrient. Finally, the scores of all the food components are summed to obtain an individual's

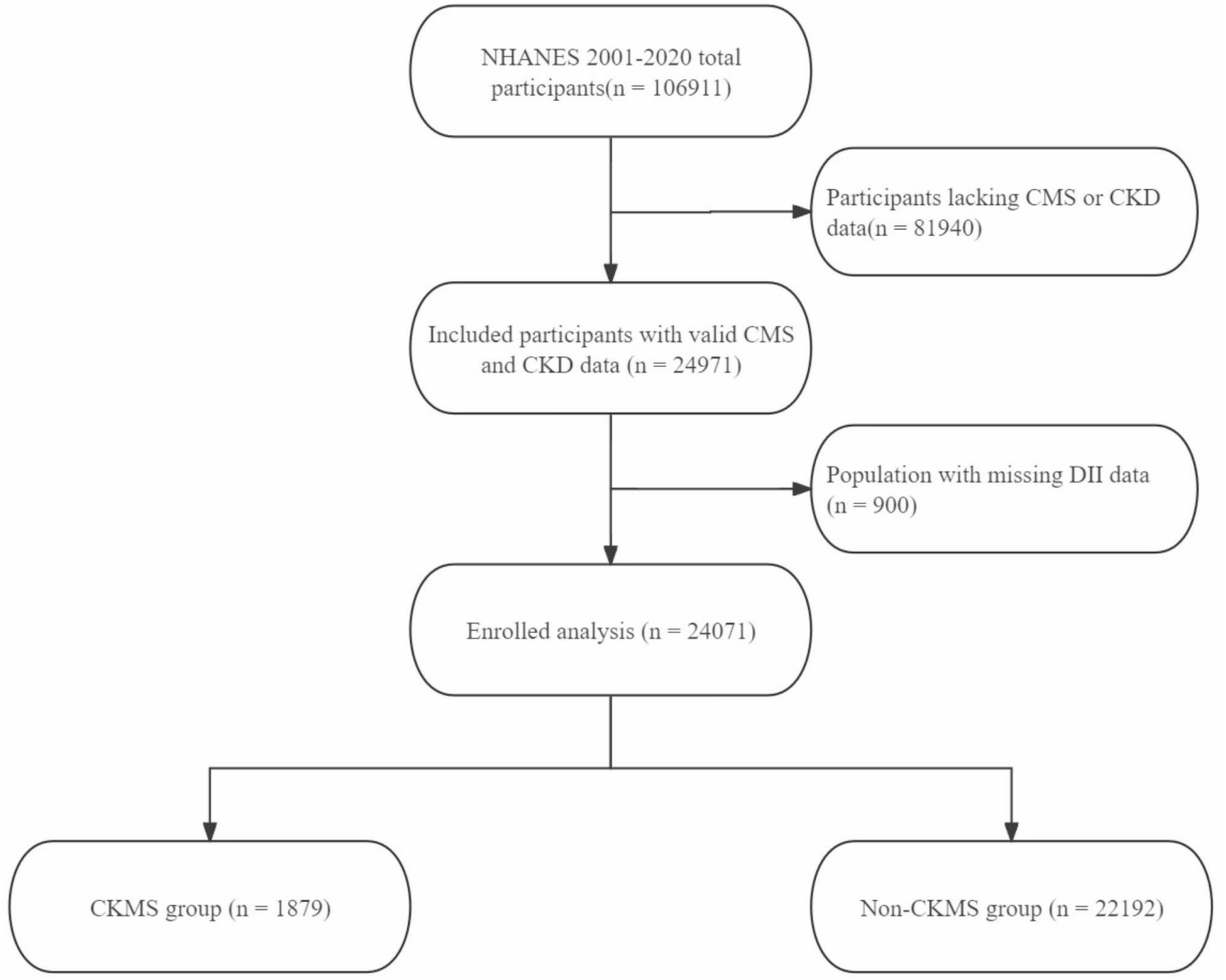

Fig. 1 Participant selection flowchart

total DII score [8]. The DII has been validated in several studies across different populations, including postmenopausal women [17], African Americans [18], and individuals with chronic diseases [19]. These validations confirm the reliability and applicability of the DII in assessing the inflammatory potential of diets in diverse groups. In this study, the DII computation includes the intakes of 26 specific nutrients, including energy; protein; carbohydrates; dietary fiber; total fat; saturated fat; monounsaturated fatty acids (MUFAs); polyunsaturated fatty acids (PUFAs); cholesterol; β-carotene; vitamins A, B1, B2, niacin, B6, folate, B12, C, D, and E; minerals, such as magnesium, iron, zinc, selenium; and caffeine and alcohol. Notably, the DII remains accurately computable even with fewer than 30 nutrients [20]. In the scoring system, foods and nutrients possessing anti-inflammatory properties are awarded negative scores, whereas those with proinflammatory effects receive positive scores [21]. Importantly, the effects of some food components may vary depending on the quantity consumed. For example, small amounts of alcohol may have anti-inflammatory effects, resulting in a negative score, whereas larger amounts may promote inflammation, leading to a positive score [22]. This dose-dependent effect is an essential aspect of the DII calculation, reflecting how different quantities of the same food component can alter its inflammatory potential.

Assessment of Cardiovascular–Kidney–Metabolic syndrome

CKMS is a systemic disorder characterized by pathological interactions among metabolic risk factors, CKD, and the cardiovascular system, leading to multiorgan dysfunction and a heightened risk of adverse cardiovascular outcomes [23]. In this research, CKMS is defined by the simultaneous presence of CKD and CMS, with CMS criteria based on the NCEP-ATP III guidelines [24]. The diagnosis of CMS requires meeting at least three of

the following criteria: central obesity with a waist circumference of ≥ 102 cm for men or ≥ 88 cm for women; hypertriglyceridemia, with serum triglycerides ≥ 150 mg/dL; low high-density lipoprotein cholesterol (HDL-C), < 40 mg/dL in men or < 50 mg/dL in women; hypertension, as indicated by a systolic blood pressure of ≥ 130 mmHg or a diastolic blood pressure of ≥ 85 mmHg, or treatment for hypertension; and hyperglycemia, defined by a fasting plasma glucose (FPG) level of ≥ 100 mg/dL or treatment for diabetes. Waist circumference, weight, and height were measured following the standard protocols outlined in the Anthropometric Standardization Reference Manual [25], and blood pressure was measured according to the latest recommendations from the American Heart Association [26]. Laboratory assessments included measurements of serum triglycerides, HDL-C, FPG, serum creatinine (SCr), and the urine albumin-to-creatinine ratio (UACR). CKD status was determined via the 2009 CKD-EPI creatinine equation. A diagnosis of CKD was indicated by an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m^2 or a UACR exceeding 30 mg/g [27, 28].

Covariates

In this survey, participants were classified into the following racial/ethnic categories: Mexican American, Non-Hispanic Black, Non-Hispanic White, Other Hispanic, and Other Race. Educational attainment was categorized as either below high school level or at high school level and above. Marital status was simplified to 'married' and 'other'. The poverty–income ratio (PIR) was employed to adjust income levels for economic inflation and family size. Self-administered questionnaires were used to collect data on smoking habits, alcohol consumption status, physical activity, and histories of diabetes and hypertension. Smoking status was categorized as never, former, or current smokers. Alcohol consumption can be divided into five categories: never drinkers (fewer than 12 drinks in a lifetime), former drinkers (at least 12 drinks in a year but did not drink last year or did not drink last year but had at least 12 drinks in a lifetime), mild drinkers (1 drink per day for females, 2 drinks per day for males), moderate drinkers (2 drinks per day for females, 3 drinks per day for males, or at least 2 days of binge drinking per month but less than 5 days), and heavy drinkers (3 drinks per day for females, 4 drinks per day for males, or at least 5 days of binge drinking per month) [29]. Physical activity levels were assessed on the basis of the participants' engagement in various activities, including walking or bicycling, tasks around home or yard, muscle-strength activities, work-related activities, and recreational activities. The assessment was conducted using a comprehensive questionnaire that captured the frequency and duration of these activities. The physical activity data were expressed in terms of weekly metabolic equivalent tasks (METs), which were calculated by multiplying the MET values of each activity by the time spent on that activity per week.

Statistical analysis

The NHANES is a multistage, stratified, probability-based survey that oversamples specific populations [15]. To account for varying sampling probabilities and nonresponses, participant data were weighted using NHANES dietary subsample weights. Data analysis was performed using the open-source software R, version 4.3.2, with data extraction and analysis conducted through the "nhanesR" package (R Core Team, 2023. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, https://www.R-project.org). The participants were divided into two groups on the basis of the presence or absence of CKMS. Continuous variables are expressed as the means ± standard deviations (SDs) and were compared using weighted t tests, whereas categorical variables are presented as frequencies (percentages) and were analyzed using chi-square tests. The DII was categorized into quartiles on the basis of the distribution of DII scores in the study sample. Specifically, the DII scores were divided into four equal parts, each representing 25% of the sample. The quartiles were derived using the following breaks: Q1 (DII < 0.46), Q2 (0.46 ≤ DII < 1.95), Q3 (1.95 ≤ DII < 3.12), and Q4 (DII ≥ 3.12). The first quartile (Q1) was used as the reference group for analysis.

Several multivariable logistic regression models were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for the association between the DII and CKMS risk. Model I was unadjusted; Model II was adjusted for age, sex, and race; and Model III was further adjusted for education level, poverty-income ratio, alcohol consumption status, smoking status, and weekly physical activity (METs). To assess the nonlinearity of the DII-CKMS relationship, restricted cubic spline (RCS) regression was applied, with knots placed at the 10th, 50th, and 90th percentiles. Subgroup analyses examined potential interactions between the DII and the risk of developing CKMS across variables such as age, sex, race, smoking status, and alcohol consumption. Multiple imputation tailored for survey datasets was used to address missing data [30]. Statistical significance was defined by a two-tailed p value of less than 0.05.

Results

Study population characteristics

The baseline characteristics of 24,071 participants, distinguishing between 22,192 individuals without CKMS and 1,879 individuals diagnosed with CKMS are presented in Table 1. The CKMS group was notably older, with an average age of 63.23 years compared with 42.57 years in

Table 1 Baseline characteristics by CKMS status

Characteristics	Overall (*n* = 24071)	Non–CKMS (*n* = 22192)	CKMS (*n* = 1879)	*p* value
Age, years	43.95 ± 0.24	42.57 ± 0.24	63.23 ± 0.49	< 0.0001***
Sex, n (%)				< 0.001***
Female	11,869 (50.42)	10,871 (50.06)	998 (55.53)	
Male	12,202 (49.58)	11,321 (49.94)	881 (44.47)	
Race, n (%)				0.13
Mexican American	4614 (8.61)	4281 (8.60)	333 (8.78)	
Non-Hispanic Black	5265 (10.96)	4890 (10.91)	375 (11.73)	
Non-Hispanic White	10,047 (68.20)	9133 (68.12)	914 (69.32)	
Other Hispanic	2003 (5.32)	1850 (5.35)	153 (4.80)	
Other Race	2142 (6.91)	2038 (7.02)	104 (5.37)	
Education level, n (%)				< 0.0001***
High school or above	18,039 (83.54)	16,833 (84.30)	1206 (72.93)	
Less than High School	6032 (16.46)	5359 (15.70)	673 (27.07)	
Marital status, n (%)				0.01*
Married	9867 (48.61)	8910 (48.32)	957 (52.69)	
Other	14,204 (51.39)	13,282 (51.68)	922 (47.31)	
Smoke, n (%)				< 0.0001***
Never	12,608 (52.20)	11,722 (52.63)	886 (46.30)	
Former	5346 (24.12)	4666 (23.29)	680 (35.72)	
Now	6117 (23.67)	5804 (24.08)	313 (17.98)	
Alcohol use, n (%)				< 0.0001***
Never	3526 (12.03)	3188 (11.60)	338 (18.05)	
Former	3994 (14.47)	3456 (13.59)	538 (26.71)	
Mild	8158 (35.98)	7556 (36.15)	602 (33.68)	
Moderate	3629 (16.85)	3467 (17.41)	162 (9.02)	
Heavy	4764 (20.67)	4525 (21.25)	239 (12.54)	
Poverty–income ratio	2.93 ± 0.03	2.95 ± 0.03	2.57 ± 0.05	< 0.0001***
Total METs/week	3511.24 ± 69.89	3574.60 ± 73.40	2625.31 ± 146.79	< 0.0001***
Body Mass Index, kg/m2	28.13 ± 0.08	27.79 ± 0.08	32.92 ± 0.23	< 0.0001***
Waist circumference, cm	96.68 ± 0.20	95.61 ± 0.20	111.55 ± 0.50	< 0.0001***
SBP, mmHg	120.16 ± 0.20	119.02 ± 0.20	136.01 ± 0.74	< 0.0001***
DBP, mmHg	69.14 ± 0.19	69.09 ± 0.19	69.81 ± 0.43	0.09
eGFR, mL/min/1.73m2	98.78 ± 0.33	100.77 ± 0.32	70.90 ± 0.90	< 0.0001***
FPG, mg/dL	104.38 ± 0.30	101.95 ± 0.25	138.30 ± 1.72	< 0.0001***
Serum Creatinine, mg/dL	0.87 ± 0.00	0.85 ± 0.00	1.13 ± 0.02	< 0.0001***
Triglycerides, mg/dL	126.41 ± 1.15	121.23 ± 1.09	198.81 ± 6.48	< 0.0001***
HDL-C, mg/dL	53.68 ± 0.19	54.17 ± 0.20	46.75 ± 0.50	< 0.0001***
UACR, mg/g	31.17 ± 1.61	17.14 ± 0.85	227.35 ± 20.43	< 0.0001***
DII	1.51 ± 0.03	1.48 ± 0.03	1.91 ± 0.06	< 0.0001***
Hypertension, n (%)				< 0.0001***
No	14,387 (58.74)	14,224 (62.30)	163 (8.89)	
Yes	9684 (41.26)	7968 (37.70)	1716 (91.11)	
Diabetes Mellitus, n (%)				< 0.0001***
No	20,339 (86.69)	19,654 (89.99)	685 (40.59)	
Yes	3732 (13.31)	2538 (10.01)	1194 (59.41)	

Enumeration data are reported as weighted means ± standard deviations, and measurement data are presented as percentages.

CKMS, Cardiovascular–Kidney–Metabolic Syndrome; MET, Metabolic Equivalent of Task; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; eGFR, estimated Glomerular Filtration Rate; FPG, Fasting Plasma Glucose; HDL-C, high-density lipoprotein cholesterol; UACR, Urinary Albumin-to-Creatinine Ratio; DII, Dietary Inflammatory Index.

* *p* value < 0.05, ** *p* value < 0.01, *** *p* value < 0.001

Table 2 Weighted logistic regression analysis assessing the relationship between the DII and the risk of developing CKMS

Characteristic	Model 1		Model 2		Model 3	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
DII	1.14 (1.09,1.19)	< 0.0001***	1.16 (1.12,1.22)	< 0.0001***	1.12 (1.08,1.18)	< 0.001***
Q1	Reference	-	Reference	-	Reference	-
Q2	1.25 (1.00,1.55)	0.05	1.23 (0.98,1.54)	0.07	1.17 (0.93,1.47)	0.18
Q3	1.55 (1.22,1.97)	< 0.001***	1.59 (1.26,2.00)	< 0.001***	1.43 (1.13,1.81)	0.003**
Q4	1.90 (1.56,2.32)	< 0.0001***	2.07 (1.69,2.54)	< 0.0001***	1.76 (1.42,2.18)	< 0.0001***
P for trend		< 0.0001***		< 0.0001***		< 0.0001***

Determined through multivariate logistic regression analysis.

Model 1: Unadjusted.

Model 2: Adjusted for age, sex, and race.

Model 3: Further adjusted for education level, the poverty–income ratio, alcohol consumption status, smoking status, and weekly physical activity in total METs, building on Model 2.

* *p* value < 0.05, ** *p* value < 0.01, *** *p* value < 0.001

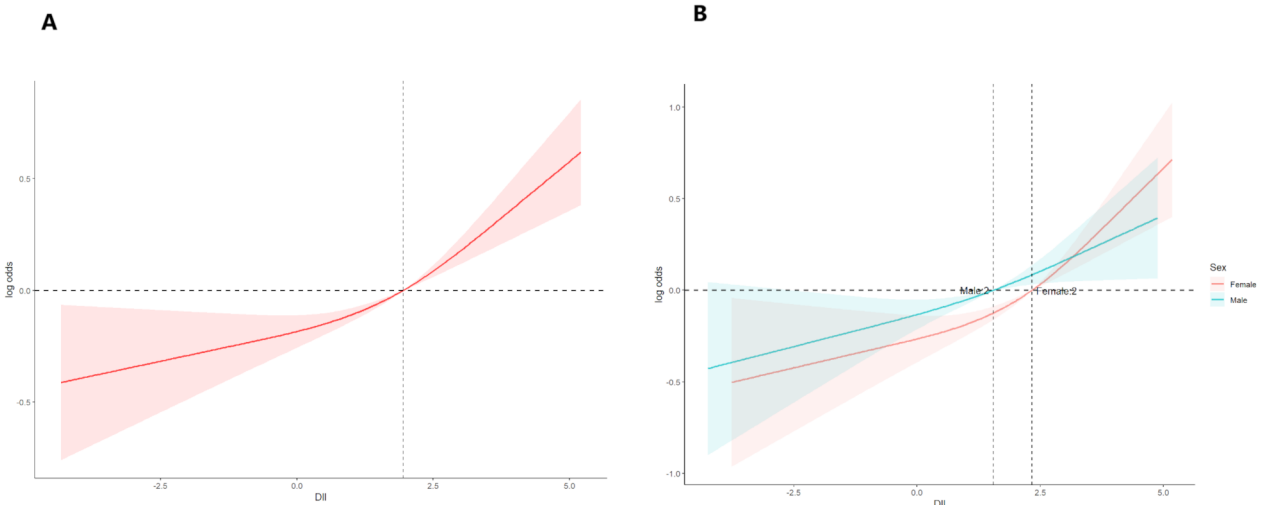

Fig. 2 (**A**) RCS curve depicting the association between the DII and the risk of developing CKMS. (**B**) RCS curves showing the relationship between the DII and the risk of developing CKMS in women (red curve) and men (blue curve), respectively

the non-CKMS group, and included a greater proportion of females (55.53% versus 50.06%). Educational levels were lower in the CKMS group, with only 72.93% having completed high school or higher, compared with 84.30% in the non-CKMS group. Poor health behaviors, such as smoking and high alcohol consumption, were more prevalent among those with CKMS. Clinically, the CKMS group presented a higher BMI, waist circumference, systolic blood pressure, fasting blood glucose, and triglyceride levels, along with a lower eGFR and HDL-C. Furthermore, as shown in Table 1, CKMS participants tended to have higher DII scores, which aligns with our initial hypothesis. Further exploration through multivariate analysis is necessary.

Association of the DII with the risk of developing Cardiovascular–Kidney–Metabolic syndrome

As shown in Table 2, sample-weighted multivariate logistic regression analysis revealed a positive association between higher DII levels and the risk of developing CKMS. After adjusting for age, sex, race, education level, the poverty–income ratio, alcohol consumption status, smoking status, and total weekly METs, a one-unit increase in the DII corresponded to a 12% higher risk of developing CKMS (OR: 1.12, 95% CI: 1.08–1.18, $p < 0.001$). Furthermore, compared with those in the lowest quartile, the adjusted ORs for CKMS in the subsequent DII quartiles were 1.17 (0.93–1.47), 1.43 (1.13–1.81), and 1.76 (1.42–2.18), respectively.

Nonlinear correlation analysis of the association between the DII and the risk of developing CKMS

Using an RCS regression model adjusted for all potential confounders, we found a nonlinear positive association between the DII and the risk of developing CKMS (**Fig. 2A**). We also explored the potential sex-specific effects of the DII on the risk of developing CKMS. In women, the relationship was nonlinear, with a more pronounced increase in the risk of developing CKMS when

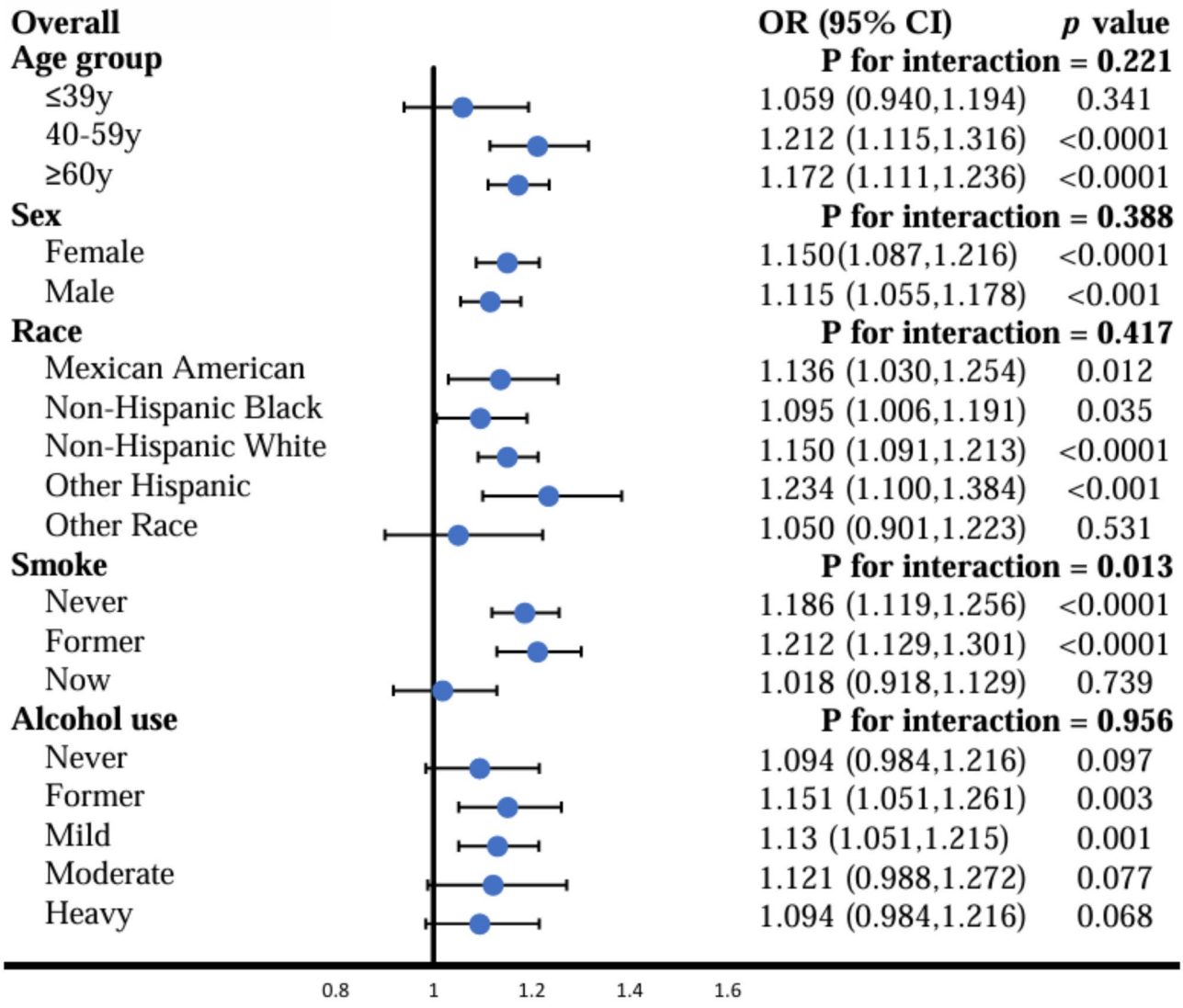

Fig. 3 Subgroups analyses for the association between the DII and the risk of developing CKMS

the DII exceeded 2. In contrast, this relationship was linear in men (**Fig. 2B**).

Subgroup analysis

In the present study, we employed multivariate logistic regression analysis and adjusted for potential confounders to examine the association between the DII and the risk of developing CKMS, with a focus on subgroups defined by age, sex, race, smoking status, and alcohol consumption (Fig. 3). In most subgroups, an increase in the OR for developing CKMS was noted for each one-unit increase in the DII, with values ranging from 1.050 to 1.234. However, this association was not statistically significant in the following subgroups: age < 39 years, other races, current smokers, and moderate to heavy drinkers ($p > 0.05$). Additionally, a significant interaction was observed between the DII and smoking status (P for interaction = 0.013), whereas interactions with other subgroups did not reach statistical significance, possibly due to the confounding effect of smoking on the DII. Independent of age, sex, race, or drinking habits, a higher dietary inflammatory status, as indicated by the DII, was confirmed to be a strong risk factor for the development of CKMS.

Discussion

An analysis of data from 24,071 participants in the 2001–2020 NHANES revealed a significant increase in the risk of developing CKMS among individuals with higher DII scores. The RCS curve indicated a nonlinear positive association between the DII and the risk of developing CKMS. We also examined the potential sex-specific effects of the DII on the risk of developing CKMS. In women, the relationship was nonlinear, with a sharper

increase in the risk of developing CKMS when the DII exceeded 2. In men, this relationship was linear. Subgroup analyses revealed that this nonlinear relationship remained consistent across most subgroups.

The DII and the risk of developing CKMS: comparative study insights

In the ongoing dialog regarding the relationship between the DII and the risk of developing CKMS, the findings of the present study align with the current scientific consensus and provide novel insights into the influence of dietary inflammation on the spectrum of chronic diseases. Our research confirms the robust positive correlation between elevated DII scores and the incidence of CKMS, a relationship previously underscored in the literature, highlighting the predictive utility of the DII in clinical practice [8]. Consistent with the findings of some studies, our findings revealed significant correlations between a high DII and specific cardiovascular risk parameters integral to the development of CKMS [31]. These results are parallel to investigations that have linked higher DII scores with an increased risk of colorectal cancer, suggesting a generalized mechanism by which inflammation exacerbates pathological states across various organ systems [32].

However, our study also distinguishes itself by the magnitude and specifics of these associations. While some studies have reported a relationship between the DII and the risk of developing cardiovascular diseases within the context of the Mediterranean diet, the findings were less pronounced than our findings, potentially because of dietary variations inherent in different cultural diets [33]. Similarly, reports from Mediterranean cohorts have shown a weaker association, likely due to the anti-inflammatory properties of the Mediterranean diet, which may mitigate the adverse effects observed in other dietary patterns [34]. Methodological differences are also pivotal in explaining the discrepancies among study results. The calculation of the DII can vary significantly on the basis of the dietary components included, which impacts the sensitivity and specificity of DII scores [35]. Furthermore, regional dietary habits have been shown to substantially influence the relationship between diet-induced inflammation and health outcomes [36]. Our findings are further supported by recent studies that have documented the biological underpinnings linking dietary inflammation to metabolic disruptions, providing a mechanistic explanation that complements our observational data [37]. This work illustrates how dietary inflammatory potential correlates with biochemical markers of inflammation and metabolic health and aligns closely with our methodological approach [34]. In conclusion, our study reinforces the validity of the DII as a predictive tool for CKMS development while emphasizing the necessity of considering local dietary patterns and methodological harmonization in future research to increase the applicability and precision of the DII across diverse populations.

Impact of diet on CKMS progression

In discussing the biological mechanisms underlying the association between the DII and the risk of developing CKMS, it is necessary to consider the roles of various metabolic abnormalities and biomarkers. Research has shown that a high DII is associated with increased levels of inflammatory markers such as CRP, IL-6, and TNF-α, which are linked to cardiovascular diseases and closely related to renal diseases [38]. Specific dietary components, such as high intake of carbohydrates, especially high glycemic index carbohydrates, are associated with increased levels of IL-6 in adolescence and early adulthood, underscoring the critical role of carbohydrates in inflammation and metabolic functions [39]. Moreover, the balance of vitamins and trace elements significantly impacts the inflammatory state and the progression of CKMS. For example, dysregulation of calcium and phosphorus metabolism, a common issue in CKD, can exacerbate cardiovascular and renal pathologies by disrupting the FGF23-αKlotho-vitamin D axis [40]. Unhealthy dietary habits, such as high intake of sugar, salt, saturated fats, and ultra-processed foods, are significant risk factors for CKD. These factors increase the production of gut-derived uremic toxins and promote inflammation and oxidative stress, thereby exacerbating the symptoms of chronic diseases [41].

Biological mechanisms linking the DII and the risk of developing CKMS

An inflammatory diet influences the progression of inflammation and CKMS through various biological pathways. For example, a high-carbohydrate diet, particularly one rich in sugars, may lead to insulin resistance and glucotoxicity, both of which exacerbate inflammation and oxidative stress, negatively impacting cardiovascular and kidney health. Additionally, high sugar intake may increase endothelial cell damage, leading to vascular dysfunction and increased atherosclerosis risk [42]. Additionally, high sugar intake may enhance endothelial cell damage, leading to increased vascular dysfunction and arteriosclerosis [43]. Cholesterol accumulation is associated with an increased risk of cardiovascular disease, particularly in patients with CKMS. Cholesterol may exacerbate these risks by promoting inflammatory responses, increasing oxidative stress, and reducing the anti-inflammatory functions of HDL-C [44, 45]. Vitamin B1 is crucial for regulating carbohydrate metabolism, and vitamin B1 deficiency can lead to decreased energy production, further exacerbating the risk of developing cardiovascular and renal diseases. Adequate intake

of vitamin B1 helps reduce oxidative stress and improve metabolic health, thereby decreasing the risk of developing CKMS [46]. Vitamin D plays a significant role in regulating inflammatory responses and immune functions. Insufficient vitamin D is associated with increased risk of developing cardiovascular diseases and renal dysfunction [47]. Supplementation with vitamin D may improve cardiovascular and metabolic health by reducing the levels of inflammatory markers such as CRP and interleukin-6, thereby lowering the risk of developing CKMS. Adequate levels of vitamin D help modulate inflammatory processes, protect cardiovascular and renal health by increasing insulin sensitivity, and reduce oxidative stress [48].

Implications for clinical practice

The findings of this study have important implications for the prevention and management of CKMS in clinical practice. Understanding the relationship between the DII and the risk of developing CKMS can guide health care professionals in developing targeted dietary interventions aimed at reducing dietary inflammation, thereby mitigating CKMS risk and severity. Health care providers should emphasize reducing the intake of high-glycemic index carbohydrates and saturated fats while promoting the consumption of anti-inflammatory foods such as fruits, vegetables, and omega-3 fatty acids. For example, a 1-unit increase in the DII could be associated with dietary changes such as decreased consumption of processed foods and increased intake of whole grains, leafy greens, and fatty fish. Additionally, ensuring adequate intake of vitamins and minerals, particularly those with anti-inflammatory properties such as vitamin D and magnesium, is crucial. The use of comprehensive dietary assessment tools such as the DII can help identify patients at high risk of developing CKMS and guide personalized nutritional counseling. By integrating these dietary recommendations into clinical practice, health care professionals can adopt a proactive approach to managing and preventing CKMS, ultimately improving patient outcomes and quality of life.

Limitations

This study has several limitations. The cross-sectional design of the NHANES data restricts the ability to establish causality between the DII and the risk of developing CKMS. Additionally, self-reported dietary data may introduce biases and inaccuracies, potentially leading to misclassification of dietary exposures. Another limitation is the exclusion of certain nutrients from the DII calculation, which may affect the comprehensiveness of the inflammatory assessment. Specifically, in this study, only 26 out of 45 possible food parameters were available to calculate the DII. The unavailable parameters included eugenol, garlic, ginger, onion, pepper, saffron, thyme/oregano, rosemary, turmeric, green/black tea, flavan-3-ol, flavones, flavonols, flavonones, anthocyanidins, isoflavones, n-3 fatty acids, n-6 fatty acids, and trans-fatty acids. The exclusion of these parameters, particularly those with known anti-inflammatory properties such as flavonoids, may have limited our ability to capture the full inflammatory potential of the diets assessed in this study. This could have resulted in an overestimation of the proinflammatory potential of the diets evaluated. Furthermore, while the DII provides valuable insights into the overall inflammatory potential of dietary patterns, its inability to account for dietary supplementation and potential inaccuracies in the determination of food parameter quantities should be acknowledged. Last, the large age difference across populations, especially with older adults who have heightened inflammatory responses, could influence the results, as this inherent factor might contribute to variations in the observed associations.

Future research directions

Future research should employ longitudinal designs to better establish causal relationships between dietary patterns and the risk of developing CKMS. Prospective cohort studies would help determine the direction of the observed relationships. Additionally, similar studies in different populations and regions are needed to validate these findings. Improving dietary assessment accuracy through biomarkers and precise tracking methods could enhance data reliability. Addressing these areas will build on the findings of the present study and contribute to a more comprehensive understanding of the role of diet in the risk of developing CKMS.

Conclusion

We found a nonlinear positive association between the DII and the risk of developing CKMS, independent of potential confounders, and identified key dietary factors related to CKMS. Given the inherent limitations of cross-sectional studies, further research is essential to verify the causality of this association and uncover the underlying mechanisms linking diet-related inflammation to CKMS.

Abbreviations

CKD	Chronic Kidney Disease
CKMS	Cardiovascular-Kidney-Metabolic Syndrome
CMS	Cardiometabolic Syndrome
CRP	C-reactive Protein
DBP	Diastolic Blood Pressure
DII	Dietary Inflammatory Index
eGFR	Estimated Glomerular Filtration Rate
FPG	Fasting Plasma Glucose
HDL-C	High-Density Lipoprotein Cholesterol
IL-1β	Interleukin-1 beta
IL-4	Interleukin-4

IL-6	Interleukin-6
IL-10	Interleukin-10
MET	Metabolic Equivalent of Task
NHANES	National Health and Nutrition Examination Survey
NCEP-ATP III	National Cholesterol Education Program Adult Treatment Panel III
PIR	Poverty–Income Ratio
RCS	Restricted Cubic Spline
SBP	Systolic Blood Pressure
TNF-α	Tumor Necrosis Factor-alpha
UACR	Urine Albumin-to-Creatinine Ratio

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Author contributions
CZ, ML, and YY contributed equally to the conceptualization and design of the study. HY, ZG, and ZY were responsible for data collection and management. CZ, ML, and CL performed the statistical analysis. YY, SY, and YZ interpreted the data and contributed to manuscript drafting. CZ supervised the project and was the major contributor to the writing of the manuscript. All the authors read and approved the final manuscript.

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Data availability
Access to the original datasets can be obtained via the NHANES website at https://www.cdc.gov/nchs/nhanes/index.htm.

Declarations

Ethics approval and consent to participate
This study adhered to the principles outlined in the Declaration of Helsinki, with approval from the Institutional Review Board (IRB) of the National Center for Health Statistics (NCHS) for all procedures involving participants. Written informed consent was obtained from all individuals involved in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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