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Dietary inflammatory index and blood inflammatory markers in relation to dyslipidemia: A cross-sectional study in American adults NHANES 2009-2018

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ABSTRACT

Background and Objectives: The presence and accumulation of inflammation may exacerbate the development of dyslipidemia. Therefore, this study aimed to explore the relationship between blood inflammatory markers and the dietary inflammatory index (DII) in American adults as well as their association with dyslipidemia. **Methods and Study Design:** This cross-sectional study included participants with complete data on lipid levels, dietary intake, and blood inflammatory markers. The associations between dyslipidemia and two sets of exposures—blood inflammatory markers and the DII—were analysed using weighted univariate and multivariate logistic regression models. **Results:** Among the 9,441 participants (2009–2018), 6,689 (70.9%) had dyslipidemia. Logistic regression analysis revealed that higher DII quartiles were significantly associated with an increased risk of dyslipidemia, with the fourth quartile exhibiting an odds ratio of 1.33 (95% CI: 1.10–1.62; $p < 0.001$). Furthermore, DII combined with various blood inflammatory markers was consistently associated with an increased dyslipidemia risk (all OR > 1.0, all $p < 0.05$). A non-linear relationship was observed between the systemic immune-inflammation index (SII) and dyslipidemia risk, which became significant when the SII exceeded 434.65. **Conclusions:** The DII and blood inflammation markers showed a positive association with dyslipidemia. Nonetheless, these findings still offer public health policymakers valuable insights for developing evidence - based strategies to prevent dyslipidemia and potentially reduce inflammation - associated dyslipidemia risk.

Key Words: dyslipidemia, dietary inflammatory index, systemic immune-inflammation index, systemic inflammation response index, National Health and Nutrition Examination Survey

INTRODUCTION

Dyslipidemia is widely recognized as a principal risk factor for cardiovascular diseases.[1] Dyslipidemia is defined by low levels of high-density lipoprotein cholesterol (HDL-C) alongside elevated concentrations of triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and total cholesterol (TC).[2, 3] From 1990 to 2019, high plasma LDL-C levels rose from the 15th to the 8th leading risk factor for death.[4] Using data from both the National Health and Nutrition Examination Survey (NHANES) and the China Health and Retirement Longitudinal Study (CHARLS), a cross-sectional study indicated that dyslipidemia is common in the United States (56.8%) and is characterized by high TC in men and low HDL-

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C in women.[5] Recent evidence has associated inflammation with the progression of dyslipidemia, subsequently increasing the risk of several chronic conditions, such as cardiovascular disease.[6] It was found that proinflammatory cytokine concentrations in the serum may increase as a result of dyslipidemia, which is induced in the early stages of inflammation, suggesting that the prevalence of dyslipidemia may increase in the absence of effective strategies to reduce inflammation and oxidative stress.[7]

Inflammation is a complex physiological process closely linked to the progression of numerous chronic illnesses, such as heart disease,[8] metabolic syndrome,[9, 10] and obesity.[11] The relationship between diet and inflammation has garnered global attention in recent decades. The dietary inflammatory index (DII) is a measure used to evaluate the relationship between diet and inflammation. The DII evaluates the inflammatory potential of food by comparing actual nutrient intake with standardized reference values. A higher DII score indicates a diet with greater proinflammatory properties, while a lower score suggests a diet with less inflammatory potential.[12] Research has revealed that diets characterized by high DII values are associated with an elevated risk of dyslipidemia progression,[13] suggesting that the consumption of foods and nutrients with high inflammatory potential may increase the body's inflammatory response. The systemic immune-inflammation index (SII) and the systemic inflammation response index (SIRI) serve as more comprehensive indicators of inflammation status compared to a single white blood cell (WBC) subpopulation.[14] A study based on a general rural population found that patients with dyslipidemia had significantly elevated levels of SII as well as SIRI.[15] The persistence and accumulation of inflammation may exacerbate the development of dyslipidemia, manifesting as reduced HDL-C and elevated TG levels.

Therefore, controlling inflammation is crucial for managing dyslipidemia, which depends on identifying factors that can be regulated or altered to mitigate inflammation. Diet is a controllable factor that affects blood lipid levels.[16-18] Logistic regression analysis 17,820 NHANES participants from a dietary perspective and revealed a strong positive correlation between DII and dyslipidemia.[19] Additionally, the association between DII and blood inflammatory markers has been investigated in individuals with cognitive dysfunction,[20, 21] periodontitis,[22] coronary heart disease,[23] and metabolic syndrome.[24, 25] However, extensive population-based research directly linking DII score and inflammatory markers within individuals with dyslipidemia remains limited. Thus, establishing the correlation between DII, blood inflammation markers, and dyslipidemia is essential, which may provide an essential

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scientific basis for reducing DII through dietary adjustment to lower the inflammation level and improve dyslipidemia.

The novelty of our study lies in its comprehensive integration of the DII with multiple blood inflammatory markers to explore their relationship with dyslipidemia. Although previous studies have explored DII or blood inflammatory markers in various diseases, few have examined their combined role in dyslipidemia. Given that inflammation plays a central role in lipid metabolism, investigating the interaction between dietary inflammation and systemic inflammatory indices could offer greater insights into the pathophysiology of dyslipidemia.

Consequently, this study sought to examine the associations between the DII, blood inflammatory markers, and dyslipidemia. The findings could inform targeted dietary interventions and clinical strategies for dyslipidemia prevention and management.

MATERIALS AND METHODS

Data source

The NHANES, conducted by the US Centers for Disease Control and Prevention, is a cross-sectional study designed to assess the health and nutritional status of adults and children in the US. Annually, it surveys a nationally representative sample of approximately 5,000 individuals. All respondents provided informed consent prior to completing the questionnaire and investigation phases. NHANES collects a wide range of data, including demographic information, dietary intake, physical examinations, laboratory tests, and questionnaire responses. All research protocols have been approved by the Ethics Review Committee of the National Center for Health Statistics, as detailed at https://wwwn.cdc.gov/nchs/nhanes/Default.aspx. A total of 49,693 individuals participated in the NHANES survey from 2009 to 2018. Individuals over 20 years of age were selected as study participants, and data from 12,218 participants were obtained by excluding those with missing HDL-C, TG, and LDL-C data and those with mean energy intake less than 500 kcal/day for all participants, 8,000 kcal/day for men, and 5,000 kcal/day for women.[26] Finally, 9,441 participants were included after excluding those with missing covariates, as shown in Figure 1.

Definition of dyslipidemia

Dyslipidemia was identified using four lipid markers: serum TC, TG, LDL-C, and HDL-C. The definitions for dyslipidemia follow the guidelines set via the 3rd report of the Expert

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Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, delineating dyslipidemia as: Criteria for dyslipidemia included TG levels ≥ 150 mg/dL, TC levels ≥ 200 mg/dL, LDL-C levels ≥ 130 mg/dL, or HDL-C levels < 40 mg/dL in males or < 50 mg/dL in females, including individuals on cholesterol-lowering medications.[27]

DII calculation

The DII was designed by the Cancer Prevention & Control Program at the University of South Carolina in Columbia to compare the inflammatory potential of diets across different populations. Researchers identified specific inflammatory effect scores, global mean intakes, and standard deviations for 45 food parameters, with 36 being anti-inflammatory and nine proinflammatory. An individual's DII score is calculated from these components.[28] These values can be employed to compute the overall DII score for an individual's diet. The overall DII score categorizes diets as anti-inflammatory (< 0), non-inflammatory (= 0), or proinflammatory (> 0). A higher DII score indicates a more proinflammatory diet, while a lower score suggests a less inflammatory diet.[29] The DII offers both qualitative and quantitative assessments of dietary inflammatory effects.[30] Furthermore, the DII can significantly predict changes in inflammatory markers, with proinflammatory diets associated with elevated levels of various inflammatory markers.[31]

This study used 28 food parameters from NHANES to calculate the DII score. These included saturated fat, energy, protein, carbohydrate, fiber, total fat, monounsaturated fatty acids, polyunsaturated fatty acids, cholesterol, vitamin E, vitamin A, β-carotene, thiamine, riboflavin, niacin, vitamin B-6, folic acid, vitamin B-12, vitamin C, vitamin D, magnesium, iron, zinc, selenium, caffeine, alcohol, n-6 fatty acids, and n-3 fatty acids.[28] Studies have shown that when the number of nutrients used to calculate the DII is less than 30, the DII is still considered effective.[28] The DII involves four distinct calculation steps: (1) DII calculation involves comparing the average daily nutrient intake of an individual against a global average intake dataset. (2) The Z-values centralization algorithm was applied to compute the Z-score for each food or nutrient. (3) Each Z-value was multiplied by its respective inflammatory effect value to generate individual DII values for every nutrient or food item. (4) Summation of the DII values from every nutrient or food item yielded the composite DII score.[28]

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Blood inflammation markers

An automated hematological analysis instrument (Coulter DxH 800 analyzer) was employed to perform a complete blood count to assess the WBC, lymphocyte (L), monocyte (M), neutrophil (N), as well as platelet (P) counts.

Several other blood inflammatory markers were also measured, including the neutrophil-to-lymphocyte ratio (NLR = N/L), platelet-to-lymphocyte ratio (PLR = P/L), and neutrophil-to-albumin ratio (NAR = N/albumin).[32] SII was calculated as P × N/L, and SIRI was determined as M × N/L.[33] C-reactive protein (CRP) and high-sensitivity CRP (hs-CRP) were excluded from further analysis due to limited data availability; CRP data were collected only during the 2009–2010 cycle, and hs-CRP data were available only for the 2015–2018 cycles.

Other covariates

The research incorporated various covariates:[34] marital status was classified as married/living with a partner, widowed/divorced/separated, or never married, chronological age, body mass index (BMI; sequential), sex (male & female), race was categorized as Mexican American, other Hispanic backgrounds, White non-Hispanic, Black non-Hispanic, and other or multiracial groups. Additionally, education level was considered, ranging from less than 9 years of education to a college degree or higher. Pre-existing health conditions heart failure (HF), coronary heart disease (CHD), angina, apoplexy (AP), cancer (CA), or malignancy (MT) were also included.[35]

Drinking status was categorized as “drinking” as > 12 times/year and “non-drinking” as ≤ 12 times/year. When “drinking” is used in the covariates section, it refers to the consumption of alcoholic beverages. This includes liquor (such as whiskey or gin), beer, wine, wine coolers, and any other type of alcoholic beverage. Smoking status was categorized as “non-smoking” as lifetime smoking ≤ 100 cigarettes and “smoking” as lifetime smoking > 100 cigarettes.[36]

Hypertension diagnosis was based on any of the following criteria:[13] (1) a confirmed clinical diagnosis of hypertension, (2) an average of three separate measurements of systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or (3) current use of anti-hypertensive medications.

Diabetes Mellitus (DM) was based on any of the following criteria:13 (1) the participant confirmed a diagnosis of DM, (2) hemoglobin levels were more than 6.5%, (3) fasting blood glucose levels ≥ 7.0 mmol/L, (4) random blood glucose levels ≥ 11.1 mmol/L, (5) 2-h post-oral glucose tolerance test levels ≥ 11.1 mmol/L, or (6) the individual was taking insulin or other diabetes medications.

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Participants were considered to have HF, CHD, angina, AP, CA, or MT if they reported a history of these conditions and had been previously diagnosed by a physician.[23]

Statistical analysis

In the analysis of the NHANES database, we used the fasting subsample weight provided by NHANES (WTSAF2YR) and the design variables listed in the demographic variables in all models. We utilized the fasting subsample weight provided by NHANES (WTSAF2YR), as lipid variables were part of the subsample component of the survey. Please refer to the content of the NHANES database catalog under the Tutorial - Weighting Module, see the URL https://wwwn.cdc.gov/nchs/nhanes/tutorials/weighting.aspx. The normality test introduced bias into the data used in this study. As a result, continuous variables are reported as medians and interquartile ranges, expressed as M (P25, P75), due to the skewed distribution. Categorical data are presented as both frequencies and percentages. Using the Chi-square testing and Mann–Whitney U testing, we compared the baseline characteristics of patients with dyslipidemia and non-dyslipidemia and the distribution of the DII and blood inflammatory markers were compared. Weighted multifactor linear regression was employed to assess the association between the DII and blood inflammation markers (N, L, M, P, NLR, PLR, NAR, SII, and SIRI) within individuals with dyslipidemia. Weighted multivariate logistic regression was employed to analyze DII, SII, and SIRI as continuous variables, which were then grouped by quartile as categorical variables to determine their impact on epidemically associated dependent variables. The influence of the grouping variables on dyslipidemia was further assessed for trends. Model 1 was the unadjusted coarse model; Model 2 was adjusted for age, sex, and race; Model 3 was based on Model 2 but additionally adjusted for BMI, marital status, education level, smoking, drinking, hypertension, DM, HF, CHD, angina, AP, CA, or MT. The assessment used a multifactorial logistic regression approach to examine the interaction between the DII and various blood inflammation markers as independent variables and their relationship with abnormal lipid levels as the dependent outcome. A Restricted Cubic Spline assessment with four knots was used to evaluate the non-linear association between dyslipidemia risk and the DII, SII, and SIRI. Statistical analyses were performed using IBM SPSS Statistics Version 26.0 and Stata 17.0, with a significance threshold of $p < 0.05$ set for all statistical analyses.

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RESULTS

General characteristics, DII, and blood inflammatory indices

Among the 9,441 participants from the NHANES database (2009–2018), 6,689 individuals (70.9%) were identified with dyslipidemia. The median participant age was 50 years, with males constituting 49.0% (4,629) and non-Hispanic whites 43.7% (4,125) of the sample. Participants with dyslipidemia were significantly older, had lower educational levels, and exhibited higher rates of comorbidities such as DM, hypertension, and CHD (all $p < 0.001$, Table 1).

Table 2 displays the participants' comprehensive baseline dietary intake and blood inflammation markers, grouped according to their lipid profiles. Individuals with dyslipidemia exhibited significantly higher DII compared to those without dyslipidemia (1.2 (-0.4, 2.6) vs. 1.0 (-0.6, 2.4)), SII (440 (317, 626) vs. 409 (290, 590)), SIRI (1.0 (0.7, 1.5) vs. 0.9 (0.6, 1.4)), hs-CRP, and blood pressure (all $p < 0.001$).

DII and blood inflammation markers in individuals with dyslipidemia

DII was positively correlated with most inflammatory markers, except for NLR and PLR, where no significant association was observed. DII was positively correlated with WBC, L, M, N, P, NAR, SII, and SIRI in individuals with dyslipidemia (all $p < 0.05$). (Table 3)

Logistic regression of DII, SII, SIRI, and dyslipidemia

Higher DII, SII, and SIRI levels were associated with an increased risk of dyslipidemia. Notably, DII remained significant across all models, while SII showed a strong association in the unadjusted and partially adjusted models. (Table 4)

Higher DII scores were associated with increased dyslipidemia risk, as evidenced by a significant odds ratio (OR) in all models (Model 3: OR = 1.05; 95% CI: 1.02–1.09; all $p < 0.05$). When participants were divided into DII quartiles, individuals in the fourth quartiles had a higher risk of developing dyslipidemia than those in the first quartile (ORQ4: 1.33; 95% CI: 1.10–1.62; all $p < 0.001$). SII demonstrated a weak association in the unadjusted and partially adjusted models but showed no significant correlation in the fully adjusted models. SIRI was only associated with the unadjusted model and exhibited no significant correlation in the fully adjusted model. (Table 4)

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Individual effects of blood inflammatory markers on lipid status

Table 5 presents the ORs and 95% CIs for the individual effects of blood inflammatory markers on lipid status. The results show that WBC, L, N, P, NLR, PLR, and NAR are significantly associated with lipid status, whereas M is not.

DII and various blood inflammatory markers

Multivariate logistic regression was employed to evaluate the impact of various blood inflammation markers (SII, SIRI, WBC, L, M, N, NLR, PLT, PLR, and NAR) on dyslipidemia after their combination with DII, as shown in Table 6. DII combined with all blood inflammatory indices was associated with an increased risk of dyslipidemia (all OR > 1.0, $p < 0.05$). Specifically, WBC (OR = 1.10, $p < 0.001$), L (OR = 1.47, $p < 0.001$), and N (OR = 1.07, $p = 0.003$) showed significant positive correlations with dyslipidemia risk. However, M, SIRI, and SII were not significantly associated with dyslipidemia ($p > 0.05$).

Dyslipidemia risk and RCS assessment

A non-linear association was observed between SII and dyslipidemia risk, particularly when SII exceeded 434.65. However, SIRI showed no significant association beyond a value of 6.02 (Figure 2).

DISCUSSION

This study examined the association between inflammation and dyslipidemia from two perspectives: DII and blood inflammatory markers. It further explored the relationship between these two inflammatory indicators.

Peripheral cell counts and inflammatory markers based on peripheral cells, such as WBC, L, M, N, P, NLR, and NAR, were more significant in individuals with dyslipidemia than those without. Systemic inflammation is typically characterized by lymphocytopenia and neutrophilia.[37] NLR and PLR are indicators of systemic inflammatory responses.[38] The peripheral WBC count is commonly used as a marker of inflammation, which is accompanied by elevated LDL-C levels in patients with an increased cardiovascular risk.[39] Coutinho et al. identified a correlation involving increased white blood cell counts and diminished HDL values.[40] Nevertheless, the relationship between WBCs and lipid levels varies according to age, sex, and the WBC subpopulation. This study found that blood inflammatory markers, including CRP and hs-CRP levels, significantly increased in individuals with dyslipidemia contrasted to those without the condition.[41-43] Elevated CRP and hs-CRP levels signify low-

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grade systemic inflammation, a condition characterized by sustained activation of inflammatory pathways leading to metabolic abnormalities, highlighting the role of local and systemic proinflammatory biomarkers in both human as well as animal models.[44] We excluded CRP/hs-CRP from the main models due to their limited availability in the NHANES dataset (2009-2018). Given the short time span and limited data points for these markers, their inclusion would have restricted the analysis to a smaller subset of participants and potentially introduced selection bias. Moreover, the inconsistent availability across cycles would have made it challenging to draw robust and generalizable conclusions. Other researchers utilizing the NHANES database to study inflammation and diseases also excluded CRP/hs-CRP. For instance, Walzik D et al. shows that NLR and PLR are significantly associated with inflammatory conditions.[45] These studies demonstrate that meaningful insights can be obtained using alternative inflammatory markers. However, we acknowledge that the exclusion of CRP/hs-CRP might have influenced our findings. Future research with more comprehensive CRP/hs-CRP data could further validate and build on our findings. Research has shown that the imbalance of lipid metabolism accelerates the inflammatory response.[46, 47] Apolipoprotein activates immune cells in local arteries and throughout the body to induce various proinflammatory pathways. LDL-C can enhance lipid-induced endothelial dysfunction, which is accompanied by the activation of circulating monocytes. Moreover, the propagation of the low-grade inflammatory response is primarily induced by LDL-C.[48]

Moreover, SII and SIRI values were notably elevated in individuals with dyslipidemia compared to those without, indicating an increased inflammation level. Recently, new biomarkers, including WBC subsets, SII, and SIRI, have emerged to describe the balance between inflammation and the immune response.[49] Dyslipidemia is closely related to the inflammatory response, and SII can comprehensively integrate various inflammatory indicators and, more precisely, show the level of inflammation within the body.[34, 50, 51] Employing a two-phase linear regression model showed a non-linear association between SII and hyperlipidemia, corroborating the findings of this study.

The non-linear association suggests that the relationship between the SII and hyperlipidemia varies across the range of SII values. Specifically, at certain levels of SII, the risk of hyperlipidemia may increase more rapidly, while at other levels, the increase in risk may slow down or even reach a plateau. This nonlinearity suggests that the impact of SII on hyperlipidemia risk is more complex than a simple linear relationship. Moreover, this finding underscores the importance of considering the full range of SII values when assessing the risk of hyperlipidemia.[34] The correlation between SIRI and dyslipidemia indicates that SIRI may

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serve as a promising marker for predicting dyslipidemia risk. A retrospective study by Lai et al. involving 148 patients with polycythemia vera demonstrated, through multifactorial analysis, that SIRI is an independent predictor of thrombosis in these patients.[52] This finding is consistent with the results of the unadjusted covariates in this study but inconsistent with the adjusted covariates, possibly because sex, age, BMI, and other factors also affect the status of blood lipids.

The DII score was weakly positively associated with dyslipidemia. Numerous global studies show a close relationship between proinflammatory diets (high DII scores) and lipid metabolic disorders. For instance, studies in Iranian populations reveal a significant link between high dietary inflammation and elevated triglycerides alongside reduced HDL-C.[53] Furthermore, Iran's cohort study demonstrates a significant positive correlation between high DII scores and an increased risk of dyslipidemia.[54] Additionally, a cardiovascular risk study in South Africa shows a significant relationship between high DII scores and poor LDL-C control, implying that dietary westernization due to rapid urbanization in Africa may undermine the metabolic protective effects of traditional diets.[55] Conversely, the more an anti-inflammatory diet reduces systemic inflammatory markers, the better the improvement in dyslipidemia.[56-58] DII was positively correlated with dyslipidemia, possibly due to the influence of certain anti-inflammatory food components (with a negative score) that can lower blood lipids. Research has shown that dietary fiber reduces the absorption and breakdown of lipids, thereby lowering TC and LDL-C levels.[59, 60] Additionally, n-3 fatty acid supplementation can enhance lipoprotein lipase activity, which is recommended as a nutritional intervention in hyperlipidemia, thereby reducing postprandial TG.[61] Cross-sectional research has shown that 25-hydroxyvitamin D is negatively associated with cholesterol and LDL and positively linked with HDL.[61] Furthermore, food components of an anti-inflammatory diet (low DII score) have been shown to may reduce inflammation-associated dyslipidemia risk. International research reviews indicate that anti-inflammatory diets are closely linked to reduced blood lipid levels.[62]

The DII score was positively associated with SII, SIRI, and other peripheral blood count inflammatory indicators in individuals with dyslipidemia, suggesting that a high-inflammatory diet may promote inflammation. Conversely, a low DII score indicated that a diet suppresses inflammation.[63] The SII included components of blood cell counts, which are derived from widely accessible, up-to-date data and are conventional, inexpensive assays that are part of routine clinical practice.[64] DII reflects the body's inflammatory state due to diet, while SII and SIRI are more comprehensive indicators of systemic inflammation. A large

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cohort study conducted in Italy suggested that individuals who consumed a diet rich in antioxidant vitamins and phytochemicals had lower plasma CRP levels. Additionally, such a diet may help reduce P and WBC counts.[65]

The combination analysis showed that DII and specific blood inflammatory markers together increased dyslipidemia risk, but the overall effects were small. This suggests that a proinflammatory diet may indirectly exacerbate lipid metabolism disorders by activating the innate immune system. However, its contribution may be partially offset by other confounding factors, such as obesity or insulin resistance.[66] WBC count, L, and N had the strongest associations, indicating that the body's immune response to an inflammatory diet may play a role in dyslipidemia.[67] This indicates that the immune response to an inflammatory diet may be one of the core mechanisms driving dyslipidemia. However, other markers like SIRI and SII did not show significant associations. This inconsistency may be attributed to the following factors. On the one hand, markers like WBC, N, and L are direct measurements of immune cell counts and may more accurately reflect inflammatory responses caused by dietary components. In contrast, composite indicators such as SII and SIRI, while useful, capture broader aspects of inflammation.[68] On the other hand, neutrophil and lymphocyte-dominated oxidative stress and cytokine release inflammatory pathways may exhibit heightened sensitivity to dietary inflammatory stimuli, thereby playing pivotal roles in early-stage dyslipidemia.[69] These factors suggest that directly measured immune cell counts may offer unique advantages in elucidating the relationship between dietary inflammation and dyslipidemia. While these small effect sizes may seem trivial, they may indicate a potential positive association. There is a possibility that the DII could increase the risk of blood or inflammatory dyslipidemia. We emphasize that even small effect sizes can have significant impacts at the population level, especially considering the widespread prevalence of dietary inflammation and its established links to chronic diseases. When applied to a large population, these small changes in ORs could translate into substantial public health benefits. For instance, in medicine, even a small effect may be clinically important. As Cohen's d effect size interpretation indicates, what may seem like a small difference can be meaningful in certain contexts.[70] In our large-scale population-based cross-sectional study, the small ORs may indicate a potential positive correlation. However, further research in other populations is needed to confirm if this correlation is truly causal. Nonetheless, our findings provide valuable clues for future studies.

The outcomes from both RCS and logistic regression analyses suggest that an increase in the DII and SII values elevates the risk of dyslipidemia, positioning both as risk factors for the

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condition. These results indicate that DII and SII are sensitive indices of dyslipidemia, especially DII. Maintaining the DII and the SII within the optimal range may be associated with a good lipid profile. From the perspective of preventing hyperlipidemia and improving dyslipidemia, an anti-inflammatory diet is crucial. Anti-inflammatory food components, such as foods rich in dietary fiber, can be increased within the diet. Moreover, SIRI emerged as a dyslipidemia risk factor within the unadjusted model. However, in the adjusted model, the findings regarding the role of SIRI in dyslipidemia do not entirely align with those of previous studies. Consistent with the results of this study, Jin et al. observed that the relationship between SIRI and dyslipidemia weakened after rigorous adjustment for covariates (OR=0.92, 95% CI: 0.85–1.01).[71] Conversely, Gu et al. reported a positive correlation between SIRI and cardiovascular risk factors, including dyslipidemia.[72] The variability in these research findings underscores the complexity of inflammatory markers and their interactions with metabolic processes. Further research is necessary to elucidate the exact mechanism of SIRI's dual role in dyslipidemia.

This study investigated the relationships between diet, blood inflammatory markers, and dyslipidemia from both dietary and clinical perspectives. The large sample size and careful adjustment for covariates strengthened the reliability and generalizability of the findings. Furthermore, the study revealed non-linear relationships among diet, inflammation, and dyslipidemia through RCS analysis, providing valuable insights for health policymakers. However, the research had certain limitations. The cross-sectional design made it difficult to establish a direct causal link between anti-inflammatory dietary interventions and their effects on low-grade inflammation and dyslipidemia. Future research with larger cohorts and prospective study designs is needed to further explore causality. Additionally, due to database limitations, only 28 nutrients were used to calculate the DII scores. Nevertheless, Shivappa et al. indicated that using no more than 30 nutrients could still be adequate to preserve the DII's predictive value for diet-related inflammation.[28]

Conclusion

This research found that while the DII and blood inflammation markers exhibited positive association with dyslipidemia, the effect sizes were relatively small, and many associations became insignificant after adjusting for other health factors. This suggests dietary inflammation might contribute to dyslipidemia, but it is likely eclipsed by factors such as obesity, DM, and hypertension. Nonetheless, these findings still provide valuable insights for public health policymakers in developing evidence-based strategies to prevent dyslipidemia

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and may reduce inflammation - associated dyslipidemia risk. The clinical significance of this study is to reduce inflammation in the body by adjusting diet and provide a scientific basis for the prevention and management of dyslipidemia.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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Table 1. Baseline demographic and clinical characteristics of participants stratified by dyslipidemia status, M (P25, P75)

Variable	Total (n = 9441)	Non-Dyslipidemia (n = 2752)	Dyslipidemia (n = 6689)	Z/χ^2	*p*
Age, years	50.0 (34.0, 64.0)	39.0 (27.0, 55.0)	54.0 (39.0, 66.0)	25.9	<0.001*
Sex, n (%)				3.1	0.080
Male	4629 (49.0)	1388 (50.4)	3241 (48.5)		
Female	4812 (51.0)	1364 (49.6)	3448 (51.6)		
Race, n (%)				56.7	<0.001*
Mexican American	1341 (14.2)	368 (13.4)	973 (14.6)		
Other Hispanic	955 (10.1)	242 (8.8)	713 (10.7)		
Non-Hispanic white	4125 (43.7)	1109 (40.3)	3016 (45.1)		
Non-Hispanic black	1857 (19.7)	644 (23.4)	1213 (18.1)		
Other race or multi-racial	1163 (12.3)	389 (14.1)	774 (11.6)		
BMI, kg/m^2	28.1 (24.3, 32.8)	25.9 (22.5, 30.4)	28.9 (25.3, 33.6)	21.4	<0.001*
BMI, kg/m^2, n (%)				475.0	<0.001*
<18.5	145 (1.5)	92 (3.3)	53 (0.8)		
18.5-25.0	2577 (27.3)	1113 (40.4)	1464 (21.9)		
25.0-30.0	3082 (32.6)	802 (29.1)	2280 (34.1)		
≥30.0	3637 (38.5)	745 (27.1)	2892 (43.2)		
Marital status, n (%)				269.0	<0.001*
Get married/live with a partner	5688 (60.3)	1531 (55.6)	4157 (62.2)		
Widowed/divorced/separated	2027 (21.5)	447 (16.2)	1580 (23.6)		
Never married	1726 (18.3)	774 (28.1)	952 (14.2)		
Education, n (%)				51.8	<0.001*
Less than 9th grade	769 (8.2)	176 (6.4)	593 (8.9)		
9–11th grade	1232 (13.1)	313 (11.4)	919 (13.7)		
High school grad/GED or Equivalent	2120 (22.5)	582 (21.2)	1538 (23.0)		
Some college or AA	2922 (31.0)	870 (31.6)	2052 (30.7)		
College graduate or above	2398 (25.4)	811 (29.5)	1587 (23.7)		
Ratio of household income to poverty, n (%)				0.5	0.764
≤1.3	2982 (31.6)	884 (32.1)	2098 (31.4)		
1.3-3.5	3595 (38.1)	1037 (37.7)	2558 (38.2)		
>3.5	2864 (30.3)	831 (30.2)	2033 (30.4)		
Drinking, n (%)	7243 (76.7)	2108 (76.6)	5135 (76.8)	0.1	0.860
Smoking, n (%)	4181 (44.3)	1084 (39.4)	3097 (46.3)	37.7	<0.001*
Hypertension, n (%)	3988 (42.2)	735 (26.7)	3253 (48.6)	384.0	<0.001*

Body mass index (BMI), Diabetes mellitus (DM), Heart failure (HF), Coronary heart disease (CHD), Apoplexy (AP), Cancer (CA), Malignancy (MT), High-density lipoprotein cholesterol (HDL-C), Triglycerides (TG), Low-density lipoprotein cholesterol (LDL-C), Total cholesterol (TC), Systolic blood pressure (SBP), Diastolic blood pressure (DBP)..
*$p < 0.05$

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Table 1. Baseline demographic and clinical characteristics of participants stratified by dyslipidemia status, M (P25, P75) (cont.)

Variable	Total (n = 9441)	Non-Dyslipidemia (n = 2752)	Dyslipidemia (n = 6689)	Z/χ^2	*p*
DM, n (%)	1852 (19.6)	280 (10.2)	1572 (23.5)	220.0	<0.001*
HF, n (%)	297 (3.2)	45 (1.6)	252 (3.8)	29.1	<0.001*
CHD, n (%)	397 (4.2)	48 (1.7)	349 (5.2)	58.4	<0.001*
Angina, n (%)	233 (2.5)	27 (1.0)	206 (3.1)	35.7	<0.001*
AP, n (%)	348 (3.7)	53 (1.9)	295 (4.4)	33.9	<0.001*
CA or MT, n (%)	905 (9.6)	172 (6.3)	733 (11.0)	49.9	<0.001*
HDL, mg/dL	52.0 (43.0, 63.0)	57.0 (50.0, 66.0)	48.0 (40.0, 60.0)	26.4	<0.001*
TG, mg/dL	98.0 (68.0, 143.0)	69.0 (51.0, 93.0)	115.0 (81.0, 164.0)	43.4	<0.001*
LDL, mg/dL	110.0 (88.0, 135.0)	95.0 (79.0, 108.0)	121.0 (94.0, 144.0)	37.1	<0.001*
TC, mg/dL	187.0 (161.0, 215.0)	169.0 (153.0, 184.0)	202.0 (169.0, 226.0)	38.3	<0.001*
Uric acid, mg/dL	5.4 (4.5, 6.4)	5.0 (4.2, 6.0)	5.5 (4.6, 6.5)	14.4	<0.001*
SBP, mmHg	120.0 (110.7, 132.7)	116.0 (107.3, 126.7)	122.0 (112.0, 134.7)	15.6	<0.001*
DBP, mmHg	70.0 (62.7, 77.3)	68.7 (62.0, 75.3)	70.7 (63.0, 78.0)	6.4	<0.001*

Body mass index (BMI), Diabetes mellitus (DM), Heart failure (HF), Coronary heart disease (CHD), Apoplexy (AP), Cancer (CA), Malignancy (MT), High-density lipoprotein cholesterol (HDL-C), Triglycerides (TG), Low-density lipoprotein cholesterol (LDL-C), Total cholesterol (TC), Systolic blood pressure (SBP), Diastolic blood pressure (DBP)..
*$p < 0.05$

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Table 2. Comparison of inflammatory markers between patients with and without dyslipidemia, M (P25, P75)

Variable	Total (n = 9441)	Non-dyslipidemia (n = 2752)	Dyslipidemia (n = 6689)	Z	*p*
DII	1.1 (-0.5, 2.5)	1.0 (-0.6, 2.4)	1.2 (-0.4, 2.6)	4.0	<0.001*
SIRI	1.0 (0.6, 1.4)	0.9 (0.6, 1.4)	1.0 (0.7, 1.5)	5.5	<0.001*
SII	431 (310, 618)	409 (290, 590)	440 (317, 626)	6.3	<0.001*
WBC, 10^9/L	6.4 (5.4, 7.8)	6.1 (5.2, 7.4)	6.6 (5.5, 8.0)	10.6	<0.001*
L, 10^9/L	1.9 (1.6, 2.4)	1.9 (1.5, 2.3)	2.0 (1.6, 2.4)	6.8	<0.001*
M, 10^9/L	0.5 (0.4, 0.6)	0.5 (0.4, 0.6)	0.5 (0.4, 0.6)	5.5	<0.001*
N, 10^9/L	3.7 (2.9, 4.7)	3.5 (2.7, 4.5)	3.8 (2.9, 4.8)	9.1	<0.001*
P, 10^9/L	229 (194, 270)	222 (189, 261)	231 (196, 274)	7.2	<0.001*
NLR	1.9 (1.4, 2.6)	1.9 (1.4, 2.5)	1.9 (1.4, 2.6)	3.4	<0.001*
PLR	119 (94.3, 148)	120 (95.6, 148)	118 (93.9, 149)	0.8	0.416
NAR	0.9 (0.7, 1.1)	0.8 (0.6, 1.1)	0.9 (0.7, 1.2)	9.9	<0.001*
CRP, mg/dL	0.2 (0.10, 0.4)	0.1 (0.1, 0.4)	0.2 (0.1, 0.5)	7.1	<0.001*
hs-CRP, mg/L	2.0 (0.8, 4.9)	1.3 (0.5, 3.7)	2.3 (1.0, 5.3)	7.4	<0.001*

Dietary inflammatory index (DII), Systemic inflammation response index (SIRI), Systemic immune-inflammation index (SII), White blood cell (WBC), Lymphocyte (L), Monocyte (M), Neutrophil (N), Platelet (P), Neutrophil lymphocyte ratio (NLR), Platelet lymphocyte ratio (PLR), Neutrophil albumin ratio (NAR), High-sensitivity C-reactive protein (hs-CRP), C-reactive protein (CRP).
*p < 0.05

Table 3. Weighted linear regression analysis of the relationship between DII and blood inflammatory markers in patients with dyslipidemia

Variable	β	95% CI	*p*
SII†	5.71	(1.14, 10.32)	0.014*
SIRI†	0.02	(0.00, 0.03) ‡	<0.001*
WBC†	0.08	(0.05, 0.11)	<0.001*
L†	0.02	(0.00, 0.03) §	0.003*
M†	0.00 ¶	(0.00, 0.01) ††	<0.001*
N†	0.05	(0.03, 0.08)	<0.001*
P†	1.51	(0.55, 2.48)	0.002*
NLR†	0.00 ‡‡	(-0.01, 0.02)	0.418
PLR†	-0.24	(-0.96, 0.48)	0.509
NAR†	7.57	(4.01, 11.13)	<0.001*

Systemic inflammation response index (SIRI), Systemic immune-inflammation index (SII), White blood cell (WBC), Lymphocyte (L), Monocyte (M), Neutrophil (N), Platelet (P), Neutrophil lymphocyte ratio (NLR), Platelet lymphocyte ratio (PLR), Neutrophil albumin ratio (NAR).
†Data were all adjusted by age, sex, race, BMI, marital status, education level, smoking, drinking, hypertension, DM, HF, CHD, angina, AP, CA or MT.
‡(0.00232, 0.03054)
§(0.00653, 0.03091)
¶0.00571
†† (0.00254, 0.00888)
‡‡0.00716.
*p < 0.05

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Table 4. Weighted logistic regression analysis of DII, SII, SIRI, and the risk of dyslipidemia

	Model1[†]		Model2[‡]		Model3[§]	
	OR (95% CI)	*p trend*	OR (95% CI)	*p trend*	OR (95% CI)	*p trend*
DII	1.05 (1.02, 1.08)		1.09 (1.05, 1.12)		1.05 (1.02, 1.09)	
Q1	Reference	0.001*	Reference	0.001*	Reference	0.001*
Q2	1.15 (0.98, 1.36)		1.24 (1.04, 1.48)		1.14 (0.95, 1.36)	
Q3	1.25 (1.06, 1.48)		1.43 (1.21, 1.71)		1.29 (1.07, 1.55)	
Q4	1.31 (1.10, 1.56)		1.54 (1.28, 1.84)		1.33 (1.10, 1.62)	
SII	1.00 (1.00, 1.00) ¶		1.00 (1.00, 1.00) ††		1.00 (1.00, 1.00) ‡‡	
Q1	Reference	<0.001*	Reference	<0.001*	Reference	<0.001*
Q2	1.32 (1.11, 1.56)		1.26 (1.06, 1.51)		1.20 (1.00, 1.44)	
Q3	1.57 (1.33, 1.86)		1.44 (1.20, 1.72)		1.28 (1.06, 1.53)	
Q4	1.66 (1.39, 1.97)		1.44 (1.20,1.73)		1.13 (0.94, 1.37)	
SIRI	1.19 (1.09, 1.30)		1.05 (0.97, 1.14)		0.95 (0.88, 1.02)	
Q1	Reference	<0.001*	Reference	<0.001*	Reference	<0.001*
Q2	1.03 (0.87, 1.22)		1.00 (0.84, 1.19)		0.92 (0.77, 1.10)	
Q3	1.39 (1.17, 1.65)		1.23 (1.03, 1.47)		1.06 (0.88, 1.27)	
Q4	1.61 (1.36, 1.92)		1.27 (1.05, 1.53)		0.97 (0.80, 1.18)	

DII: XXXX; SII: XXXX; SIRI: XXXX.
†Model 1 unadjusted.
‡Model 2 adjusted for age, sex, and race.
§Model 3 adjusted for age, sex, race, BMI, marital status, education level, smoking, drinking, hypertension, DM, HF, CHD, angina, AP, CA or MT.
¶1.00064 (1.00040,1.00087); ††1.00043 (1.00019, 1.00068); ‡‡1.00011 (0.99988, 1.00034)..
*p < 0.05

Table 5. Individual effects of blood inflammatory markers on lipid status

Variable	OR (95% CI)	*p*
WBC effects[†]	1.08 (1.05, 1.11)	0.001*
L effects†[†]	1.47 (1.35, 1.59)	<0.001*
M effects[†]	1.08 (0.83, 1.40)	0.579
N effects[†]	1.04 (1.01, 1.08)	0.008*
P effects[†]	1.00 (1.00, 1.00) ‡	<0.001*
NLR effects[†]	0.92 (0.88, 0.96)	<0.001*
PLR effects[†]	1.00 (1.00, 1.00) §	0.038*
NAR effects[†]	1.14 (1.01, 1.29)	0.038*

Dietary inflammatory index (DII), Systemic inflammation response index (SIRI), Systemic immune-inflammation index (SII), White blood cell (WBC), Lymphocyte (L), Monocyte (M), Neutrophil (N), Platelet (P), Neutrophil lymphocyte ratio (NLR), Platelet lymphocyte ratio (PLR), Neutrophil albumin ratio (NAR). Change format to → DII: dietary inflammatory index; SIRI: systemic inflammation response index; xxxxx
[†]The data were adjusted for age, sex, race, BMI, marital status, education level, smoking, drinking, hypertension, DM, HF, CHD, angina, AP, CA or MT.
[‡]1.00358 (1.00272, 1.00444); §0.99896 (0.99798, 0.99994)
*p < 0.05

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Table 6. Combined effects of DII and blood inflammatory markers on lipid status

Combination	OR (95% CI)	*p*
Combination1[†]		
DII effects	1.05 (1.02, 1.09)	0.003[*]
SII effects	1.00 (1.00, 1.00) [‡]	0.431
Combination2[†]		
DII effects	1.05 (1.02, 1.09)	0.002[*]
SIRI effects	0.94 (0.87, 1.01)	0.111
Combination3[†]		
DII effects	1.05 (1.01, 1.08)	0.009[*]
WBC effects	1.10 (1.06, 1.14)	<0.001[*]
Combination4[†]		
DII effects	1.05 (1.01, 1.08)	0.006[*]
L effects	1.47 (1.31, 1.65)	<0.001[*]
Combination5[†]		
DII effects	1.05(1.02, 1.09)	0.003[*]
M effects	1.34 (0.94, 1.92)	0.107
Combination6[†]		
DII effects	1.05 (1.01, 1.09)	0.005[*]
N effects	1.07 (1.02, 1.12)	0.003[*]
Combination7[†]		
DII effects	1.05 (1.01, 1.08)	0.006[*]
P effects	1.00 (1.00, 1.00) [§]	<0.001[*]
Combination8[†]		
DII effects	1.05 (1.02, 1.09)	0.002[*]
NLR effects	0.93 (0.88, 0.98)	0.007[*]
Combination9[†]		
DII effects	1.05 (1.02, 1.09)	0.002[*]
PLR effects	1.00 (1.00, 1.00) [¶]	0.152
Combination10[†]		
DII effects	1.05 (1.02, 1.09)	0.004[*]
NAR effects	1.00 (1.00, 1.00)[††]	0.036[*]

Dietary inflammatory index (DII), Systemic inflammation response index (SIRI), Systemic immune inflammation index (SII), White blood cell (WBC), Lymphocyte (L), Monocyte (M), Neutrophil (N), Platelet (P), Neutrophil lymphocyte ratio (NLR), Platelet lymphocyte ratio (PLR), Neutrophil albumin ratio (NAR). Change format to → DII: dietary inflammatory index; SIRI: systemic inflammation response index; xxxxx

[†]The data were adjusted for age, sex, race, BMI, marital status, education level, smoking, drinking, hypertension, DM, HF, CHD, angina, AP, CA or MT.

Models 1-10 show the effects of DII and WBC, N, M, L, P, NLR, PLR, NAR, SII, and SIRI on dyslipidemia, respectively.

[‡]1.00009 (0.99986, 1.00032); §1.00410 (1.00290, 1.00529); ¶0.99900 (0.99764, 1.00036); ††1.00033 (1.00002, 1.00064)

*p < 0.05

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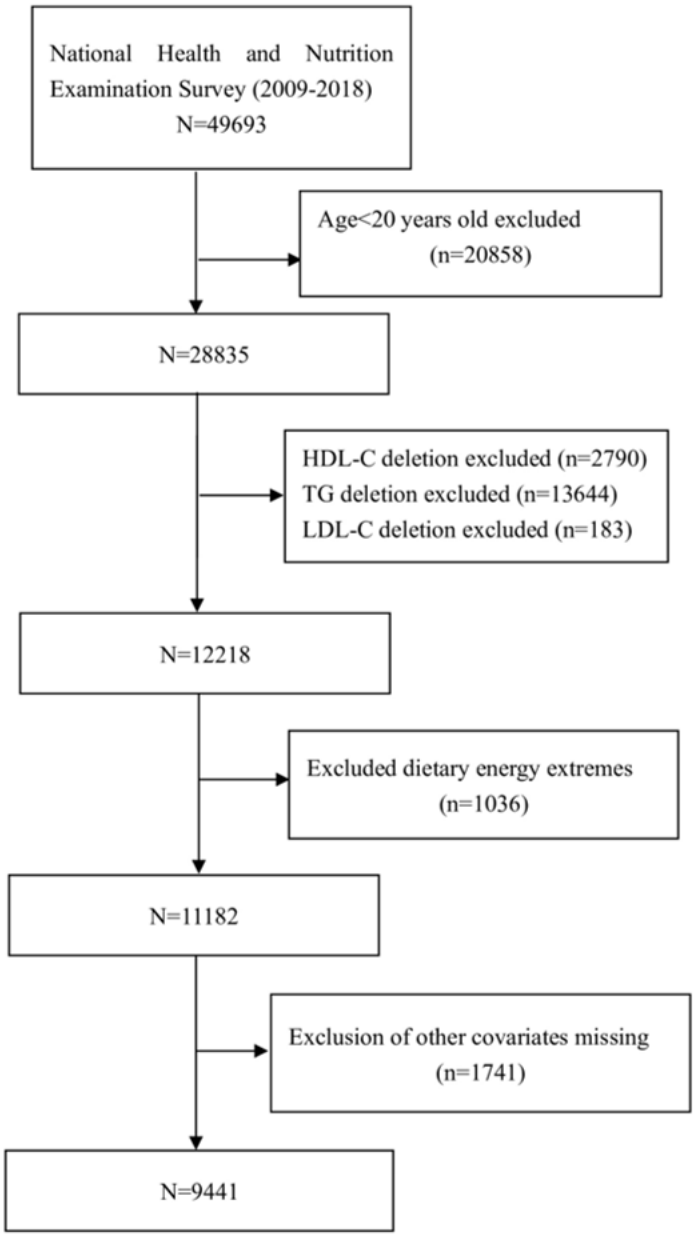

Figure 1. Participant selection process flowchart

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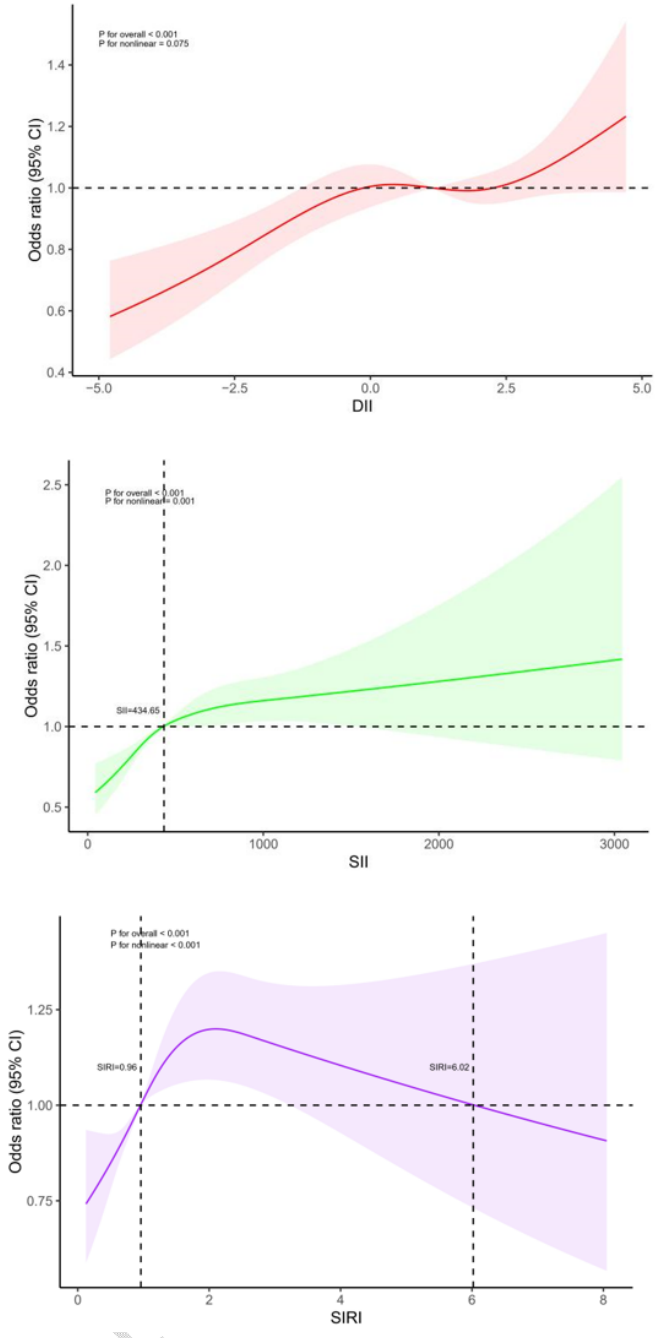

Figure 2. RCS analysis of DII, SII and SIRI and the risk of dyslipidemia. Critical inflection points represent inflammatory thresholds

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Supplementary Table 1. Complete list of food parameters

Number	Food parameter
1	Alcohol (g)†
2	Vitamin B-12 (μg)†
3	Vitamin B-6 (mg)†
4	β -Carotene (μg)†
5	Caffeine (g)†
6	Carbohydrate (g)†
7	Cholesterol (mg)†
8	Energy (kcal)†
9	Total fat (g)†
10	Fibre (g)†
11	Folic acid (μg)†
12	Fe (mg)†
13	Mg (mg)†
14	MUFA (g)†
15	Niacin (mg)†
16	n-3 Fatty acids (g)†
17	n-6 Fatty acids (g)†
18	Protein (g)†
19	PUFA (g)†
20	Riboflavin (mg)†
21	Saturated fat (g)†
22	Se (μg)†
23	Thiamin (mg)†
24	Vitamin A (RE)†
25	Vitamin C (mg)†
26	Vitamin D (μg)†
27	Vitamin E (mg)†
28	Zn (mg)†
29	Eugenol (mg)
30	Garlic (g)
31	Ginger (g)
32	Onion (g)
33	Saffron (g)
34	Trans fat (g)
35	Turmeric (mg)
36	Green/black tea (g)
37	Flavan-3-ol (mg)
38	Flavones (mg)
39	Flavonols (mg)
40	Flavonones (mg)
41	Anthocyanidins (mg)
42	Isoflavones (mg)
43	Pepper (g)
44	Thyme/oregano (mg)
45	Rosemary (mg)

†food parameters used in this study

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