Nutrition, Metabolism & Cardiovascular Diseases (xxxx) xxx, xxx

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

RESEARCH PAPER

Association of a dietary inflammatory index with cardiometabolic, endocrine, liver, renal and bones biomarkers: cross-sectional analysis of the UK Biobank study

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Received 8 November 2023; received in revised form 4 March 2024; accepted 7 March 2024
Handling Editor: S Stranges
Available online ■ ■ ■

KEYWORDS
Diet inflammatory index;
Biomarkers;
Diet

Abstract *Background and aims:* Research into the relationship between an Energy-adjusted Diet-Inflammatory Index (E-DII) and a wider health-related biomarkers profile is limited. Much of the existing evidence centers on traditional metabolic biomarkers in populations with chronic diseases, with scarce data on healthy individuals. Thus, this study aims to investigate the association between an E-DII score and 30 biomarkers spanning metabolic health, endocrine, bone health, liver function, cardiovascular, and renal functions, in healthy individuals.
Methods and results: 66,978 healthy UK Biobank participants, the overall mean age was 55.3 (7.9) years were included in this cross-sectional study. E-DII scores, based on 18 food parameters, were categorised as anti-inflammatory (E-DII $<$ -1), neutral (-1 to 1), and pro-inflammatory (>1). Regression analyses, adjusted for confounding factors, were conducted to investigate the association of 30 biomarkers with E-DII. Compared to those with an anti-inflammatory diet, individuals with a pro-inflammatory diet had increased levels of 16 biomarkers, including six cardiometabolic, five liver, and four renal markers. The concentration difference ranged from 0.27 SD for creatinine to 0.03 SD for total cholesterol. Conversely, those on a pro-inflammatory diet had decreased concentrations in six biomarkers, including two for endocrine and cardiometabolic. The association range varied from -0.04 for IGF-1 to -0.23 for SHBG.

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https://doi.org/10.1016/j.numecd.2024.03.010

Conclusion: This study highlighted that a pro-inflammatory diet was associated with an adverse profile of biomarkers linked to cardiometabolic health, endocrine, liver function, and renal health.

1. Introduction

Poor diet has been associated with increased risk and premature mortality of many chronic diseases [1]. In fact, over 11 million deaths worldwide are attributable to not meeting healthy dietary recommendations [1]. Despite the substantial evidence supporting associations between different dietary patterns and health outcomes, the exact mechanisms linking diet and health are complex and the mechanisms underlying these associations are poorly understood. Inflammation has been proposed as the substrate for key mechanistic drivers linking diet with multiple non-communicable diseases [2].

Although the anti- and pro-inflammatory properties of different food items and nutrients are well known, investigating single foods or nutrients with health provides only a partial understanding of the role of the inflammatory potential of diet on intermediate and long-term health outcomes [3]. The Dietary Inflammatory Index (DII®) was developed to assess the overall inflammatory potential of whole diets on a continuum from anti-to pro-inflammatory. Evidencing that DII and energy-adjusted DII (E-DII™) are strongly associated with indicators of systemic inflammation [4–7] and with risk of multiple chronic, inflammation-related conditions, including cardiovascular disease (CVD) and cancer [8–10]. In a recent meta-analysis, individuals with the highest DII scores had a 36% increased risk of CVD incidence and mortality, relative to those with the lowest DII scores [11].

Despite the well-known association between inflammatory biomarkers [4–7] and inflammation-related to chronic diseases [11,12], the association between a DII and intermediate biomarkers of cardiometabolic health has been less explored. Several, but not all, studies have shown that higher DII is associated with higher blood pressure, abnormal lipid profile [13,14] and with poorer glycaemic control [15]. However, most of this evidence has been derived from small-scale studies and in populations with existing multimorbidity which introduces a potential for reverse causation bias [13–15]. There is also limited evidence for other biomarkers related to bone health, liver disease, and cancer [16–18]. Therefore, the purpose of this study is to assess the specific benefits on the levels of 30 biomarkers linked to metabolic, endocrine, bone, liver, cardiovascular and renal health in healthy participants enrolled in the UK Biobank study, by comparing the effects of an anti-inflammatory diet versus a pro-inflammatory diet.

2. Methods

Out of 502,535 participants recruited in UK Biobank between 2006 and 2010, 329,036 were excluded due to having existing chronic illness at baseline (Supplementary Table 1). A total of 66,978 participants with available data for biomarkers, dietary exposure and covariates were included in this study (Supplemental Figure 1). Participants (aged 37–73 years) were enrolled across 22 assessment centers from England, Wales, and Scotland. All participants gave informed written consent to data collection which included physical measurements, biological samples and, a touch-screen questionnaire. A complete detailed description of the protocol and baseline assessments is available (https://www.ukbiobank.ac.uk/).

2.1. Diet inflammatory index (DII) and energy-adjusted DII (E-DII)

The Oxford WebQ questionnaire (WebQ), which queried 206 foods and 32 beverages consumed during the past 24 h (h), was used to collect dietary information. Nutrient intake was calculated using McCance and Widdowson's Composition of Foods Tables [19]. Results from a validation study showed that the mean Spearman correlation coefficient between the Oxford WebQ and interviewer-administered 24 h dietary recall for 21 nutrients was $\approx$0.6, with the majority ranging from 0.5 to 0.9 [20].

DII scores were calculated based on the mean of the available Oxford WebQ dietary data using the methodology described elsewhere [21]. To account for differences in total energy intake, the energy-adjusted DII (E-DII™) was estimated. The rationale and description of E-DII methodology were published in 2019 [2,22]. In about -two-thirds of studies, the E-DII has better predictive ability than DII. 18 of the possible 45 food parameters were used for DII calculation in UK Biobank and data on 17 food parameters for calculation of E-DII (as energy was in the denominator) was finally used as described elsewhere [23]. E-DII score was used as a continuous variable and classified into three categories following a previous study (Ref Michael) - from anti-inflammatory (scores down to − 4.39) to pro-inflammatory (scores up to 3.45): i) anti-inflammatory ($<$-1); ii) neutral ($\geq$-1 to $\leq$ 1); and iii) pro-inflammatory ($>$1).

2.2. Biomarkers

Thirty biomarkers were determined in blood and urine samples collected in non-fasted condition at baseline [24].

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The biomarkers included were C-reactive protein (CRP), calcium, phosphate, vitamin D, alkaline phosphatase (ALP), albumin, total protein, total bilirubin, direct bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT), cholesterol, low-density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, apolipoprotein A (apoA), apolipoprotein B (apoB) lipoprotein A, urea, creatinine, cystatin C, urate, haemoglobin A1c (HbA1c), glucose, testosterone, oestradiol, sex hormone-binding globulin (SHBG), IGF-1 and rheumatoid factor. A summary of the biomarkers and their links to health can be found in Supplementary Table 2.

2.3. Covariates

Age was calculated from the date of birth and the date of baseline assessment. Ethnicity was self-reported and categorised as White, south Asian, Black, Chinese and mixed or other ethnic backgrounds. The Townsend deprivation index score is constructed using data pertaining to unemployment rates, car ownership, household overcrowding, and owner occupation, all aggregated at the geographic level of postcode area. Each study participant was allocated a Townsend score based on their residential address at the time of recruitment, with calculations based on the preceding national census data from 2001. A higher Townsend score signifies a heightened degree of socioeconomic deprivation. Smoking status, assessed at baseline was categorised as never, former, or current smoker. Alcohol categorised as risk (>14 unit/week) or no risk (<14 unit/week). We assessed physical activity levels through self-report using the validated International Physical Activity Questionnaire, which estimates the total metabolic equivalent of task (MET) per week. These activity levels were categorised as inactive, moderately active, and active.

2.4. Patients' involvement

No patients were involved in the conception of the research question or in the choice of outcome measures. They were not involved in the design or implementation of the study. No patients were asked to share suggestions on interpreting the finding or in drafting this manuscript.

2.5. Ethics approval

The UK Biobank study was approved by the North West Multi-Centre Research Ethics Committee (NHS National Research Ethics Service 16/NW/0274). Participants provided written informed consent for data collection, data analysis, and record linkage. This study is part of UK Biobank project 7155.

2.6. Statistical analyses

Descriptive characteristics were classified by sex and E-DII category. Numerical variables were presented as means with standard deviation and categorical variables as percentage.

Biomarker values are presented in their traditional units of measurement as well as z-score (per standard deviation, SD). Using standardized units allows for easier comparisons of the magnitude of associations of each biomarker with the E-DII score.

The associations between each biomarker, expressed as z-score and as their traditional units, and the E-DII categories (pro, neutral and anti-inflammatory) were obtained through linear regression analysis. The results were presented as regression coefficients with their respective 95% confidence intervals (CI). In the analyses, adjustments were made for age, sex, ethnicity, deprivation, smoking, alcohol consumption, physical activity, and BMI. When evaluating testosterone and oestradiol as outcomes, that the analyses were restricted exclusively to men and women, respectively. The interaction between covariates and the E-DII score was evaluated by incorporating a multiplicative interaction term between each covariate and the E-DII into the regression model. Our analysis did not reveal any significant interactions; hence, the results were not further stratified based on the covariates.

Data were analysed using Stata statistical software, version 14.0. Statistical significance was defined as p-value of <0.0004 after Bonferroni correction for multiple testing.

3. Results

Of the 66,978 participants included in this study, the overall mean age was 55.3 (7.9) years and 53.9% were women. Briefly, participants who reported consuming an anti-inflammatory diet, based on the E-DII score, were slightly older, more likely to be highly educated, physically active and less likely to be obese or a current smoker than their counterparts classified in the pro-inflammatory E-DII (Table 1).

3.1. Renal function

The associations of the standardized biomarkers with categories of the E-DII are presented in Fig. 1. Compared with individuals with an anti-inflammatory diet, those with a pro-inflammatory diet had significative higher concentrations of four renal (creatinine, urate, cystatin C and urea). The difference in biomarker concentration between those with ant- and pro-inflammatory diets ranged from 0.27 SD for creatinine (equivalent to 5.1 μmol/L). Among people with a pro-inflammatory compared with an anti-inflammatory diet, there were significative lower concentrations of one renal biomarker (phosphate).

Biomarkers concentration among people with an anti-inflammatory diet compared with those in people with a neutral E-DII are shown in Fig. 2. Individuals with an anti-inflammatory diet also had significative lower concentrations of four renal biomarkers (creatinine, urate, urea and cystatin C). The lowest concentration was observed for creatinine (−0.15 SD, equivalent to −2.95 μmol/L) (Fig. 2 and Supplementary Table 3).

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Table 1 Baseline characteristics by E-DII categories

	Total	Anti-inflammatory	Neutral	Pro-inflammatory
Sociodemographic				
Total, n	66,978	20,095	35,128	11,755
E-DII, Mean (SD)	−0.28 ± 1.31	−1.84 ± 0.59	−0.01 ± 0.56	1,57 ± 0.44
E-DII, (Min-Max range)		−4.39; −1.00	−0.99; 0.99	1.00; 3.45
Age (y), mean (SD)	55.3 ± 7.9	54.3 ± 7.7	53.3 ± 7.8	52.2 ± 7.8
Sex, n (%)				
Women	36,126 (53.9)	12,937 (64.4)	18,135 (51.6)	5054 (43.0)
Men	30,852 (46.1)	7158 (35.6)	16,993 (48.4)	6701 (57.0)
Education Qualifications, n (%)				
College or University	37,073 (55.4)	11,530 (57.4)	19,773 (56.3)	5770 (49.1)
A levels/AS levels or eq.	9807 (14.6)	2947 (14.7)	5078 (14.5)	1782 (15.2)
0 levels/GCSEs or eq.	13,678 (20.4)	3951 (19.6)	7054 (20.1)	2667 (22.7)
SEs/NVQ, HND or HNC	6426 (9.6)	1667 (8.3)	3223 (9.2)	1536 (13.1)
Ethnicity, n (%)				
White	63,947 (95.5)	19,196 (95.5)	33,647 (95.7)	11,104 (94.4)
Mixed	445 (0.6)	122 (0.61)	224 (0.64)	99 (0.84)
South Asian	944 (1.4)	295 (1.47)	468 (1.33)	181 (1.54)
Black	864 (1.3)	238 (1.18)	398 (1.13)	228 (1.94)
Chinese	258 (0.4)	69 (0.34)	145 (0.41)	44 (0.37)
Others	520 (0.8)	175 (0.87)	246 (0.70)	99 (0.84)
Townsend Deprivation index, n (%)				
Lower deprivation	14,697 (21.9)	4470 (22.2)	7791 (22.1)	2436 (20.7)
Middle Lower deprivation	14,096 (21.0)	4395 (21.8)	7377 (21.0)	2324 (19.7)
Middle deprivation	13,882 (20.7)	4139 (20.6)	7370 (20.9)	2373 (20.2)
Middle higher deprivation	13,711 (20.5)	4091 (20.4)	7130 (20.3)	2490 (21.2)
Higher deprivation	10,592 (15.8)	3000 (14.9)	5460 (15.5)	2132 (18.1)
Anthropometric				
BMI ($kg.m^{-2}$), mean (SD)	25.8 ± 3.9	25.5 ± 3.9	25.8 ± 3.9	26.5 ± 4.3
BMI category, n (%)				
Underweight	456 (0.68)	185 (0.92)	205 (0.58)	66 (0.56)
Normal	30,350 (45.4)	9965 (46.68)	15,795 (45.03)	4590 (39.14)
Overweight	27,106 (40.5)	7611 (37.9)	14,424 (41.13)	5071 (43.2)
Obese	8947 (13.4)	2298 (11.4)	4649 (13.26)	2000 (17.05)
Fitness and lifestyle				
Smoking status, n (%)				
Current	5346 (8.0)	1131 (5.6)	2746 (7.8)	1469 (12.5)
Previous	20,427 (30.5)	6405 (31.9)	10,650 (30.4)	3372 (28.7)
Never	41,107 (61.5)	12,525 (62.4)	21,681 (61.8)	6901 (58.7)
IPAQ activity group, n (%)				
Inactive	9665 (16.4)	2218 (12.5)	5351 (17.2)	2096 (20.4)
Moderate active	24,978 (42.3)	7326 (41.2)	13,241 (42.7)	4411 (42.9)
Active	24,427 (41.3)	8222 (46.3)	12,434 (40.1)	3771 (36.7)
Alcohol Consumption, mean (SD)	16.2 ± 16.3	14.4 ± 14.2	17.1 ± 16.8	16.4 ± 17.4
Alcohol Intake Category, n (%)				
No risk (<14 unit)	35,916 (56.8)	11,528 (60.7)	18,112 (54.5)	6276 (57.2)
Risk (>14 unit)	27,281 (43.2)	7472 (39.3)	15,123 (45.5)	4686 (42.7)

Data presented as mean and standard deviation for continuous variables and as frequency and % for categorical variables.

Compared with participants with a neutral E-DII diet, those with a pro-inflammatory diet had higher concentrations of four kidney biomarkers (creatinine, cystatin C, urate and urea), Those with a neutral E-DII also had lower concentrations, the biggest concentration differences were for creatinine (0.11 SD, equivalent to 2.2 μmol/L) (Fig. 3 and Supplementary Table 3).

3.2. Cardiovascular function

Compared with individuals with an anti-inflammatory diet those with a pro-inflammatory diet had significative higher concentrations of six cardiometabolic (Total cholesterol, TG, LDL, apolipoprotein B, HbA1c and CRP), The difference in biomarker concentration between those with ant- and pro-inflammatory diets ranged from 0.27 SD for creatinine (equivalent to 5.1 μmol/L) to 0.03 SD for total cholesterol (equivalent to 0.035 mmol/L). Among people with a pro-inflammatory compared with an anti-inflammatory diet, there were significative lower concentrations of two bio cardiometabolic markers (apolipoprotein A and HDL).

Biomarkers concentration among people with an anti-inflammatory diet compared with those in people with a neutral E-DII are shown in Fig. 2. Two biomarkers showed a significative higher concentration (HDL and apolipoprotein A). Individuals with an anti-inflammatory diet also had significative lower concentrations of thirteen biomarkers, including five cardiometabolic biomarkers (TG, LDL cholesterol, apolipoprotein B, HbA1c and CRP),

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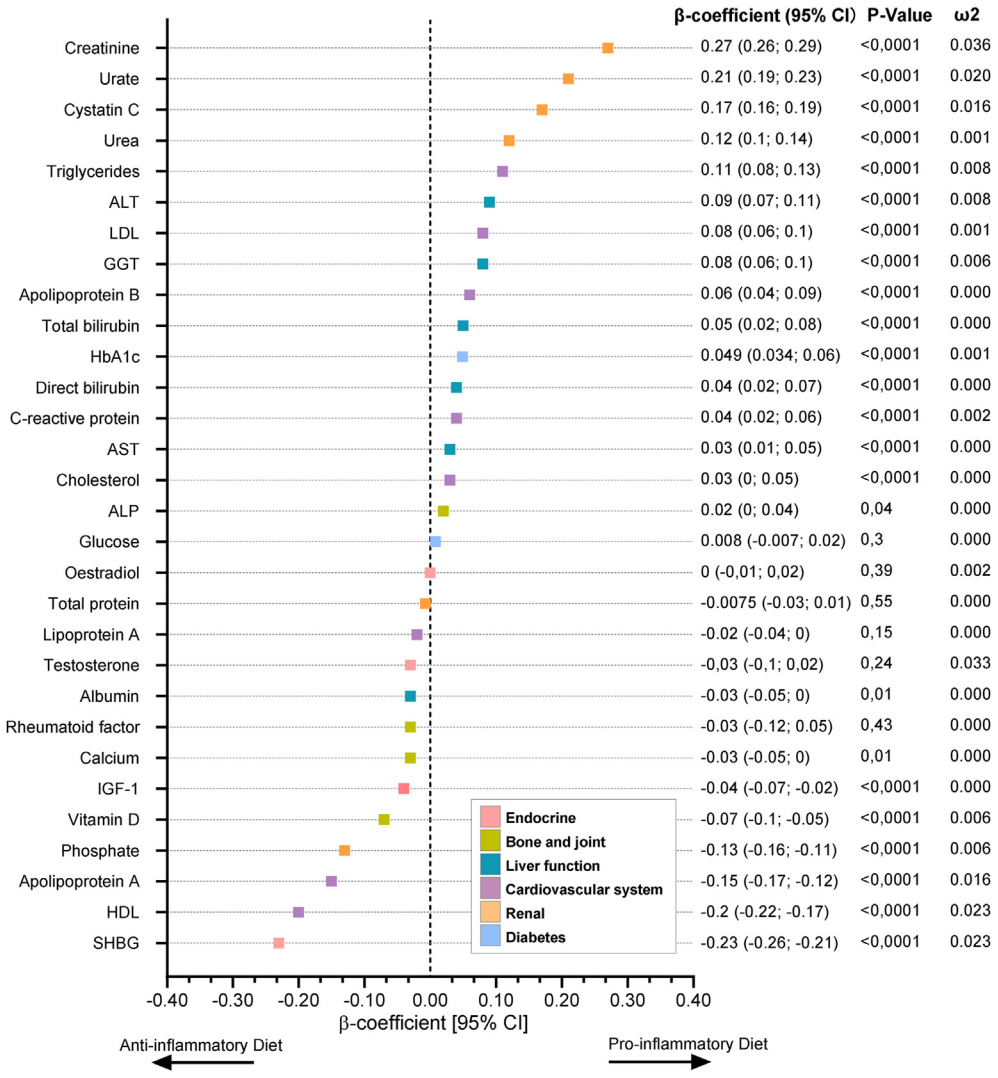

Figure 1 Differences in Biomarker Concentrations between Individuals Following Pro-inflammatory vs. Anti-inflammatory E-DII Diet. Data are presented as the standardized beta coefficient. This coefficient represents the difference in biomarker concentrations between individuals with anti-inflammatory and pro-inflammatory E-DII diet. A positive coefficient indicates that the biomarker concentration was higher with a pro-inflammatory diet, while a negative coefficient suggests it was higher with an anti-inflammatory diet. Statistical significance was set at $p < 0.0004$ after applying a Bonferroni correction. Analyses were adjusted for age, sex, deprivation, smoking, alcohol consumption, physical activity, and BMI.

Compared with participants with a neutral E-DII diet, those with a pro-inflammatory diet had higher concentrations of three cardiometabolic biomarkers (TG, LDL cholesterol and apolipoprotein B). Those with a neutral E-DII also had lower concentrations of three cardiometabolic biomarkers (HDL cholesterol, vitamin D and apolipoprotein A. The lowest concentration differences were for HDL cholesterol (−0.1 SD, equivalent to −0.039 nmol/L) (Fig. 3 and Supplementary Table 3).

3.3. Liver function

The associations of the standardized biomarkers with categories of the E-DII are presented in Fig. 1. Compared with individuals with an anti-inflammatory diet, those with a pro-inflammatory diet had significative higher concentrations of five liver function (ALT, GGT, total bilirubin, direct bilirubin and AST).

Biomarkers concentration among people with an anti-inflammatory diet compared with those in people with a neutral E-DII are shown in Fig. 2. Individuals with an anti-inflammatory diet had significative lower concentrations of four liver function biomarkers (ALT, direct bilirubin, total bilirubin and GGT). Compared with participants with a neutral E-DII diet, those with a pro-inflammatory diet had higher concentrations of two liver biomarkers (GGT and ALT.

3.4. Endocrine function

Compared with individuals with pro -inflammatory diet those with anti-inflammatory diet had significative lower concentrations of six biomarkers including two endocrine biomarkers (IGF-1 and SHBG), two cardiometabolic biomarkers (apolipoprotein A and HDL). The range of associations varies from −0.04 for IGF-1 (equivalent to

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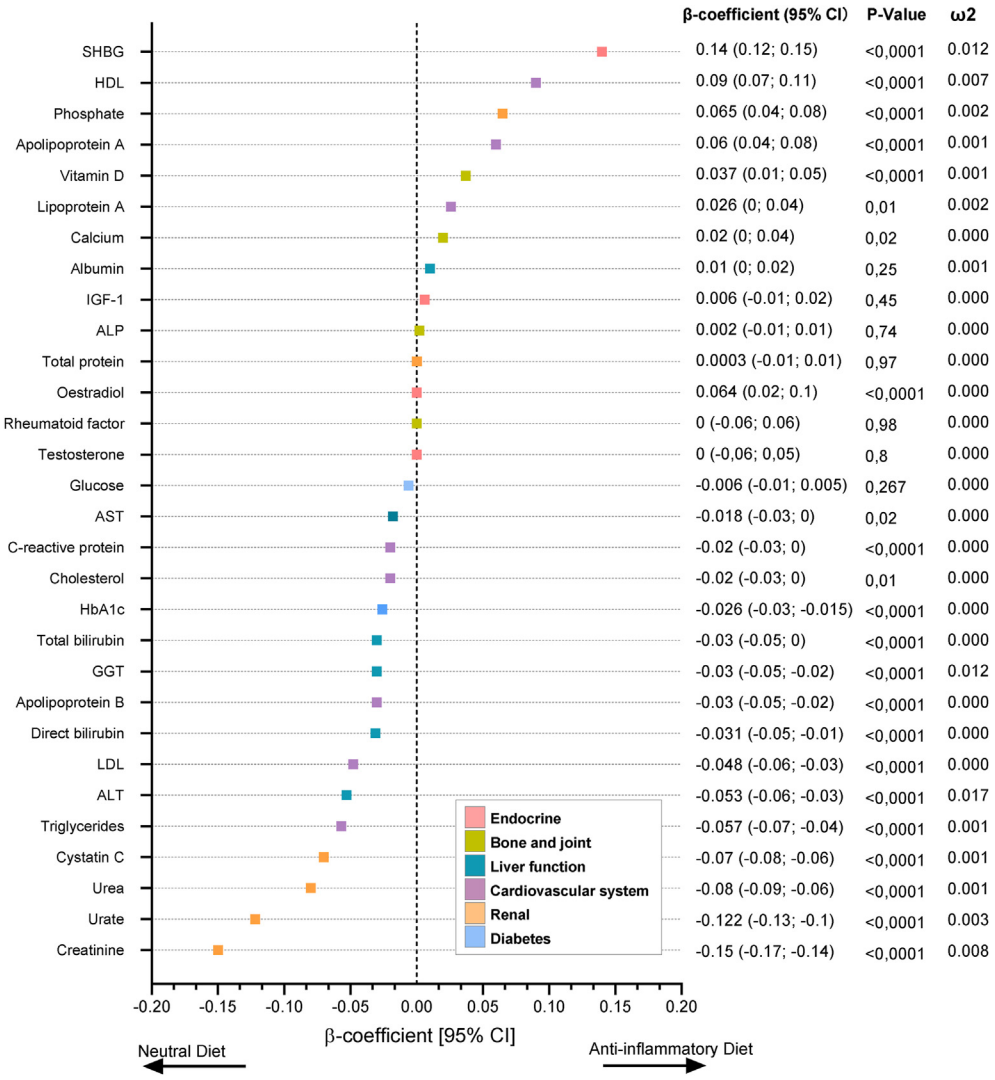

Figure 2 Differences in Biomarker Concentrations between Individuals Following Anti-inflammatory vs. Neutral E-DII Diet. Data are presented as the standardized beta coefficient. This coefficient represents the difference in biomarker concentrations between individuals with anti-inflammatory and neutral E-DII diet. A positive coefficient indicates that the biomarker concentration was higher with an anti-inflammatory diet, while a negative coefficient suggests it was higher with neutral diet. Statistical significance was set at $p < 0.0004$ after applying a Bonferroni correction. Analyses were adjusted for age, sex, deprivation, smoking, alcohol consumption, physical activity, and BMI.

−0.28 nmol/L) to −0.23 (equivalent to −6.6 nmol/L) for SHBG in individuals with a pro-inflammatory versus an anti-inflammatory diet (Fig. 1 and Supplementary Table 3).

Biomarkers concentration among people with an anti-inflammatory diet compared with those in people with a neutral E-DII are shown in Fig. 2 one endocrine biomarker (SHBG). The largest differences were found for SHBG (0.14 SD, equivalent to 3.9 nmol/L).

Compared with participants with a neutral E-DII diet, those with a pro-inflammatory diet had higher concentrations of one endocrine biomarker (testosterone). Those with a neutral E-DII also had lower concentrations of two endocrine biomarkers (IGF-1 and SHBG).

3.5. Bone health

Among people with a pro-inflammatory compared with an anti-inflammatory diet, there were a lower concentrations of vitamin D. Biomarkers concentration among people with an anti-inflammatory diet compared with those with a neutral E-DII are shown in Fig. 2. Two bone biomarkers showed a significantly higher concentration (vitamin D and phosphate). The largest differences were found for SHBG (0.14 SD, equivalent to 3.9 nmol/L) and the lowest for vitamin D (0.037 SD, equivalent to 0.78 nmol/L).

In Supplementary Table 3, we present the mean concentrations of biomarkers, expressed in their respective clinical units, stratified by E-DII into anti-inflammatory, neutral, and pro-inflammatory categories.

4. Discussion

Our study offers new insights into the association between 30 health-related biomarkers and indicators of an anti-inflammatory diet according to E-DII among healthy individuals. We found that participants with a pro-

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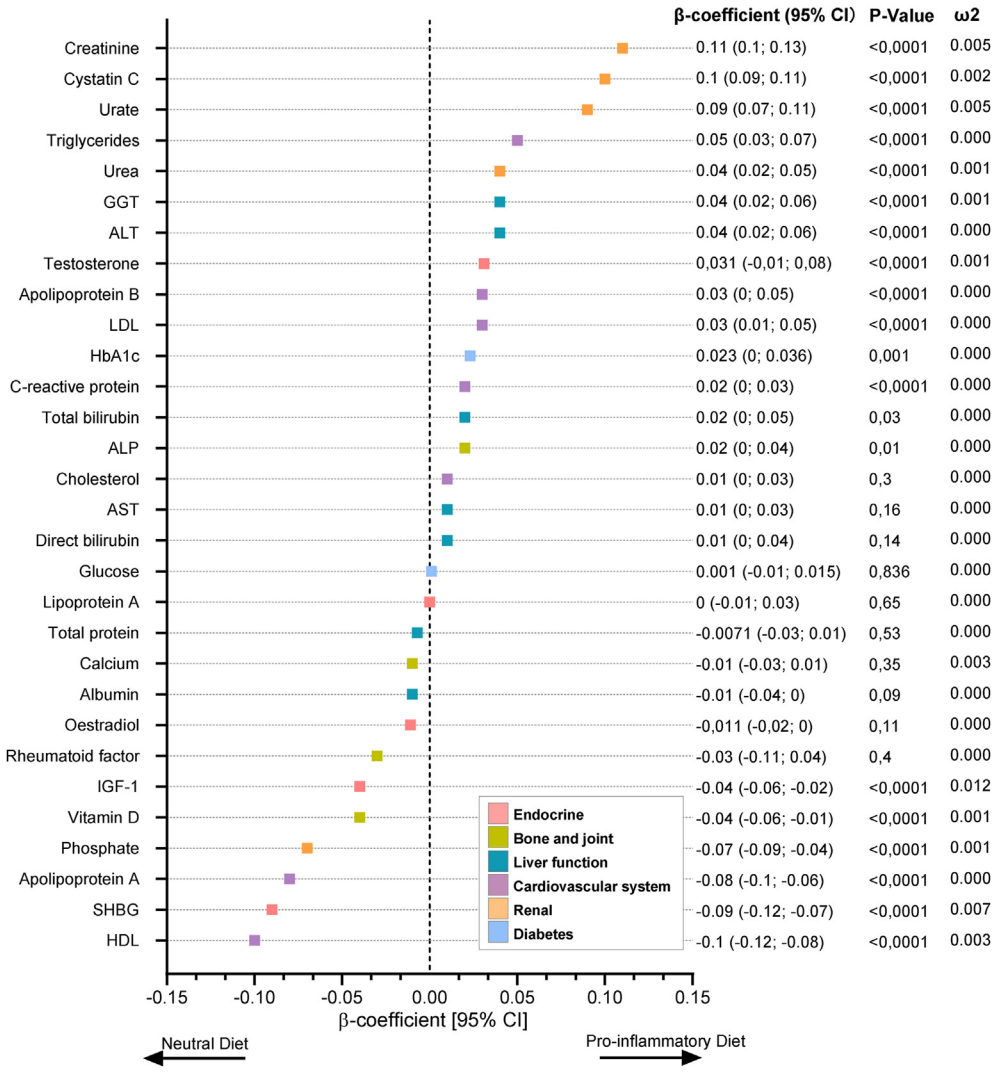

Figure 3 Differences in Biomarker Concentrations between Individuals Following Pro inflammatory vs. Neutral E-DII Diet. Data are presented as the standardized beta coefficient. This coefficient represents the difference in biomarker concentrations between individuals with pro-inflammatory and neutral E-DII diet. A positive coefficient indicates that the biomarker concentration was higher with a pro-inflammatory diet, while a negative coefficient suggests it was higher with neutral diet. Statistical significance was set at $p < 0.0004$ after applying a Bonferroni correction. Analyses were adjusted for age, sex, deprivation, smoking, alcohol consumption, physical activity, and BMI.

inflammatory diet had elevated levels of 16 biomarkers, with renal biomarkers displaying the most significant differences. These differences were observed independently of age, sex, BMI, and other lifestyle factors. Conversely, a pro-inflammatory diet was linked to lower concentrations of seven biomarkers, among which SHBG, HDL, and apolipoprotein A showed the lowest concentrations relative to an anti-inflammatory diet. Our findings contribute novel evidence to the field by shedding light on associations between E-DII and health-related biomarkers pertinent to a range of chronic diseases, including cardiovascular, metabolic, renal and liver conditions.

4.1. Renal function

In our study, participants who reported an anti-inflammatory diet showed the lowest concentrations of renal function biomarkers, including cystatin C, urate, urea, and creatinine. In contrast, those with a pro-inflammatory diet had elevated levels of these markers. The elevated creatinine and urate levels observed in the pro-inflammatory diet group could be attributed to the higher meat content in their diets [25,26]. Creatinine originates from creatine during muscle breakdown and from dietary protein [27]. Thus, protein-rich diets are likely to increase creatinine levels [25,26]. These results are consistent with earlier research indicating a higher incidence of kidney disease among individuals with pro-inflammatory diets [28]. Specifically, previous studies have demonstrated a positive association between DII score and elevated creatinine and urea nitrogen concentrations, particularly in men [29]. Poor nutrition and increased inflammation are linked to higher mortality rates and diminished quality of life in chronic kidney disease patients [30]. Furthermore, high urea concentrations have been associated with a greater incidence of CVD,

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insulin resistance, bowel disorders, and anemia, in people with and without chronic kidney disease [31]. In addition, raised concentrations of cystatin C predict higher risk of cardiovascular events in various clinical settings [32]. The relationship between pro-inflammatory dietary patterns and renal biomarkers is becoming a key focus in nephrological research. A diet characterized by high levels of saturated fats, sugars, and sodium, coupled with a lack of fibre, fruits, and vegetables, is thought to trigger systemic inflammation, adversely impacting renal function [28,33].

4.2. Cardiovascular function

Our study indicates that participants consuming anti-inflammatory diets exhibited a more favourable lipid profile, characterized by reduced LDL cholesterol, total cholesterol, Apo-B, and triglycerides, with higher HDL and apolipoprotein A concentrations. Additionally, these participants had lower concentrations of CRP an acute-phase protein produced by the liver and a well-established marker of systemic inflammation. These findings are in line with previous research [34], which has reported less favourable lipoprotein profiles and elevated concentrations of CRP in those with higher E-DII scores, indicative of a pro-inflammatory diet. Such dietary patterns have been associated with a raised risk of CVD and metabolic syndrome [34,35].

4.3. Endocrine function

We observed a positive association between an anti-inflammatory diet and higher concentrations of SHBG, which might confirm findings from a cross-sectional study conducted among American women [34,35]. There are several hypotheses to explain this relationship. One prominent hypothesis focuses on insulin sensitivity. Diets rich in anti-inflammatory components—typically high in fibre, omega-3 fatty acids and antioxidants—are associated with improved insulin sensitivity, which is linked with higher SHBG concentrations [36–38]. Additionally, anti-inflammatory diets reduce systemic inflammation which could affect SHBG concentrations indirectly [39]. Furthermore, since E-DII is positively associated with adiposity [40], an anti-inflammatory diet may facilitate weight management, leading to reduced fat mass which is associated with higher SHBG concentrations [41].

4.4. Liver function

We found that pro-inflammatory diets were linked to higher serum concentrations of key liver function markers, including ALT, GGT, AST, and total bilirubin. Although previous research involving multi-ethnic populations established an association between the AST:ALT ratio and the DII [42], fewer studies have investigated links with total bilirubin, albumin, and GGT [17]. A recent study on 4189 US adults aged 20–80 years showed contrasting findings: those participants with pro-inflammatory diets had higher concentrations of GGT and a higher AST:ALT ratio, while concentrations of both ALT and AST were lower among those with a more pro-inflammatory diet [17]. The higher concentrations of ALT and AST with pro-inflammatory diets in our study may be because we focused on healthy individuals. In contrast, the study by Ramirez-Velez et al. was based on a nationally representative sample of the American adult population and, therefore, included both healthy and unhealthy individuals. Alternatively, the divergent findings may be explained by differences in the covariates included in the statistical models in the two studies. The liver function markers we examined are low-cost, non-invasive and they hold promise as early indicators of liver damage, including Non-Alcoholic Fatty Liver Disease, that could result from a pro-inflammatory diet [43].

4.5. Bone health

We found no association between the E-DII and ALP but vitamin D concentrations were higher among those consuming anti-inflammatory diets. These findings differ from previous research, which has suggested that anti-inflammatory diets are associated with higher ALP concentrations [44]. While our study identifies elevated vitamin D concentrations among participants adhering to a more anti-inflammatory diet, existing literature primarily focuses on individuals with chronic conditions, leaving a gap in evidence concerning the relationship between vitamin D and E-DII in healthy individuals [45,46].

4.6. Strength and limitations

The primary strengths of this study lie in the extensive range of health-related biomarkers evaluated and the large sample size of healthy people drawn from the UK Biobank cohort. To the best of our knowledge, this is the first study to examine the associations between an E-DII and a comprehensive array of clinically relevant biomarkers. However, caution is advised in interpreting our findings. Since this is an observational study, causality cannot be firmly established, and diet may have been changed because of suboptimal biomarker level. Additionally, findings from the study may not be generalizable to the whole UK population since the UK Biobank sample is slightly skewed towards higher socio-economic status and healthier behaviours compared with the general UK population. While our analyses are adjusted for key covariates, residual confounding may affect interpretation of the findings. It is also important to note that DII scores were derived from self-reported dietary questionnaires, which may introduce reporting bias. Another limitation is related to the cross-sectional design of the study, the biomarkers investigated are a snapshot and not necessarily reflective of long-term biomarker status. Despite these limitations, this is the first large study to explore the relationship between E-DII and a range of clinically used biomarkers reporting on health of multiple body systems. Confirming these associations and their potential causal association in independent studies and using Mendelian Randomization

Please cite this article as: Carrasco-Marín F et al., Association of a dietary inflammatory index with cardiometabolic, endocrine, liver, renal and bones biomarkers: cross-sectional analysis of the UK Biobank study, Nutrition, Metabolism & Cardiovascular Diseases, https://doi.org/10.1016/j.numecd.2024.03.010

analysis may offer valuable insights for predicting chronic diseases, thus presenting an opportunity to mitigate their prevalence. Finally, about the observed differences in means we acknowledge that these differences are statistically significant ($p < 0.0001$ for all comparisons). However, it is crucial to contextualize these differences from a clinical perspective as while they may be statistically significant due to the large sample size, the clinical relevance of some of these variations may be limited.

5. Conclusions and implications

This study highlighted that a pro-inflammatory diet was associated with an adverse profile of biomarkers linked to cardiometabolic health, endocrine, liver function, and renal health. Notably, these associations remained significant even after adjusting for adiposity and other socio-demographic and lifestyle-related confounding factors.

Specifically, individuals following a pro-inflammatory diet have elevated levels of biomarkers associated with kidney function, such as creatinine and uric acid, suggesting a potential risk of chronic kidney disease. In addition, the relationship between pro-inflammatory dietary patterns and liver markers indicates a possible link with liver damage, including non-alcoholic fatty liver disease. On the other hand, those following an anti-inflammatory diet have a more favourable lipid profile and protein concentrations associated with cardiovascular health, suggesting a lower risk of cardiovascular and metabolic diseases. The positive association between an anti-inflammatory diet and higher concentrations of sex hormone binding globulin (SHBG) supports the importance of these dietary patterns on endocrine function, potentially improving insulin sensitivity.

Our findings contribute to an enhanced understanding of how dietary components and overall diet quality may influence biological processes in healthy individuals. Understanding how diet changes disease risk mechanistically could offer a way to monitor and potentially anticipate disease risk, thereby creating opportunities to reverse or delay its onset.

Financial Support

None of the authors have funding for conducting this study. However, UK Biobank was established by the Wellcome Trust, Medical Research Council, Department of Health, Scottish Government and the Northwest Regional Development Agency. It has also had funding from the Welsh Assembly Government and the British Heart Foundation, United Kingdom.

Authorship contributions

F.C-M, FH and C.C-M., contributed to the conception and design of the study, advised on all statistical aspects, and interpreted the data. J.M and M.W created the E-DII. All authors critically reviewed this and previous drafts. All authors approved the final draft for submission, with final responsibility for publication.

Ethical standards disclosure

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the North West Multi-Centre Research Ethics Committee (NHS National Research Ethics Service 16/NW/0274). Written informed consent was obtained from all subjects/patients.

Conflict of interest

The authors have no conflict of interest to declare.

Acknowledgements

We are grateful to UK Biobank participants. This research has been conducted using the UK Biobank resource under application number 7155.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2024.03.010.

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