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Association between dietary phytochemical index, inflammation and oxidative stress with sleep duration and sleep quality in Iranian adults

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We aimed to explore the link between dietary phytochemical index (DPI) and sleep quality/duration, along with oxidative stress and inflammatory biomarkers in Iranian adults. The present cross-sectional investigation was carried out on 535 adults (54% male) with a mean age of 42.6 years. Sleep quality and duration were assessed using the Pittsburgh Sleep Quality Index, and dietary intake was evaluated using a 168-item food frequency questionnaire. DPI was calculated as a percentage of energy intake derived from phytochemical-rich foods. An overnight fasting blood sample was collected from each participant to evaluate serum malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPX), and high-sensitivity C-reactive protein (hs-CRP) levels. Participants in the third tertile of DPI had 43% lower odds of having short sleep duration (OR = 0.57, 95%CI: 0.32–0.99) and 53% lower odds of having poor sleep quality (OR = 0.47, 95%CI: 0.26–0.86). Regarding specific domains of poor sleep quality, an inverse association was observed between sleep latency (OR = 0.39, 95%CI: 0.17–0.89) and sleep disturbances (OR = 0.40, 95%CI: 0.16–1.02). Higher scores of DPI were associated with marginally lower odds of having short sleep duration in overweight/obese individuals (OR = 0.55, 95%CI: 0.27–1.09) and males (OR = 0.42, 95%CI: 0.18–1.01). A significant inverse relationship was observed between DPI and having poor sleep quality in normal-weight subjects (OR = 0.20, 95%CI: 0.06–0.74) and females (OR = 0.40, 95%CI: 0.17–0.94). A marginally inverse association was observed between each tertile increment in DPI and hs-CRP levels (B (non-standardized β) =-0.31 mg/L, 95%CI: -0.64, 0.01; *P* = 0.06). Individuals with good quality of sleep also had lower serum levels of MDA than those with poor quality of sleep (162.0 vs. 185.5 nmol/mL; *P* = 0.01). However, no significant association was observed regarding SOD, GPX, and hs-CRP levels and sleep quality. Iranian adults with higher DPI scores had lower odds of having short sleep duration and poor sleep quality. MDA and hs-CRP might be intermediate factors for this association.

Keywords Sleep, Dietary phytochemical index, Oxidative stress, Inflammation

Abbreviations

BMI	Body mass index
CI	Confidence interval
DPI	Dietary phytochemical index
ELISA	Enzyme-linked immunosorbent assay
FFQ	Food Frequency Questionnaire

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GPX	Glutathione peroxidase
hs-CRP	high-sensitivity C-reactive protein
IPAQ	International Physical Activity Questionnaire
MDA	Malondialdehyde
MED	Mediterranean
MIND	Mediterranean-DASH intervention for neurodegenerative delay
MUFA	Mono unsaturated fatty acid
OR	Odds ratio
OSA	Obstructive sleep apnea
PA	Physical activity
PSQI	Pittsburgh Sleep Quality Index
STOP-Bang	Snoring, Tiredness, Observed apnea, blood Pressure, Body mass index, Age, Neck circumference and Gender
PUFA	Poly unsaturated fatty acid
REM	Rapid eye movement
SD	Standard deviation
SE	Standard error
SES	Socioeconomic status
SFA	Saturated fatty acid
SOD	Superoxide dismutase
HEPA	Health-Enhancing Physical Activity

Sleep is an important element of human biological life needed for optimal metabolism, homeostasis, and proper function of the brain and other organs of the body[1]. Overall well-being is significantly impacted by the quantity and quality of sleep[2]. Poor or inadequate sleep is associated with chronic conditions such as metabolic syndrome, type 2 diabetes, cognitive impairment, and obesity[3], highlighting a staggering economic burden on healthcare systems[4]. Based on evidence, one-third of the general population in the globe, as well as Iranians, suffers from sleep disorders[5,6]. Therefore, it is crucial to identify strategies that reduce the risk of sleep disorders and associated chronic conditions.

The etiology of sleep disorders is complex, and both genetic and modifiable risk factors such as diet, physical activity, and stress are involved[7]. Plant-based foods such as fruits, vegetables (except for potatoes), whole grains, nuts, legumes, and oil seeds are rich sources of phytochemicals, and their link with sleep quality and duration has received a great deal of attention[8,9]. The dietary phytochemical index (DPI), suggested by McCarty, is a validated tool previously developed in epidemiological studies which reflects the total content of phytochemicals in the diet. DPI is described as the percentage of energy consumption obtained from foods rich in phytochemicals[10]. Based on literature review, no previous study has investigated the relationship between DPI and sleep quality and duration in the globe.

In recent years, the interrelationship and mediating effect of oxidative stress and inflammation on sleep disorders has been explored[11,12]. Oxidative stress is an imbalance between the production and scavenging of reactive oxygen species (ROS) by the antioxidant defense system, which can cause inflammation. Evidence supports the idea that oxidative stress and inflammation play a crucial role in sleep disorders[13]. A previous study indicated that serum malondialdehyde (MDA) level, a lipid peroxidation metabolite, was substantially lower in subjects with adequate sleep[14]. In addition, prior experimental studies found significant decreases in superoxide dismutase (SOD)[15] and glutathione peroxidase (GPX) activities[16], as antioxidant enzymes, in sleep-deprived rats. A recent cross-sectional study on 9,184 Iranian adults found that serum pro-oxidant/antioxidant balance was significantly higher in subjects with very short sleep duration[17]. However, no association was observed regarding SOD activity[17]. Additionally, a previous cross-sectional study on 1,020 Taiwanese adults found no significant relationship between CRP levels and sleep quality[18]. However, they indicated a positive association between long sleep duration and CRP levels[18]. Also, another cross-sectional study in the United Kingdom (UK) found no significant link between sleep duration and CRP levels[19]. However, a previous prospective study on 74,867 Korean adults found that long sleep duration and poor sleep quality were related to higher levels of hs-CRP[20]. Moreover, another cross-sectional study by He et al. on 8,170 Chinese adults showed that long sleep duration was positively related to higher hs-CRP levels[21]. Okun et al. also indicated that poor sleep quality was associated with higher CRP levels; however, this association was not significant regarding sleep duration[22]. To the best of our knowledge, the relationship between biomarkers of oxidative stress and inflammation concurrently with sleep quality/duration has not been examined in Iranian adults. Therefore, in the present study, we aimed to investigate the association between DPI and sleep quality/duration regarding the potential role of oxidative stress and inflammation in Iranian adults.

Methods and material

Study design and participants

The present cross-sectional study was undertaken among a somewhat representative sample of Iranian adults in 2021. The sample size of this study was estimated according to a prior study, which reported a prevalence of 35% for sleep deprivation among Iranian adults[23]. At least 519 individuals were required for this study by considering a type I error of 5%, a power of 80%, and a precision (d) of 4.1%. More information in the case of study design has been published previously[24]. Considering the possibility of a low response rate due to the COVID-19 pandemic during data collection, 600 participants were invited to take part in this study. Individuals were selected from staff of 20 schools in Isfahan, Iran, using a multistage cluster random sampling method. Participants with varying socioeconomic statuses were randomly selected from various job categories in chosen schools

as employees, teachers, school administrators, assistants, and crews. The response rate was 90.5%. Individuals with the following criteria were precluded from the investigation: (1) reported a total energy intake outside the range of 800–4200 kcal/day (A single, non–sex-specific cutoff was applied to all participants, based on previous literature[25]; (2) had left more than 70 items blank on the food frequency questionnaire; and (3) refused blood draw. At the end, 535 adults were included in this analysis. This survey was conducted in compliance with the Declaration of Helsinki. An informed consent form was provided from each participant. The Ethics Committee of Isfahan University of Medical Sciences has granted ethical approval for the study protocol (no. 2404188).

Assessment of dietary intake

A validated semi-quantitative 168-item food frequency questionnaire (FFQ) in a Willett format was employed to evaluate dietary intake of subjects over the past year[26]. Reasonable correlations between dietary intakes evaluated from this FFQ and twelve 24-hour dietary recalls were revealed in the prior validation study of this questionnaire[26]. The reproducibility of the FFQ was assessed by comparing nutrient intakes obtained from this FFQ on two occasions, 1 year apart. Accordingly, this questionnaire could provide valid and reliable measures of usual dietary intakes of Iranian adults[26]. A trained nutritionist instructed participants how to complete the FFQ by reporting the frequency and amount of each food item they consumed over the previous year. Using household measures, the serving sizes of consumed items were transformed into grams per day[27]. Afterwards, all food items were entered into the Nutritionist IV software (Version 7; First Databank, Hearst Corp, San Bruno, CA, USA) to calculate total energy and nutrient intakes. This software, which was based on the United States Department of Agriculture (USDA) food composition database, was modified for Iranian food items[28].

Assessment of DPI

An equation proposed by McCarty was used to compute DPI[10]: (DPI = energy derived from phytochemical-rich foods (kcal/d)/overall energy consumption (kcal/day) × 100. This calculation included legumes, nuts, seeds, fruits and vegetables, juices from fruits and vegetables, tomato sauces, whole grains, olives, olive oil, and soy products. Potato was not included in the DPI calculation, because of its limited phytochemical content.

Assessment of biochemical indices

Following a 12-hour overnight fast, a 10-ml sample of peripheral blood was collected from each participant. Blood samples were immediately centrifuged at 3500 rpm for 10 min to separate serum. These serum samples were kept at -80 °C for further tests. The commercial enzyme-linked immunosorbent assay (ELISA) kits were used for assessing hs-CRP (turbidimetry kit, latex-enhanced turbidimetric method, Delta.DP). Commercial kits from Kiazist (Hamedan, Iran) were used to assess MDA, SOD, and GPX.

Assessment of sleep habits

In order to evaluate measures of quality and quantity of sleep, the Pittsburgh Sleep Quality Index (PSQI) questionnaire was utilized[29]. The validity and reliability of this questionnaire have previously been approved among Iranian adults with a sensitivity of 85% and specificity of 84%[30]. The PSQI consists of 9 questions, which include 19 items evaluating 7 domains: sleep duration, habitual sleep efficiency, subjective sleep quality, sleep disturbances, sleep latency, use of sleep medications, and daytime dysfunction. Each domain was rated on a four-point scale (0–3). Finally, the total score of all domains was summed to get a total score ranging from 0 to 21 which lower scores indicating higher sleep quality. Participants were categorized into two groups: good and average sleep quality (score up to 5), and poor sleep quality (score of ≥ 6)[29]. In order to assess sleep duration, the fourth question of the PSQI was used: "How many hours do you sleep per night?" Individuals with less than 7 hours of sleep per night were considered as short sleepers[31,32].

Assessment of other variables

Weight and height of individuals were measured while standing with minimum clothes and barefoot. Weight was measured to the nearest 0.01 kg, using a body composition analyzer (Tanita MC-780MA, Tokyo, Japan). Height assessment was done to the nearest 0.1 cm by a wall-mounted tape. In order to calculate body mass index (BMI), weight (kg) was divided by height squared (m^2). Information about age, sex, education, and marital status was gathered through a self-reported questionnaire. Home ownership and family size were considered as the main items of socioeconomic status (SES) of individuals. The STOP-Bang questionnaire, a self-administered screening tool consisting of eight "yes or no" questions related to snoring, fatigue, observed apnea, hypertension, BMI greater than 35 kg/m^2, age over 50 year, neck size exceeding 40 cm, and male sex was utilized to define obstructive sleep apnea (OSA). Participants who answered positively to ≥ 5 questions were categorized as having high risks of OSA. In addition, the physical activity (PA) of individuals was assessed by a validated International Physical Activity Questionnaire-short form (IPAQ-SF), in which subjects were classified in three categories: (1) inactive (< 600 MET.min/week), (2) minimally active (≥ 600 to < 3000 MET.min/week), and (3) active (≥ 3000 MET.min/week)[33].

Statistical analysis

The Kolmogorov–Smirnov test was used to examine the normality of quantitative variables. Subjects were distributed into tertiles of DPI (T1: <25.24, T2: 25.24–36.29, and T3: >36.29% of total energy intake). Continuous (mean ± SD/SE) and categorical (percentage) variables were respectively compared across tertiles of DPI through one-way ANOVA and chi-square tests. To assess adjusted dietary intake of participants across tertiles of DPI, the ANCOVA test was used. Binary logistic regression was applied to investigate the association between DPI and outcomes of interest by reporting odds ratio (OR) and 95% confidence interval (CI) in crude and adjusted models. In the first model, age, sex, and total energy intake were taken into account. In the second model,

further adjustments were made for marital status, education, home ownership, family size, physical activity levels, history of diabetes, tea and coffee intake after 8 pm, use of antidepressant medicine, and OSA. In the last model, BMI was added to the prior adjustments. The first tertile of DPI was considered as the reference category. To determine P for trends, tertiles of DPI were regarded as an ordinary variable. Additionally, stratified analyses were performed in terms of BMI levels (normal-weight vs. overweight/obesity) and sex (women vs. men). Linear regression analysis was used to provide MDA, SOD, GPX, and hs-CRP values by each tertile increase in DPI through controlling for age and sex (in the first model), and further adjustment for BMI (in the second model). All analyses were conducted using SPSS software version 26 (IBM, Chicago, IL). P-values below 0.05 were regarded as statistically significant.

Ethics approval

The study procedure was performed according to the declaration of Helsinki and the STROBE checklist.

Consent to participate

All participants provided informed written consent. The study protocol was approved by the local Ethics Committee of Isfahan University of Medical Sciences.

Results

Five hundred and thirty-five participants (54% male) with a mean age of 42.60 years and a BMI of 26.90 kg/m^2 participated in this study. General characteristics of study participants in different DPI tertiles are shown in Table 1. Individuals in the highest tertile of DPI, in comparison with the lowest tertile, were more likely to be older, female, higher educated, house owners, and have lower weight and lower intake of coffee/tea after evening (8 pm). No other significant differences were observed.

Multivariable-adjusted intakes of selected nutrients and food groups of study participants across tertiles of DPI are presented in Table 2. Participants in the top tertile of DPI consumed greater amounts of energy, carbohydrate, vitamin C, pyridoxine, folate, total fiber, fruits, vegetables, nuts, and legumes and lower amounts of fat, saturated fatty acid, iron, refined grain, and red and processed meat.

Among the participants being studied, 70.10% experienced short sleep duration and 28.60% reported poor or low sleep quality. Figure 1 displays the prevalence of individuals with short sleep duration and poor sleep quality in various DPI groups. In the first, second, and third tertiles of DPI, 70.20%, 74.90%, and 65.20% of participants had short sleep duration, respectively. However, there was no significant difference in short sleep duration prevalence across tertiles of DPI ($P = 0.13$). Moreover, no significant difference in prevalence of poor sleep quality was observed across tertiles of DPI ($P = 0.08$).

Multivariable-adjusted ORs for short sleeping and poor sleep quality across tertiles of DPI are provided in Table 3. The highest score of DPI was not associated with odds of having short sleep duration in the crude model (OR = 0.79, 95% CI: 0.51–1.24; P_{trend}=0.30). After adjusting for potential confounders, individuals in the top tertile of DPI, in comparison with those in the bottom tertile, had lower odds of having short sleep duration (OR = 0.57, 95% CI: 0.32–0.99; P_{trend}=0.04). Participants in the highest tertile of DPI compared to those with the lowest tertile had lower chance of having poor sleep quality (OR = 0.59, 95% CI: 0.37–0.94; P_{trend}=0.03). This association also existed after considering potential confounders (OR = 0.47, 95% CI: 0.26–0.86; P_{trend}=0.01).

Multivariable-adjusted ORs for individual domains of sleep quality across DPI tertiles are presented in Table 4. Regarding sleep latency, a significant inverse association was observed in individuals in the third tertile of DPI in comparison with those in the first tertile (OR = 0.50, 95% CI: 0.26–0.97; P_{trend}=0.04). This association persisted after taking all potential confounders into account (OR = 0.39, 95% CI: 0.17–0.89; P_{trend}=0.03). Higher level of DPI compared to lower category, was associated with a lower likelihood of sleep disturbances (OR = 0.34, 95% CI: 0.16–0.74; P_{trend}=0.01). However, this association was marginally significant after adjustment for all potential confounders (OR = 0.40, 95% CI: 0.16–1.02; P_{trend}=0.07).

Multivariate adjusted ORs and 95% CIs for short sleeping and poor quality of sleep across tertiles of DPI, stratified by sex and BMI categories are shown in Table 5. With regard to short sleeping, males (OR = 0.42, 95% CI: 0.18–1.01; P_{trend}=0.05) and overweight/obese individuals (OR = 0.55, 95% CI: 0.27–1.09; P_{trend}=0.08) in the top tertile of DPI had marginally lower odds of having short sleep duration. In terms of quality of sleep, females (OR = 0.40, 95% CI: 0.17–0.94; P_{trend}=0.04) and normal-weight participants (OR = 0.20, 95% CI: 0.06–0.74; P_{trend}=0.02) in the third tertile of DPI had a lower likelihood of having poor quality of sleep.

Linear associations between each tertile increase in DPI and serum levels of MDA, GPX, SOD, and hs-CRP are shown in Fig. 2. In the crude model, for each tertile increase in DPI, MDA levels decreased by 4.37 (B (non-standardized β) = -4.37 nmol/mL, 95% CI: -13.98, 5.24; $P = 0.37$). After controlling for potential confounders, this association strengthened; however, it was still not statistically significant (B (non-standardized β) = -6.44 nmol/mL, 95% CI: -16.58, 3.71; $P = 0.21$). Regarding SOD and GPX, after adjusting confounders, each tertile increase in DPI was accompanied by a slight increase in SOD and GPX levels; however, these associations were not statistically significant (SOD: B (non-standardized β) = 0.04 U, 95% CI: -0.02, 0.09; $P = 0.21$; GPX: B (non-standardized β) = 0.26 mU/mL, 95% CI: -0.16, 0.68; $P = 0.22$). Each tertile increment in DPI was associated with a slight decrease in hs-CRP levels in the crude model (B (non-standardized β) = -0.22 mg/L, 95% CI: -0.53, 0.08; $P = 0.15$). After controlling for potential confounders, this association strengthened (B (non-standardized β) = -0.31 mg/L, 95% CI: -0.64, 0.01; $P = 0.06$). No significant association was found for serum levels of these biomarkers in individuals with adequate duration of sleep, in comparison with those with inadequate duration of sleep. Regarding quality of sleep, individuals with good/moderate quality of sleep compared to individuals with poor quality of sleep had lower MDA levels (162.9 vs. 186.0 nmol/mL; $P = 0.01$). No significant association was observed

	DPI tertiles			
	T1 ($n=178$) (< 25.24)	T2 ($n=179$) (25.24–36.29)	T3 ($n=178$) (> 36.29% of energy intake)	*P*-value[2]
Age (y)	39.77 ± 11.43	41.28 ± 9.68	46.69 ± 11.08	< 0.001
Sex (%)				< 0.001
Male	64.00	55.90	42.10	
Female	36.00	44.10	57.90	
Marital status (%)				0.26
Single	21.00	12.30	16.00	
Married	77.80	86.60	82.30	
Divorced or widow	1.10	1.10	1.70	
Education status (%)				< 0.001
Diploma or lower	16.30	5.10	12.00	
Higher than diploma	83.70	94.90	88.00	
OSA (%)				0.28
No	62.20	65.70	71.20	
Borderline	33.50	27.30	24.10	
Yes	4.30	7.00	4.70	
Home ownership (%)				0.02
Yes	70.50	71.50	82.60	
No	29.50	28.50	17.40	
Family size (%)				0.47
≥ 4 members	84.70	83.60	88.10	
< 4 members	15.30	16.40	11.90	
Weight (kg)	76.16 ± 14.80	77.41 ± 14.47	73.62 ± 14.14	0.04
BMI (kg/m^2)	26.45 ± 4.36	27.27 ± 4.16	27.00 ± 4.69	0.20
Waist circumference (cm)	92.23 ± 12.01	93.70 ± 11.00	92.00 ± 11.39	0.32
Physical activity (HEPA)				0.17
Inactive	59.10	58.10	52.50	
Minimally active	30.10	35.80	40.70	
Active	10.80	6.10	6.80	
History of diabetes				0.06
Yes	2.20	5.60	7.90	
No	97.80	94.40	92.10	
Drinking tea/coffee after 8 pm				< 0.001
Yes	65.70	60.30	47.20	
No	34.30	39.70	52.80	
Antidepressant drug intake				0.85
Yes	4.60	5.80	5.70	
No	95.40	94.20	94.30	
SOD (U)	1.14 ± 0.04	1.10 ± 0.04	1.13 ± 0.04	0.75
GPX (mU/mL)	1.81 ± 0.22	1.89 ± 0.34	2.22 ± 0.29	0.57
MDA (nmol/mL)	168.95 ± 6.65	179.37 ± 92.13	160.27 ± 7.09	0.15
hs-CRP (mg/L)	3.56 ± 0.26	2.88 ± 0.20	3.11 ± 0.20	0.09

Table 1. General characteristics of study participants across tertiles of DPI1. [1] Values are Mean ± SD for socioeconomic factors, and Mean ± SE for SOD, GPX, MDA, and CRP.[2] Obtained from ANOVA and $\chi 2$ test for quantitative and categorical variables, respectively. DPI, Dietary phytochemical index; y, year; kg, kilogram; mg, milligram; m, meter; cm, centimeter; BMI: Body mass index; n, number; mg, milligram; mL, milliliter; U, unit; OSA, obstructive sleep apnea; SOD, Superoxide dismutase; GPX, Glutathione peroxidase; MDA, Malondialdehyde; hs-CRP, High-sensitivity C-reactive protein; HEPA, Health-Enhancing Physical Activity.

between SOD, GPX, and hs-CRP levels and having good/moderate vs. poor sleep quality (SOD: 1.14 vs. 1.09 U, $P=0.29$; GPX: 1.98 vs. 1.96 mU/mL, $P=0.95$; hs-CRP: 3.20 vs. 3.14 mg/L, $P=0.83$).

Discussion

In this cross-sectional survey, individuals with higher DPI scores were less likely to have a short duration of sleep and lower quality of sleep. Regarding individual domains of sleep quality, DPI was inversely related to sleep latency and sleep disturbances. Based on stratified analysis, males and overweight/obese participants

	DPI tertiles			
	T1 ($n=178$) (< 25.24)	T2 ($n=179$) (25.24–36.29)	T3 ($n=178$) (> 36.29)	*P*-value[2]
Energy, kcal	2158.81 ± 51.71	2296.68 ± 50.58	2358.71 ± 52.65	0.03
Protein, % of E	14.42 ± 0.22	14.48 ± 0.21	13.87 ± 0.22	0.11
Carbohydrate, % of E	58.69 ± 0.61	59.91 ± 0.59	63.79 ± 0.62	< 0.001
Fat, % of E	28.11 ± 0.51	27.49 ± 0.50	25.10 ± 0.52	< 0.001
Saturated fatty acid, gr	24.34 ± 0.59	22.55 ± 0.58	20.05 ± 0.60	< 0.001
Vitamin C, mg	134.99 ± 6.66	191.16 ± 6.49	267.36 ± 6.77	< 0.001
Pyridoxine, mg	1.55 ± 0.04	1.79 ± 0.03	2.06 ± 0.04	< 0.001
Vitamin E, mg	6.51 ± 0.24	6.92 ± 0.23	7.15 ± 0.24	0.18
Folate, mcg	281.47 ± 7.93	346.66 ± 7.73	395.96 ± 8.06	< 0.001
Iron, mg	18.49 ± 0.31	17.78 ± 0.30	17.14 ± 0.31	0.01
Calcium, mg	884.33 ± 28.50	955.81 ± 27.76	921.04 ± 28.97	0.20
Total fiber, gr	16.02 ± 0.39	20.81 ± 0.38	26.57 ± 0.39	< 0.001
Sodium, mg	3887.92 ± 194.47	3930.57 ± 189.44	3504.16 ± 197.65	0.26
Food groups				
Vegetables, g	252.80 ± 16.64	323.97 ± 16.21	454.88 ± 16.91	< 0.001
Fruits, g	332.74 ± 20.25	531.80 ± 19.72	794.54 ± 20.58	< 0.001
Dairy, g	311.42 ± 20.27	337.13 ± 19.74	295.83 ± 20.60	0.34
Whole grains, g	118.88 ± 6.12	108.05 ± 5.96	108.31 ± 6.22	0.37
Refined grain, g	328.71 ± 11.79	280.52 ± 11.49	209.62 ± 11.99	< 0.001
Nuts and legumes, g	38.19 ± 2.81	56.97 ± 2.74	57.68 ± 2.85	< 0.001
Red and processed Meat, g	73.48 ± 3.43	70.59 ± 3.34	59.27 ± 3.49	0.01
White meat, g	40.54 ± 2.54	35.18 ± 2.47	40.57 ± 2.58	0.21

Table 2. Multivariable-adjusted intakes of selected nutrients and food groups of study participants across tertiles of DPI1. [1] Values are Mean ± SE; energy intake and macronutrients are adjusted for age and sex; all other values are adjusted for age, sex and energy intake.[2] Obtained from ANCOVA. DPI, Dietary phytochemical index; g: gram; mg: milligram; mcg: microgram.

with higher DPI scores had a slightly lower chance of short duration of sleep. In the case of poor sleep quality, an inverse association was observed among normal-weight participants and females. Moreover, higher scores of DPI were associated with lower hs-CRP levels. Individuals with good quality of sleep had lower levels of MDA.

Inadequate levels of sleep quality and duration lead to increased risk of cardiovascular morbidity[34], diabetes mellitus[35], obesity[36], hypertension[37], and impaired functioning[38]. Results of the present investigation indicated that individuals with higher DPI scores might have better sleep quality and duration. Thus, individuals could be recommended to switch their dietary intakes to a phytochemical-rich diet to improve their sleep health.

While numerous studies have highlighted the positive impact of phytochemicals on health, a limited number of studies have examined the link between the consumption of these bioactive compounds and sleep habits. Our results revealed that higher scores of DPI were associated with lower odds of having short sleep duration and poor quality of sleep. In agreement with our findings, a recent cross-sectional study on 278 overweight and obese Iranian women reported that higher polyphenol intake was negatively associated with poor sleep quality[39]. However, another cross-sectional study by Bayram et al. found no significant association between polyphenol intake and sleep quality among Turkish adults[40]. These conflicting results could be explained by differences in the investigated population and study design.

Phytochemicals are key elements in plant-based dietary patterns such as the Mediterranean (MED) diet and the Mediterranean-DASH intervention for neurodegenerative delay (MIND) diet, all of which show protective links with sleep habits. In line with our findings, higher adherence to a healthy plant-based pattern was associated with better sleep quality and duration in a cohort study on Chinese adults[41]. However, in a cross-sectional study of Iranian female adults with obesity, higher adherence to a healthy plant-based diet was not related to sleep quality[8]. Another cross-sectional study on 1,314 Italian adults indicated that high adherence to the MED diet was linked to better sleep quality[42]. Moreover, a cross-sectional study in Iran revealed that greater adherence to the MIND diet was associated with a lower chance of having poor sleep quality in adult males[43]. The conflicting results of prior investigations may be justified by differences in the studied population, study design, statistical methods used, and covariates considered in the analyses.

In the present study, higher scores of DPI in overweight/obese individuals and males were marginally associated with lower odds of having short sleep. Evidence suggests that inflammation linked to obesity may change sleep-wake cycles by triggering the release of sleep-inducing cytokines, resulting in extended sleep duration in individuals with overweight/obesity[44]. The duration spending in the first two stages of sleep as well

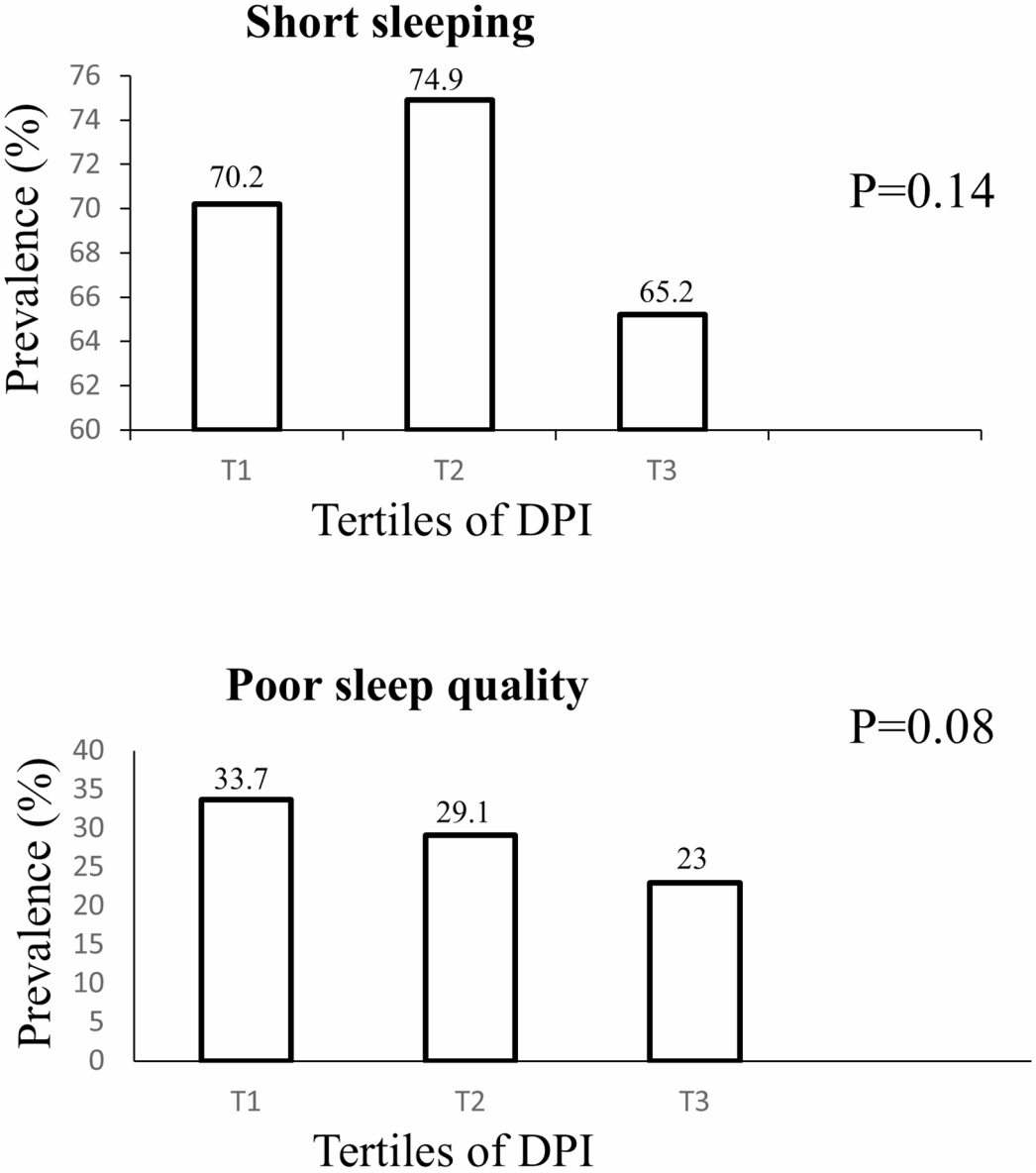

Fig. 1. Prevalence of individuals with short sleep and low sleep quality in various DPI groups.

as the rapid eye movement (REM) stage is believed to be longer in males than females, which could result in longer sleeping[45].

Regarding poor sleep quality, an inverse association was observed among normal-weight participants and females. Females are believed to get more deep sleep and having higher melatonin levels that might lead to better sleep quality than males[45]. It is also possible that there are physical effects of carrying excess weight itself, which impacts sleep quality in individuals with overweight/obesity[44]. Future studies, particularly prospective in design, are required to investigate to what extent the relationship between DPI and sleep quality/duration may vary among individuals with different BMI classifications and sexes.

Findings of the present survey revealed that hs-CRP levels were relatively lower in individuals with higher DPI scores. Our findings were in line with results of previous studies on other populations such as adults with obesity[46] and metabolic syndrome[47]. To date, the association between DPI and hs-CRP has not been examined in individuals with sleep disorders.

In our study, the mean hs-CRP level among participants was 3.18 mg/L, reflecting a moderate baseline inflammatory status. The observed decrease of approximately 0.31 mg/L in hs-CRP with each tertile in DPI tertile, although modest and not clinically significant, represented a slight improvement in systemic inflammation. Previous studies support these findings; for example, a recent meta-analysis demonstrated that similar reductions in hs-CRP were associated with significant decreases in cardiovascular events in patients with coronary artery disease[48]. Additionally, a cohort study on patients with type 2 diabetes found that small decreases in hs-CRP correlated with improved inflammatory profiles and reduced cardiovascular risk[49]. While

	DPI tertiles			
	T1 (< 25.24)	T2 (25.24–36.29)	T3 (> 36.29)	P_{trend}[2]
Short sleeping				
Cases/participants (n)	125/178	134/179	116/178	
Crude	1.00 (ref)	1.26 (0.79–2.01)	0.79 (0.51–1.24)	0.30
Model 1[3]	1.00 (ref)	1.24 (0.77–1.99)	0.72 (0.44–1.16)	0.18
Model 2[4]	1.00 (ref)	0.96 (0.57–1.62)	0.57 (0.33–0.99)	0.05
Model 3[5]	1.00 (ref)	0.96 (0.56–1.62)	0.57 (0.32–0.99)	0.04
Poor sleep quality				
Cases/participants (n)	60/178	52/179	41/178	
Crude	1.00 (ref)	0.81 (0.51–1.26)	0.59 (0.37–0.94)	0.03
Model 1[3]	1.00 (ref)	0.74 (0.47–1.17)	0.48 (0.29–0.80)	0.01
Model 2[4]	1.00 (ref)	0.72 (0.42–1.22)	0.47 (0.26–0.86)	0.01
Model 3[5]	1.00 (ref)	0.72 (0.42–1.22)	0.47 (0.26–0.86)	0.01

Table 3. Multivariable-adjusted odds ratio for short sleeping and poor sleep quality across tertiles of DPI1. [1] All values are odds ratios and 95% confidence intervals.[2]P_{trend} was obtained by the use of tertiles of DPI as an ordinal variable in the model.[3] Model 1: Adjusted for age, sex, and energy intake.[4] Model 2: Additionally adjusted for marital status, education, home ownership, family size, physical activity levels (HEPA), history of diabetes, tea and coffee intake after 8 pm, use of antidepressant medicine, and OSA.[5] Model 3: More adjustments for body mass index.Abbreviations: n, number; HEPA, Health-Enhancing Physical Activity.

the cross-sectional design of our study limits the ability to infer causality, these findings suggest a potential anti-inflammatory benefit of a phytochemical-rich diet.

Some pieces of evidence suggest that inflammatory and oxidative stress pathways are closely involved in the regulation and disruption of sleep. Elevated concentrations of pro-inflammatory cytokines, including IL-1β, TNF-α, and CRP, have been associated with sleep disorders[50]. These mediators can penetrate the blood-brain barrier and trigger neuroinflammatory responses that interfere with key neurotransmitter systems such as the glutamatergic pathway, affecting the sleep–wake cycle[51]. Concurrently, oxidative stress reflected by increased levels of MDA and diminished activity of antioxidant enzymes such as SOD and GPX contributes to neuronal dysfunction by promoting lipid peroxidation, protein oxidation, and DNA damage[52]. The brain's high metabolic rate renders it particularly vulnerable to reactive oxygen and nitrogen species, which can impair circadian regulation by modifying redox-sensitive components of the suprachiasmatic nucleus[52].

In the present study we found that participants with higher quality of sleep have lower MDA levels. No significant association was found between SOD, GPX, and hs-CRP with sleep quality and duration. In contrast with our findings, a previous study on Indonesian adults indicated an inverse association between serum MDA level and sleep duration[14]. However, a recent cross-sectional study on 9,184 Iranian adults found no significant relationship between short sleep duration and SOD levels, which was in line with our findings[17]. Moreover, a previous cross-sectional investigation on Taiwanese adults by Dowd et al. indicated no significant link between CRP levels and sleep quality[18]. However, they found that long sleep duration was associated with higher CRP levels[18]. Additionally, another cross-sectional study by Taheri et al. in 2007 revealed no relationship between sleep duration and CRP levels[19]. In contrast with our findings, a prospective study on 74,867 Korean adults found that long sleep duration and poor sleep quality were related to higher serum hs-CRP[20]. Moreover, another cross-sectional study on 8,170 Chinese adults showed that long sleep duration was positively related to higher hs-CRP levels[21]. Okun et al. also indicated that poor sleep quality was associated with higher CRP levels; however, sleep duration was not related to this biomarker[22].

DPI may influence sleep duration and quality via various potential mechanisms. DPI contains fruits, vegetables, legumes, and nuts that contain high levels of tryptophan, an amino acid that controls circadian rhythms and is recognized as a potent sleep inducer[53]. Inflammation may be the key factor in the causes of poor sleep quality[12]. Increased consumption of foods rich in phytochemicals might positively affect sleep habits by reducing inflammation[54]. DPI includes foods that promote sleep, potentially enhancing hormones like serotonin and melatonin; it is well known that melatonin and serotonin are related to sleep-wake brain centers, and reduced serotonin levels may result in inadequate sleep quality or quantity[55]. Moreover, fruits and vegetables provide abundant fiber and other vital nutrients that can positively influence the gut's microbial makeup[56], potentially leading to enhanced sleep quality[57].

Certain strengths of this research ought to be emphasized. This is the first survey that investigated DPI in relation to sleep quality and duration, along with oxidative stress and inflammatory biomarkers in a representative sample of Iranian adults. Moreover, we employed valid questionnaires to evaluate DPI and sleep health condition of participants. Nonetheless, various limitations must be considered when interpreting our results. The primary limitation of our research was its cross-sectional design, which complicated the inference of a causal link between DPI and sleep habits. It is important to note that the observed links might be biased due to reverse causation, as those with sleep disorders may alter their lifestyle habits. Therefore, future prospective studies are necessary to establish a causal link between DPI and sleep outcomes. Although we assessed dietary

	DPI tertiles			
	T1 (< 25.24)	T2 (25.24–36.29)	T3 (> 36.29)	P_{trend}[2]
Subjective sleep quality				
Cases (n)	22	23	13	
Model 1[3]	1.00 (ref)	1.09 (0.58–2.06)	0.59 (0.28–1.27)	0.21
Fully-adjusted model[4]	1.00 (ref)	1.17 (0.56–2.42)	0.49 (0.19–1.23)	0.17
Sleep latency				
Cases (n)	27	23	21	
Model 1[3]	1.00 (ref)	0.72 (0.39–1.34)	0.50 (0.26–0.97)	0.04
Fully-adjusted model[4]	1.00 (ref)	0.69 (0.33–1.42)	0.39 (0.17–0.89)	0.03
Sleep duration				
Cases (n)	68	77	68	
Model 1[3]	1.00 (ref)	1.19 (0.77–1.82)	0.89 (0.56–1.40)	0.63
Fully-adjusted model[4]	1.00 (ref)	1.03 (0.63–1.69)	0.74 (0.43–1.27)	0.28
Habitual sleep efficiency [5]				
Cases (n)	0	1	1	
Model 1[3]	1.00 (ref)	-	-	-
Fully-adjusted model[4]	1.00 (ref)	-	-	-
Sleep disturbances				
Cases (n)	23	21	12	
Model 1[3]	1.00 (ref)	0.80 (0.42–1.52)	0.34 (0.16–0.74)	0.01
Fully-adjusted model[4]	1.00 (ref)	1.01 (0.47–2.16)	0.40 (0.16–1.02)	0.07
Use of sleeping medications				
Cases (n)	7	4	7	
Model 1[3]	1.00 (ref)	0.44 (0.12–1.59)	0.50 (0.16–1.61)	0.26
Fully-adjusted model[4]	1.00 (ref)	0.51 (0.11–2.33)	0.46 (0.10–2.18)	0.33
Daytime dysfunction				
Cases (n)	30	23	20	
Model 1[3]	1.00 (ref)	0.75 (0.42–1.38)	0.73 (0.38–1.41)	0.33
Fully-adjusted model[4]	1.00 (ref)	0.95 (0.48–1.88)	0.74 (0.34–1.62)	0.47

Table 4. Multivariable-adjusted odds ratio for individual domains of sleep quality across DPI tertiles1. [1]All values are odds ratios and 95% confidence intervals.[2]P trend was obtained by considering the tertiles of DPI as ordinal variable. For each domain of sleep quality, the odds was reported for score 2–3 of that domain (as poor quality); while score 0–1 was considered as the reference category.[3]Model 1 adjusted for age, sex, and energy intake.[4]Fully adjusted model: Adjusted for age, sex, energy intake, marital status, physical activity (HEPA), homeownership, anti-depressing medication, education status, obstructive sleep apnea (OSA), family size, history of diabetes, coffee and tea intake after 8 pm, and BMI.[5]OR (95% CI) could not be calculated, due to not having cases in one tertile.

intakes of participants through a validated FFQ, recall bias or other potential reporting biases were unavoidable and could have influenced our results. Even though we took into account certain potential confounders in our analyses, residual confounding cannot be dismissed and might have influenced the results. The COVID-19 pandemic led to a decrease in sleep quality, as indicated by earlier research[58], which might, in turn, influence our findings. The phytochemical composition of calorie-free foods, including nonalcoholic drinks like tea and various spices, as well as the bioavailability of these phytochemicals, has not been taken into account in DPI calculations, potentially influencing the outcomes. Last but not least, a high percentage of participants in the current study had academic education, so extrapolating these results to the entire Iranian adult population should be done with cautious. Consequently, additional research in various nations is necessary.

In conclusion, we found that adults with higher DPI scores had a lower chance of having short sleep duration and poor sleep quality. This link was also stronger in subjects with overweight/obesity and males for sleep duration and those with normal-weight and females in the case of sleep quality. Our results showed that MDA and hs-CRP could be intermediate factors for this association. Future prospective studies should be performed to confirm whether higher DPI causally improves sleep outcomes and reduces inflammation or oxidative stress.

	DPI tertiles			
	T1 (< 25.24)	T2 (25.24–36.29)	T3 (> 36.29)	P_{trend}[2]
Short sleeping				
Males				
Cases (n)	85	77	51	
Model 1[3]	1.00 (ref)	1.06 (0.56–2.01)	0.58 (0.28–1.17)	0.16
Fully-adjusted model[4]	1.00 (ref)	0.60 (0.28–1.30)	0.42 (0.18–1.01)	0.05
Females				
Cases (n)	40	57	65	
Model 1[3]	1.00 (ref)	1.57 (0.77–3.21)	0.88 (0.45–1.72)	0.60
Fully-adjusted model[4]	1.00 (ref)	1.15 (0.51–2.59)	0.66 (0.29–1.50)	0.26
Poor quality of sleep				
Males				
Cases (n)	29	28	13	
Model 1[3]	1.00 (ref)	1.12 (0.60–2.07)	0.59 (0.27–1.29)	0.26
Fully-adjusted model[4]	1.00 (ref)	1.15 (0.54–2.45)	0.61 (0.24–1.60)	0.40
Females				
Cases (n)	31	24	28	
Model 1[3]	1.00 (ref)	0.45 (0.22–0.90)	0.37 (0.19–0.73)	0.01
Fully-adjusted model[4]	1.00 (ref)	0.50 (0.22–1.15)	0.40 (0.17–0.94)	0.04
Short sleeping				
Normal-weight participants				
Cases (n)	48	36	36	
Model 1[3]	1.00 (ref)	1.27 (0.54-3.00)	0.80 (0.33–1.91)	0.65
Fully-adjusted model[4]	1.00 (ref)	1.47 (0.50–4.28)	0.66 (0.23–1.93)	0.45
Participants with overweight/obesity				
Cases (n)	77	98	80	
Model 1[3]	1.00 (ref)	1.25 (0.70–2.23)	0.70 (0.39–1.26)	0.22
Fully-adjusted model[4]	1.00 (ref)	0.93 (0.49–1.76)	0.55 (0.27–1.09)	0.08
Poor quality of sleep				
Normal-weight participants				
Cases (n)	21	15	8	
Model 1[3]	1.00 (ref)	0.87 (0.38–1.98)	0.27 (0.10–0.75)	0.02
Fully-adjusted model[4]	1.00 (ref)	0.79 (0.27–2.32)	0.20 (0.06–0.74)	0.02
Participants with overweight/obesity				
Cases (n)	39	37	33	
Model 1[3]	1.00 (ref)	0.69 (0.40–1.20)	0.59 (0.33–1.08)	0.09
Fully-adjusted model[4]	1.00 (ref)	0.64 (0.34–1.22)	0.57 (0.27–1.19)	0.13

Table 5. Multivariate adjusted odds ratio (OR) and 95% confidence interval (CI) for short sleeping and poor quality of life across tertiles of DPI, stratified by sex and BMI categories1. [1]All values are odds ratios and 95% confidence intervals.[2]Obtained by the use of tertiles of DPI as an ordinal variable in the model.[3]Model 1: Adjusted for age, and energy intake in stratified analysis for sex categories. Adjusted for age, sex, and energy intake in stratified analysis for BMI categories.[4]Fully-adjusted model: Additionally adjusted for marital status, physical activity (HEPA), homeownership, anti-depressing medication, education status, obstructive sleep apnea (OSA), family size, history of diabetes, coffee and tea intake after 8 pm, and BMI in stratified analysis for sex categories. Additionally adjusted for marital status, physical activity (HEPA), homeownership, anti-depressing medication, education status, obstructive sleep apnea (OSA), family size, history of diabetes, coffee and tea intake after 8 pm in stratified analysis for BMI categories.

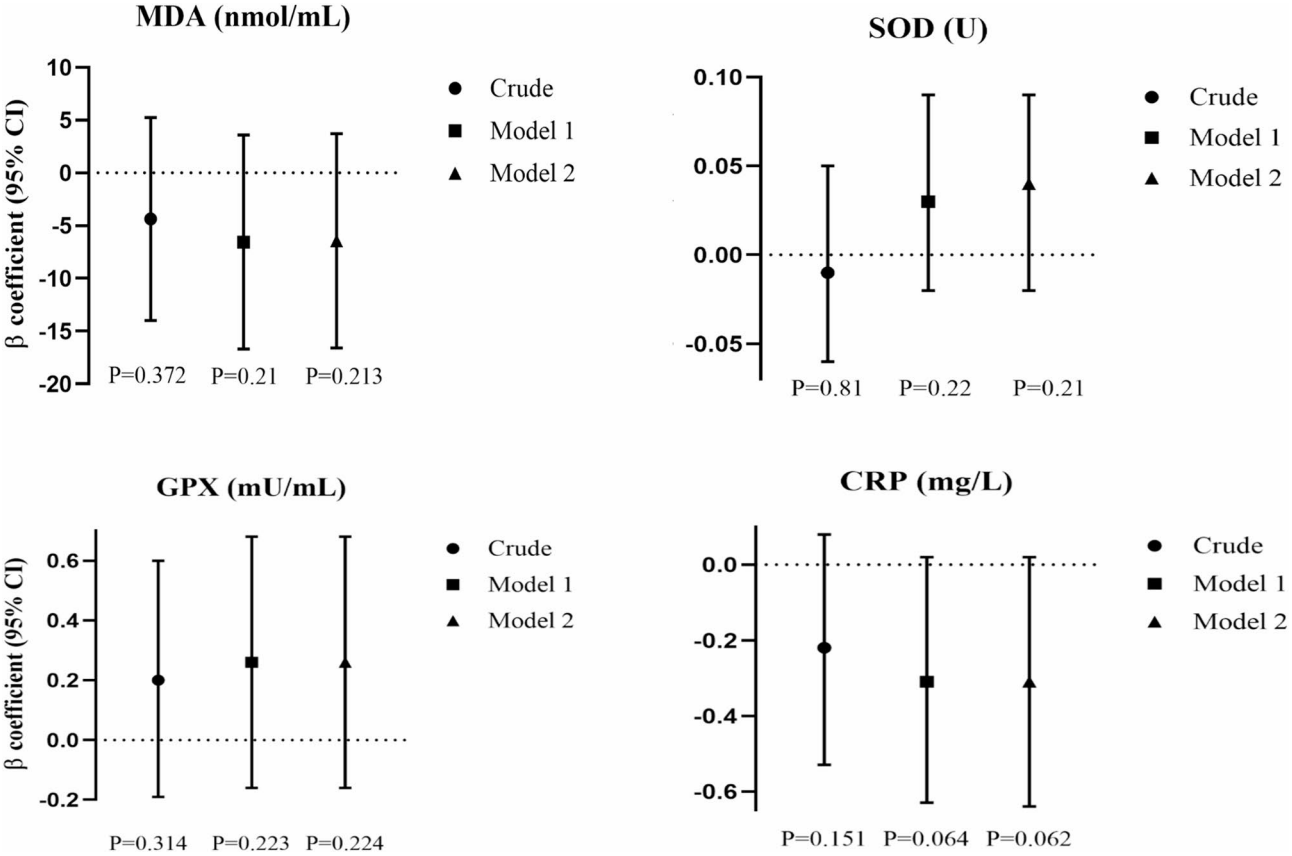

Fig. 2. Linear association between tertiles of DPI and serum levels of malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPX), and C-reactive protein (CRP). Values are β (non-standardized) regression coefficients (or B) (and 95% confidence intervals) for MDA, SOD, GPX, and CRP concentrations per one tertile increase in DPI. Model 1: Adjusted for age, and sex; Model 2: More adjustments for body mass index (BMI).

Data availability

Data described in the manuscript will be made available upon reasonable request pending application and approval to the corresponding author.

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Author contributions
AB, DP, FS, PR, and PS contributed to the conception, design, data collection, data interpretation, manuscript drafting and approval of the final version of the manuscript, and agreed on all aspects of the work.

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Declarations

Competing interests
The authors declare no competing interests.

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