

ORIGINAL STUDY

Dietary inflammatory index and dietary energy density are associated with menopausal symptoms in postmenopausal women: a cross-sectional study

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Abstract

Objectives: No previous study has evaluated the association of the dietary inflammatory index (DII) and dietary energy density (DED) with menopausal symptoms and its subclasses in postmenopausal women. The aim of this study was to evaluate the association of DII score and DED with menopausal symptoms and its subtypes in Iranian postmenopausal women.

Methods: This cross-sectional study was conducted on 393 postmenopausal women who attended health centers in the south of Tehran, Iran. The DII score was calculated using dietary factors obtained by a validated food frequency questionnaire. DED was defined as average daily energy intake (kcal) per gram of food. The Menopause Rating Scale questionnaire was used to evaluate the menopausal symptoms. The total Menopause Rating Scale score (TMRSS) was the sum of the somatic score (SS), psychological score (PS), and urogenital score. Linear regression analysis was used to assess the association of the DII score and DED with menopausal symptoms.

Results: After adjusting for covariates, participants in the highest tertile of DII score had greater SS compared to those in the lowest tertile ($\beta_{\text{DII}3\text{vs}1} = 0.032$, 95% confidence interval (CI): 0.004-0.068, $P = 0.04$). No significant relationship was found between DII score and PS, urogenital score or TMRSS. Furthermore, higher DED was associated with greater SS ($\beta_{\text{DED}3\text{vs}1} = 0.071$, 95% CI: 0.028-0.115, $P = 0.001$), PS ($\beta_{\text{DED}3\text{vs}1} = 0.065$, 95% CI: 0.012-0.121, $P = 0.01$) and TMRSS ($\beta_{\text{DED}3\text{vs}1} = 0.053$, 95% CI: 0.017-0.088, $P = 0.004$).

Conclusion: A proinflammatory diet was associated with higher menopause-specific somatic symptoms and higher DED was positively associated with menopausal symptoms.

Key Words: Diet – Dietary inflammatory index – Inflammation – Menopause.

Menopause is a natural process, characterized by a gradual reduction of ovarian hormones including progesterone, estrogen, testosterone, and androstenedione. This condition results in somatic, psychological, and urogenital symptoms.¹ Epidemiologic studies have shown

that approximately 80% of women in the postmenopausal period experience symptoms such as vasomotor menopausal symptoms (VMS) (including hot flashes and sweating), heart discomfort, irritability, and fatigue that may adversely affect their quality of life.^{2,3} Despite the role of hormone therapy

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(HT) in improving menopausal symptoms, several studies have demonstrated a positive association between HT and breast cancer, thromboembolism, and stroke.^{4,5} Therefore, heightened attention has focused on lifestyle factors, such as physical activity and dietary intake, that may reduce menopausal symptoms.^{6,7}

Diet is an important modulator of biological processes, which may play an effective role in the production and metabolism of estrogen and its related climacteric symptoms.⁸

Following the restriction of ovarian function in menopause, proinflammatory biomarkers such as tumor necrosis factor- α (TNF- α), interleukin (IL)-6, and IL-1 increase in postmenopausal women.⁹ In addition, the deposition of visceral fat increases in menopause, which can lead to the production and release of these inflammatory cytokines.¹⁰ Although visceral fat is associated with chronic conditions, such as obesity, cancer, type 2 diabetes mellitus, and cardiovascular diseases (CVDs),¹¹⁻¹⁸ the relationship between inflammation and menopausal symptoms has not been studied sufficiently. Several studies have demonstrated an inverse association between menopausal symptoms and adherence to anti-inflammatory dietary prescriptions. In a cross-sectional study conducted in Chinese postmenopausal women, higher adherence to a whole-plant food pattern was associated with reduced depression risk, whereas greater consumption of processed foods was positively related to stress.¹⁹ In another study conducted in postmenopausal women, adherence to a dietary pattern rich in vegetables and fruits was inversely associated with menopause-specific physical, mental, and general complaints. In contrast, high intake of mayonnaise, liquid oils, sweets, and desserts was positively linked to general and genitourinary symptoms of menopause. Furthermore, adherence to a dietary pattern high in solid fats, snacks, sugars, and processed meat was associated with higher scores in menopause-specific mental complaints in the same study.²⁰ Findings from a cohort study conducted in middle-aged women showed that high consumption of a Mediterranean-style diet or fruit was linked to fewer VMS. Also, a high intake of fat and sugar was associated with an increased risk of hot flushes and night sweats.²¹ In another cross-sectional study, consumption of soy foods, fruits, vegetables, and high omega-3 plant foods was associated with a lower severity of physical and vasomotor symptoms. In addition, high intake of flesh food and sweets was positively associated with severity of both vasomotor and physical symptoms.²²

The dietary inflammatory index (DII) was designed by Shivappa et al, to evaluate inflammatory load of the overall diet.²³ Evidence of the association between the DII with serum level of IL-6 and TNF- α receptor 2 (TNF α -R2) in postmenopausal women has been shown.²⁴ Other studies have reported a positive link between the DII and colorectal²⁵ and breast cancer,²⁶ lower lumbar spine bone mineral density,²⁷ and osteopenic and osteosarcopenic obesity among postmenopausal women.²⁸

Dietary energy density (DED) is a tool developed to measure diet quality based on the ratio of energy intake to food weight. DED can be calculated for each food item, daily meals, and total consumed foods.²⁹ The results of several studies have shown that high consumption of vegetables and fruits, which are nutrient dense and energy sparse,²⁹ was associated with fewer menopausal symptoms.^{19,20,30} In contrast, higher consumption of fat, sweets, and desserts, which are energy dense,³¹ was positively related to menopausal symptoms.²⁰ Although some studies have assessed the relationship between a single food item and the DED³² or dietary patterns and menopausal symptoms,^{19,20,30} there is no study evaluating the association between DED and menopausal symptoms.

A high-energy-density diet was positively associated with serum inflammatory biomarkers such as high-sensitivity C-reactive protein,^{33,34} whereas adopting a low-energy-dense diet was related to a decreased level of chronic inflammation.³⁵

Given that there is a high prevalence of menopausal symptoms among postmenopausal women³⁶ and the absence of any studies evaluating the association of the DII score and DED with menopausal symptoms, the current study was designed to investigate the association of the DII score and DED with climacteric symptoms and its subclasses in postmenopausal women.

MATERIALS AND METHODS

Study participants

Complete details of this cross-sectional study have been described elsewhere.³⁷ Briefly, this study was conducted from September 2016 to September 2017 on 393 postmenopausal women living in southern regions of Tehran, Iran. Figure 1 shows the participants' enrollment. The following describes the sampling methods. Two out of six southern areas of Tehran were selected through random sampling. In the next phase, 10 urban health centers from 2 areas affiliated with Tehran University of Medical Sciences were randomly selected for the data collection. Study participants were postmenopausal women with at least 1 year since the last menstrual period. Individuals with body mass index (BMI) 40 kg/m² or more, currently smoking habit, or having medical conditions such as cancer, diabetes, stroke, multiple sclerosis, dementia, and hyper- or hypothyroidism diagnosed by a physician or any long-term dietary modification and women who had taken any form of HT for at least 6 months before the study were excluded. All eligible participants who agreed to participate in the study provided written informed consent. The Research Ethics Committee of Tehran University of Medical Sciences approved the study protocol.

Assessment of general characteristics, socioeconomic status, anthropometry, and physical activity

Data on sociodemographic and current chronic diseases including CVDs, musculoskeletal, endocrine, and metabolic diseases; intake of medication; and dietary supplements were recorded by standard questionnaire administered by trained interviewers during face-to-face interviews.

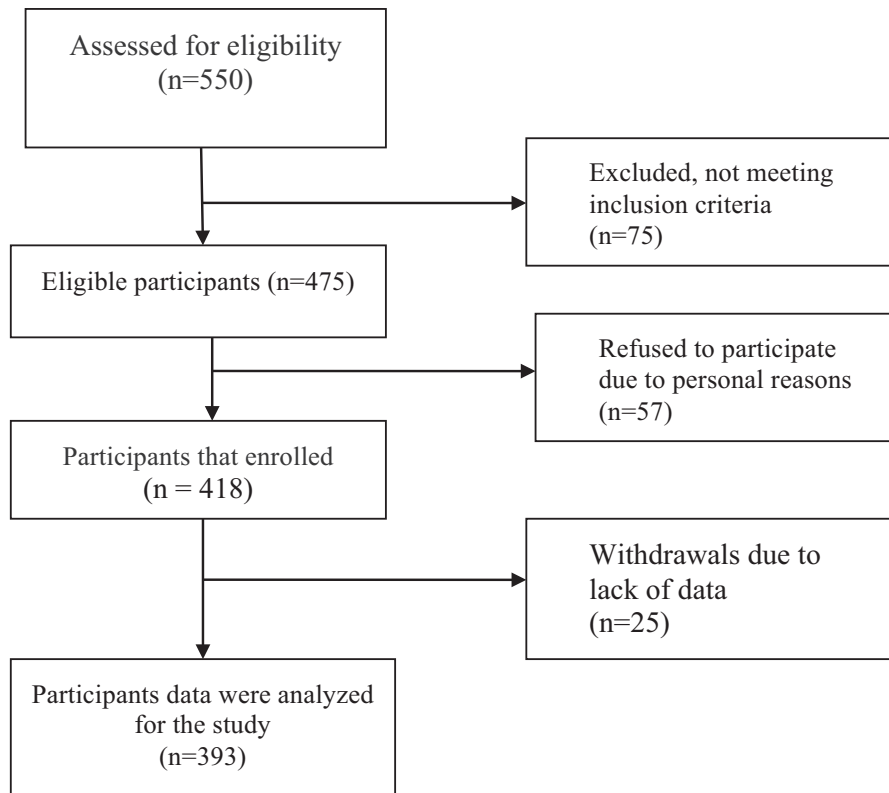


FIG. 1. Flow diagram of participant enrollment.

Socioeconomic status (SES) was assessed by summing the number of possessions, including home or car, freezer, computer, flat-screen television, handmade carpet, dishwasher, villa or additional home, and microwave. Participants with three or few possessions were categorized as low SES, women with four to six possessions were categorized as moderate SES and those with seven or more possessions were categorized as high SES.³⁸

Anthropometric measures were determined by standard protocol. Height and weight were recorded with participants wearing light clothing and in bare feet using a wall-mounted stadiometer to the nearest 0.5 cm and digital scale (Seca725 GmbH & Co., Hamburg, Germany) to the nearest 0.1 kg, respectively. To measure waist circumference, a flexible tape was held at the midpoint between the lowest rib and the iliac crest while participants were standing and breathing out. Height (m) and weight (kg) measures were collected to calculate BMI (kg/m^2).

Physical activity was determined by the short form of the International Physical Activity Questionnaire. Physical activity was defined as reporting the times spent on strenuous, moderate, and mild physical activity over the previous week, multiplied by their metabolic equivalent quantities and cumulative values were reported as metabolic equivalent (min/wk).³⁹ The reliability and validity of the International Physical Activity Questionnaire across 12 countries were assessed and the result showed that it can be used in different languages.⁴⁰

Dietary assessment

A validated 147-item food frequency questionnaire (FFQ) was administered by the trained dietitian to gain data on dietary intake of participants during the past year. This questionnaire has been tested for validity and reliability in a healthy population⁴¹ in Tehran. The participants reported the frequency of each food item consumed (the standard serving size) on daily, weekly, or monthly basis. Data obtained from the FFQ were then transformed into grams per day to describe the daily food intake. The nutrient and energy composition of the foods were computed using the Nutritionist 4 software (First Databank; Hearst, San Bruno, CA) developed for Iranian foods. Spice items, such as turmeric and thyme, were included in the FFQ.

Calculation of the DII and DED

The DII score was computed based on the dietary data obtained from the FFQ. Full details of procedure applied for development of this index have been reported elsewhere.²³ In brief, 1,943 articles reporting on the effect of dietary components on inflammatory biomarkers (including IL-1 β , IL-4, IL-6, IL-10, TNF- α , and C-reactive protein) and they were evaluated and scored, with +1 applied to dietary components with proinflammatory properties, -1 assigned to anti-inflammatory dietary factors, and 0 assigned to dietary factors without any impact on inflammatory biomarkers. A total of 45 dietary factors were identified from this extensive

literature search. In order to compute DII, the dietary data including macronutrients, micronutrients, food items, spices, and flavonoids were first linked to the worldwide database that provided a robust estimate of a mean and standard deviation (SD) for each of them. Then these dietary factors were used to compute the *z*-score by subtracting the “global mean intake” from the reported intake of each dietary factor and then dividing the obtained value by the world SD. Global mean intake and SD for each dietary factor were determined through datasets of 11 countries including New Zealand, South Korea, USA, Australia, Denmark, UK, Bahrain, India, Japan, Taiwan, and Mexico. To reduce the effect of “right skewing,” the obtained *z* score for each dietary factor was converted to a proportion score with values from 0 to 1. Then, to obtain a symmetrical distribution which ranged from -1 to $+1$ and centered on 0, the proportion score for each dietary factor was multiplied by 2 and then 1 was subtracted from it. The achieved value for each dietary factor was multiplied by overall dietary factor-specific inflammatory effect score to capture dietary factor-specific DII score. Finally, all dietary factor-specific DII scores were summed to calculate the DII score for each participant.

Theoretically, the total DII score can range from -8.87 to $+7.98$, although values within individual studies were rarely outside the range of -5.5 to $+5.5$. Lower values of the DII score reflect a more anti-inflammatory diet, whereas a higher DII score indicates a more proinflammatory diet.

In this study, the DII score was obtained using 34 dietary factors. The proinflammatory component included energy, total fat, protein, carbohydrate, cholesterol, saturated fatty acids, iron, and vitamin B12 and the anti-inflammatory components were ginger, turmeric, thyme, garlic, onion, pepper, black tea, zinc, selenium, magnesium, monounsaturated fatty acids (MUFAs), polyunsaturated fatty acids (PUFAs), n-3 and n-6 fatty acids, fiber, thiamin, riboflavin, niacin, vitamin B6, folic acid, vitamin A, vitamin C, vitamin D, vitamin E, β -carotene, and caffeine. The other dietary factors of DII score (ie, alcohol, eugenol, anthocyanidins, flavan-3-ol, flavones, flavonols, flavonones, isoflavones, trans fat, saffron, and rosemary) were not used in the computation of DII score due to lack of data on the amount of their daily intake. Before computation of the DII score, all dietary factors were adjusted for energy intake by the residual method.⁴² Then, obtained values for dietary factors were summed to create the DII score calculation. Fortified foods consumption was not reported by any of the participants. In addition, because there were no data available on the amount of nutrients from supplements, nutrient intakes from supplements were not taken into account for the computation of DII score.

The DED was calculated by dividing the daily energy intake (kcal) of consumed food by its total weight (g). In the current study, the DED was calculated by using foods and beverages, excluding water.⁴³

Assessment of menopausal symptoms

Data on menopausal symptoms were obtained through the Menopause Rating Scale questionnaire.⁴⁴ The validity and

reliability of this questionnaire among Iranian menopausal-aged women have been assessed previously.⁴⁵ This questionnaire consists of 11 items that are categorized into three subscales: somatic symptoms (hot flushes, sweating, sleep problems, heart discomfort, joint and muscle complaints), psychological symptoms (depression, irritability, anxiety, physical and mental exhaustion), and genitourinary symptoms (dryness of vagina, sexual problems, and bladder complaints). Women scored each complaint from 0 (no symptom) to 4 (1, mild; 2, moderate; 3, severe; 4, extremely severe) based on the severity they experienced within the last month. The total Menopause Rating Scale score (TMRSS) was assessed by summing somatic score (SS), psychological score (PS), and urogenital score (US), producing scores ranging from 0 to 44.⁴⁴

Statistical analysis

Variables were examined for normality using the Kolmogorov-Smirnov test. Logarithm (log) transformations were conducted for variables with nonnormal distribution. The DII score and DED were analyzed as categorical (tertiles) variables. Findings on quantitative variables across the tertiles of DII score and DED were presented as means \pm SDs or median (interquartile range) for normal and nonnormal variables, respectively. In addition, qualitative variables were expressed as the number (percentage). One-way analysis of variance test was performed to compare the mean values of general characteristics, intake of energy, and micro and macronutrients with normal distribution across the DII and DED tertiles. Furthermore, Kruskal-Wallis test was used for comparing medians of variables with skewed distribution. Comparison of the percentage of categorical variables across the DII tertiles was made using the χ^2 test. Moreover, linear regression models were used to assess the relation of the DII score and DED with TMRSS and each subscale. Linear trend for TMRSS and its three subscales across the DII and DED tertiles was achieved by entering the DII and DED tertiles in the regression model as an independent variable in the crude model (Model I) and in an adjusted model (Model II). Age, time since menopause, marital status, educational level, physical activity, SES, BMI, dietary tea and coffee, energy intake, dietary supplement use (yes, no), and CVDs (yes, no) for the DII score in Model II. Furthermore, for the DED in Model II, these covariates were controlled: age, time since menopause, marital status, educational level, physical activity, SES, BMI, tea and coffee, dietary supplement use (yes, no), and CVDs (yes, no). All statistical analyses were performed using SPSS version 20 software package for windows (SPSS Inc., Chicago, IL). A *P* value less than 0.05 was regarded as demarcating statistical significance.

RESULTS

In this study, a total of 393 postmenopausal women aged 40 to 76 years were recruited. Table 1 shows the distribution of general characteristics of participants across the DII and DED tertiles. There was no association between the DII score and

TABLE 1. Characteristics of study population according to tertiles of dietary inflammatory index score and dietary energy density score, Tehran, Iran, 2016-2017

Characteristics	Tertiles of DII score			P	Tertiles of DED			P ^a
	T ₁ (n = 131) -4.33, -0.82	T ₂ (n = 131) -0.83, 0.72	T ₃ (n = 131) 0.73, 4.21		T ₁ (n = 131) 0.45, 0.82	T ₂ (n = 131) 0.83, 0.95	T ₃ (n = 131) 0.96, 1.96	
Age, y ^b	57.0 (53.0, 64.0)	56.0 (52.0, 61.0)	56.0 (53.0, 60.0)	0.1 ^c	57.0 (53.0, 64.0)	56.0 (52.0, 60.0)	56.0 (53.0, 60.0)	0.3 ^c
Educational level, y ^b	4.0 (0.0, 6.0)	4.0 (0.0, 6.0)	2.0 (0.0, 5.0)	0.1 ^c	4.0 (0.0, 6.0)	5.0 (0.0, 6.0)	2.0 (0.0, 5.0)	0.04 ^e
Time since menopause, y ^b	7.0 (3.0, 15.0)	5.5 (3.0, 12.0)	6.0 (2.0, 11.0)	0.2 ^c	7.0 (3.0, 14.0)	7.0 (3.0, 14.0)	5.0 (2.0, 10.0)	0.08 ^e
Body weight, kg ^d	73.7 ± 10.8	73.6 ± 10.9	74.4 ± 11.0	0.8 ^a	73.4 ± 10.9	74.2 ± 10.6	74.3 ± 11.2	0.7 ^a
Height, cm ^d	156.0 ± 6.1	155.8 ± 6.1	155.7 ± 6.7	0.9 ^a	155.3 ± 6.3	156.5 ± 6.1	155.7 ± 6.4	0.3 ^a
BMI, kg/m ^{2d}	30.3 ± 4.1	30.3 ± 4.3	30.7 ± 4.4	0.6 ^a	30.4 ± 4.1	30.3 ± 4.2	30.6 ± 4.5	0.7 ^a
WC (cm) ^d	104.7 ± 10.7	103.7 ± 11.3	104.6 ± 11.7	0.7 ^a	104.2 ± 10.9	104.3 ± 11.0	104.5 ± 11.9	0.9 ^a
Total PA, MET-min/wk ^b	572.5 (231.0, 973.0)	462.0 (240.0, 945.0)	462.0 (198.0, 993.0)	0.5 ^c	522.0 (198.0, 988.5)	492.7 (240.0, 891.0)	431.5 (212.0, 990.0)	0.6 ^c
Marital status ^e								
Single/divorced/widowed	31 (7.9)	29 (7.4)	30 (7.6)	0.9 ^f	27 (6.9)	33 (8.4)	30 (7.6)	0.6 ^f
Married	100 (25.4)	102 (26.0)	101 (25.7)		104 (26.5)	98 (24.9)	101 (25.7)	
Occupation ^e								
Housekeeper	123 (31.3)	125 (31.8)	126 (32.1)	0.6 ^f	124 (31.6)	122 (31.0)	128 (32.6)	0.2 ^f
Employee/retiree	8 (2.0)	6 (1.5)	5 (1.3)		7 (1.8)	9 (2.3)	3 (0.8)	
SES ^{e,g}								
Low	94 (23.9)	77 (19.6)	85 (21.6)	0.08 ^f	90 (22.9)	85 (21.6)	81 (20.6)	0.5 ^f
Average/high	37 (9.4)	54 (13.7)	46 (11.7)		41 (10.4)	46 (11.7)	50 (12.7)	
Dietary supplement use ^e								
Yes	76 (19.3)	71 (18.1)	62 (15.8)	0.2 ^f	67 (17.0)	74 (18.8)	68 (17.3)	0.6 ^f
No	55 (14.0)	60 (15.3)	69 (17.6)		64 (16.3)	57 (14.5)	63 (16.0)	
CVDs ^e								
Yes	48 (12.2)	38 (9.7)	46 (11.7)	0.3 ^f	48 (12.2)	44 (11.2)	40 (10.2)	0.5 ^f
No	83 (21.1)	93 (23.7)	85 (21.6)		83 (21.1)	87 (22.1)	91 (23.2)	

BMI, body mass index; CVD, cardiovascular disease; MET, metabolic equivalent; PA, physical activity; SES, socioeconomic status; WC, waist circumference.

^aP values obtained using one-way analysis of variance test.

^bValues are median (interquartile range).

^cP values obtained using Kruskal-Wallis test.

^dValues are means ± SD.

^eNumber of participants having the characteristic (%).

^fP values obtained using Chi-square test.

^gSocioeconomic status represents having three or lesser living items for low status, four to six living items for average status, and seven to nine living items at home for high status.

general characteristics of the participants. Furthermore, we observed no association between the DED and general characteristics of postmenopausal women except for educational level (P value = 0.04). Individuals with a greater DED had lower educational levels compared to those with a lower DED.

The distribution of dietary intakes of participants based on the tertiles of the DII and DED is shown in Table 2. Participants in the highest category of the DII score had higher intake of energy, total fat, and saturated fatty acid (P value <0.01), and lower intake of carbohydrates, proteins, β -carotene, vitamin C, and fiber (all P values <0.05). Moreover, postmenopausal women in the highest category of the DED had greater intake of energy, MUFA, PUFA, and n-6 fatty acids (P value <0.05) and lower intake of proteins, β -carotene, and vitamin C (P value <0.01).

The association between the DII score and menopausal symptoms and its subclasses is presented in Table 3. After adjusting for covariates, participants in the highest tertile of DII score had higher log of SS compared to those in the first quartile as reference in both the crude ($\beta_{\text{DII}3\text{vs}1} = 0.034$, 95% confidence interval [CI]: 0.001-0.069, P value = 0.04) and the multivariable model ($\beta_{\text{DII}3\text{vs}1} = 0.032$, 95% CI: 0.004-0.068, P value = 0.04). In the crude model, the DII score was inversely associated with log of US ($\beta_{\text{DII}3\text{vs}1} = -0.045$, 95% CI: -0.088 to -0.003, P value = 0.03), although this association did not remain significant after adjusting for the potential confounders. The association of the DII score with PS and TMRSS was not statistically significant in the crude and multivariable models. The DII score was positively correlated with DED (P value <0.001, correlation coefficient = 0.65).

The association between the DED (as categorical variable) and menopausal symptoms and its subclasses is shown in Table 4. After adjusting for covariates, individuals with a higher DED had greater log of SS compared to those in the first tertile as reference in crude ($\beta_{\text{DED}3\text{vs}1} = 0.041$, 95% CI: 0.006-0.076, P value = 0.02) and multivariable models ($\beta_{\text{DED}3\text{vs}1} = 0.071$, 95% CI: 0.028-0.115, P value = 0.001). Moreover, participants in the highest category of the DED had a higher log of PS compared to those in the first tertile of the DED ($\beta_{\text{DED}3\text{vs}1} = 0.065$, 95% CI: 0.012-0.121, P value = 0.01). Postmenopausal women with a higher DED had greater log of TMRSS compared to those in the first tertile ($\beta_{\text{DED}3\text{vs}1} = 0.053$, 95% CI: 0.017-0.088, P value = 0.004). No significant association was observed between the DED and log of US.

Sensitivity analyses were performed by removing women who were obese (BMI >29.9 kg/m²) or had CVDs from the statistical analysis. The results, however, remained unchanged (Tables 5 and 6).

DISCUSSION

Findings from our study provided evidence that participants with higher DII scores had higher somatic symptoms compared to those with an anti-inflammatory diet. In addition, individuals with a higher DED had greater somatic, psychological, and total

menopause symptoms compared to those with a lower DED as reference. These findings support the hypothesis that consuming proinflammatory and energy-dense diets may put women at a higher risk of adverse menopausal symptoms. To the best of our knowledge, no study has been conducted to examine the association of the DII score and DED with menopausal symptoms.

The results of the present study showed that there was a positive association between the DII score and DED with somatic symptoms, which was consistent with previous studies reporting the association between healthy/high-quality diets and menopausal symptoms, particularly VMS. For example, results from the Australian Longitudinal Study on Women's Health over 9 years of follow-up showed that diets adhering to a Mediterranean-style dietary pattern were associated with a lower risk of reporting VMS.²¹ Furthermore, healthy dietary patterns, including high intake of vegetables, fruits, legumes, seeds, and nuts and whole-plant food diet and low intake of sweets, mayonnaise and liquid oils, desserts, potatoes, refined grains, and little or no animal foods were associated with fewer VMS.^{20,46} A cross-sectional study conducted on Chinese postmenopausal women reported that a higher consumption of whole plant foods was inversely related to nonspecific symptoms of menopause.³⁰ A recent study evaluating VMS and physical symptoms among vegan and omnivorous women aged 45 to 80 years found that perimenopausal women following the vegan diets reported fewer discomforting VMS and physical symptoms as compared with omnivores.²² The link between the DII score and somatic symptoms is further supported by evidence from clinical trials that revealed supplementation with nutrients that are known to be anti-inflammatory including vitamin E, omega 3, and polyphenol antioxidant (proanthocyanidin) decreased the severity and frequency of hot flashes, anxiety, and insomnia in postmenopausal women.⁴⁷

No significant relationship was observed between DII and psychological symptoms. In contrast to this finding, previous evidence indicated an increased risk of depression among middle-aged women with a higher DII score.^{48,49} Moreover, another study revealed a positive link between the consumption of processed foods and stress in postmenopausal women. Conversely, higher consumption of whole plant foods was inversely associated with depression.¹⁹ The findings of our study regarding the positive association between DED and psychological symptoms is supported by a study among Chinese postmenopausal women that revealed poor-quality diets, such as intake of processed foods, was associated with higher depression and perceived stress and lower self-esteem score. By contrast healthy diets, such as whole-plant foods, were associated with a lower risk of depression and psychological symptoms.¹⁹ The reasons for the inconsistent findings could be attributed to the difference in the design of the studies; characteristics of participants, including various ethnicities; outcome measures; variable food components in the diet; and different geographic, environmental, cultural, and social conditions.²⁰ We, however, speculate that variability

TABLE 2. Daily dietary intakes of the study participants according to the tertiles (T) of dietary inflammatory index score and dietary energy density score, Tehran, Iran, 2016-2017^a

	Tertiles of DII score			Tertiles of DED			P
	T ₁ (n = 131)	T ₂ (n = 131)	T ₃ (n = 131)	T ₁ (n = 131)	T ₂ (n = 131)	T ₃ (n = 131)	
Energy, kcal ^b	2149.24 ± 533.65	2127.31 ± 530.66	2361.01 ± 478.92	2049.67 ± 548.86	2231.67 ± 506.07	2311.22 ± 497.77	0.003 ^c
Carbohydrates, g ^d	332.60 (316.82, 347.59)	329.12 (311.66, 349.04)	319.50 (287.09, 347.54)	329.91 (309.23, 349.19)	327.89 (313.59, 345.93)	325.73 (294.27, 350.23)	0.4 ^c
Total fat, g ^d	69.20 (63.59, 77.07)	71.20 (63.41, 81.84)	76.83 (64.76, 93.18)	71.72 (63.52, 80.99)	71.78 (64.22, 81.27)	71.94 (62.72, 88.42)	0.5 ^c
Proteins, g ^b	84.41 ± 10.17	77.47 ± 10.40	74.18 ± 10.38	80.12 ± 11.82	80.08 ± 11.22	75.86 ± 9.84	0.002 ^c
SFA, g ^d	19.08 (16.30, 21.92)	20.24 (17.23, 22.49)	22.31 (18.74, 25.50)	20.51 (16.89, 23.15)	20.56 (17.52, 22.80)	20.38 (17.24, 23.75)	0.9 ^c
MUFA, g ^d	23.44 (20.92, 27.28)	24.12 (20.82, 28.96)	25.33 (20.03, 34.56)	23.36 (19.81, 27.62)	23.78 (20.68, 28.95)	25.33 (21.55, 31.17)	0.01 ^e
PUFA, g ^d	16.16 (14.01, 19.00)	15.91 (12.18, 20.76)	15.47 (11.65, 22.67)	15.36 (13.10, 18.47)	15.37 (12.33, 19.76)	17.17 (13.61, 22.96)	0.006 ^c
n-3 Fatty acids, g ^d	1.18 (0.89, 1.54)	1.13 (0.84, 1.51)	1.08 (0.78, 1.76)	1.08 (0.83, 1.51)	1.11 (0.85, 1.56)	1.27 (0.82, 1.72)	0.3 ^c
n-6 Fatty acids, g ^d	13.58 (11.60, 16.37)	13.71 (10.30, 18.48)	13.19 (10.14, 19.84)	12.79 (10.52, 16.10)	13.21 (10.09, 17.39)	15.27 (11.72, 20.62)	0.002 ^c
β-Carotene, μg ^b	6498.68 ± 1927.92	4600.57 ± 1541.62	3417.16 ± 1596.13	5407.86 ± 2054.80	5243.57 ± 2204.47	3864.99 ± 1726.95	<0.001 ^c
Vitamin C, mg ^d	233.25 (197.92, 274.50)	177.32 (146.36, 222.01)	142.47 (103.86, 193.73)	222.01 (174.61, 287.94)	200.47 (156.95, 252.67)	142.86 (105.11, 187.37)	<0.001 ^c
Vitamin E, mg ^b	14.71 ± 4.20	13.17 ± 4.10	13.93 ± 4.84	13.95 ± 4.21	13.38 ± 4.29	13.94 ± 4.79	0.4 ^c
Fiber, g ^b	61.21 ± 14.13	57.53 ± 16.89	51.35 ± 17.62	54.47 ± 15.21	57.33 ± 15.34	58.29 ± 19.25	0.1 ^c

MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid, SFA, saturated fatty acid.

^aNutrient intakes expressed as energy-adjusted residuals.

^bValues are means ± SD.

^cP values obtained using analysis of variance test.

^dValues are median (interquartile range).

^eP values obtained using Kruskal-Wallis test.

TABLE 3. Multivariate linear regression analyses of dietary inflammatory index for menopausal symptoms and its subclasses, Tehran, Iran, 2016-2017^a

Model I ^{a,d}	DII tertiles	Somatic score ^b			Psychological score ^b			Urogenital score ^b			Total MRS score ^b			
		T ₁	T ₂	T ₃	P	T ₁	T ₂	T ₃	P	T ₁	T ₂	T ₃	P	
Model I ^{a,d}	T ₁	(-4.33, -0.82)												
	n = 131													
	T ₂	(-0.83, 0.72)	0.026 (-0.009, 0.062)	0.1	0.019 (-0.025, 0.062)	0.3	-0.051 (-0.093, -0.008)	0.02	0.004 (-0.025, 0.033)					0.7
	n = 131													
	T ₃	(0.73, 4.21)	0.034 (0.001, 0.069)	0.04	0.035 (-0.009, 0.078)	0.1	-0.045 (-0.088, -0.003)	0.03	0.016 (-0.013, 0.044)					0.2
Model II ^{c,e}	T ₁	(-4.33, -0.82)												
	n = 131													
	T ₂	(-0.83, 0.72)	0.029 (-0.005, 0.064)	0.08	0.018 (-0.024, 0.061)	0.3	-0.040 (-0.082, 0.002)	0.06	0.007 (-0.021, 0.035)					0.6
	n = 131													
	T ₃	(0.73, 4.21)	0.032 (0.004, 0.068)	0.04	0.035 (-0.010, 0.079)	0.1	-0.043 (-0.086, 0.001)	0.056	0.015 (-0.015, 0.044)					0.3
Model II ^{c,e}	P-trend		0.04		0.1		0.052							
	n = 131													

DII, dietary inflammatory index; MRS, Menopause Rating Scale.

^aData presented as β (95% confidence interval).

^bSomatic score; psychological score; urogenital score; and total MRS score were log 10-transformed.

^cLinear regression was used.

^dCrude model.

^eAdjusted for age, time since menopause, marital status, educational level, physical activity, socioeconomic status, body mass index, dietary tea and coffee, energy intake, dietary supplement use (yes, no), and cardiovascular diseases (yes, no).

TABLE 4. Multivariate linear regression analyses of dietary energy density for menopausal symptoms and its subclasses, Tehran, Iran, 2016-2017^a

Model I ^{c,d}	DED tertiles	Somatic score ^b	P	Psychological score ^b	P	Urogenital score ^b	P	Total MRS score ^b	P
		Reference		Reference		Reference		Reference	
	T ₁ (0.45, 0.82) n = 131	-0.006 (-0.040, 0.029)	0.7	0.028 (-0.016, 0.071)	0.2	0.008 (-0.035, 0.051)	0.7	0.011 (-0.018, 0.039)	0.4
	T ₂ (0.83, 0.95) n = 131	0.041 (0.006, 0.076)	0.02	0.042 (-0.001, 0.085)	0.055	-0.035 (-0.078, 0.008)	0.1	0.024 (-0.005, 0.053)	0.1
	T ₃ (0.96, 1.96) n = 131	0.02	-	0.055	-	0.1	-	0.1	-
	P-trend	Reference		Reference		Reference		Reference	
	T ₁ (0.45, 0.82) n = 131	0.014 (-0.024, 0.052)	0.4	0.044 (-0.003, 0.091)	0.06	0.035 (-0.012, 0.082)	0.1	0.029 (-0.002, 0.060)	0.06
	T ₂ (0.83, 0.95) n = 131	0.071 (0.028, 0.115)	0.001	0.065 (0.012, 0.121)	0.01	0.009 (-0.045, 0.063)	0.7	0.053 (0.017, 0.088)	0.004
	T ₃ (0.96, 1.96) n = 131	0.001	-	0.01	-	0.8	-	0.004	-
	P-trend	Reference		Reference		Reference		Reference	

DED, dietary energy density; MRS, Menopause Rating Scale.

^aData presented as β (95% confidence interval).

^bSomatic score; psychological score; urogenital score; and total MRS score were log 10-transformed.

^cLinear regression was used.

^dCrude model.

^eAdjusted for age, time since menopause, marital status, educational level, physical activity, socioeconomic status, body mass index, dietary tea and coffee, dietary supplement use (yes, no), and cardiovascular diseases (yes, no).

TABLE 5. Multivariate linear regression analyses of dietary inflammatory index for menopausal symptoms and its subclasses in women without obesity and cardiovascular disease, Tehran, Iran, 2016-2017^a

Model I ^{c,d}	DII tertiles	Somatic score ^b	P	Psychological score ^b	P	Urogenital score ^b	P	Total MRS score ^b	P
		Reference		Reference		Reference		Reference	
	T ₁ (-4.33, -0.72) n = 49	0.019 (-0.042, 0.081)	0.1	0.032 (-0.043, 0.065)	0.2	-0.082 (-0.128, -0.012)	0.02	-0.002 (-0.054, 0.049)	0.8
	T ₂ (-0.71, 0.69) n = 50	0.042 (0.007, 0.074)	0.03	0.044 (-0.032, 0.087)	0.1	-0.053 (-0.088, -0.018)	0.01	0.020 (-0.032, 0.072)	0.2
	T ₃ (0.70, 3.78) n = 49	0.03	-	0.1	-	0.01	-	0.3	-
	P-trend	Reference		Reference		Reference		Reference	
	T ₁ (-4.33, -0.72) n = 49	0.032 (-0.001, 0.075)	0.1	0.020 (-0.056, 0.096)	0.2	-0.065 (-0.098, 0.001)	0.06	0.01 (-0.064, 0.041)	0.4
	T ₂ (-0.71, 0.69) n = 50	0.045 (0.010, 0.086)	0.04	0.053 (-0.029, 0.085)	0.1	-0.042 (-0.076, 0.001)	0.06	0.022 (-0.035, 0.079)	0.2
	T ₃ (0.70, 3.78) n = 49	0.04	-	0.1	-	0.06	-	0.2	-
	P-trend	Reference		Reference		Reference		Reference	

DII, dietary inflammatory index; MRS, Menopause Rating Scale.

^aData presented as β (95% confidence interval).

^bSomatic score; psychological score; urogenital score; and total MRS score were log 10-transformed.

^cLinear regression was used.

^dCrude model.

^eAdjusted for age, time since menopause, marital status, educational level, physical activity, socioeconomic status, body mass index, dietary tea and coffee, energy intake, and dietary supplement use (yes, no).

TABLE 6. Multivariate linear regression analyses of dietary energy density for menopausal symptoms and its subclasses in women without obesity and cardiovascular disease, Tehran, Iran, 2016-2017^a

Model I ^{c,d}	DED tertiles	Somatic score ^b	P	Psychological score ^b	P	Urogenital score ^b	P	Total MRS score ^b	P
		Reference		Reference		Reference		Reference	
	T ₁ (0.45, 0.83) n = 49	0.004 (-0.057, 0.065)	0.7	0.016 (-0.059, 0.090)	0.2	0.018 (-0.052, 0.088)	0.4	0.008 (-0.043, 0.060)	0.3
	T ₂ (0.84, 0.97) n = 50	0.054 (0.008, 0.088)	0.02	0.068 (-0.007, 0.098)	0.07	-0.067 (-0.098, 0.015)	0.08	0.029 (-0.022, 0.081)	0.1
	T ₃ (0.98, 1.82) n = 49 P-trend	0.02 Reference	-	0.06 Reference	-	0.08 Reference	-	0.1 Reference	-
Model II ^{c,e}	DED tertiles								
		Reference		Reference		Reference		Reference	
	T ₁ (0.45, 0.83) n = 49	0.026 (-0.044, 0.095)	0.6	0.022 (-0.003, 0.062)	0.09	0.062 (-0.015, 0.095)	0.1	0.027 (-0.031, 0.085)	0.08
	T ₂ (0.84, 0.97) n = 50	0.084 (0.033, 0.135)	0.003	0.075 (0.012, 0.147)	0.03	0.008 (-0.089, 0.065)	0.6	0.056 (0.015, 0.095)	0.007
	T ₃ (0.98, 1.82) n = 49 P-trend	0.003 Reference	-	0.03 Reference	-	0.7 Reference	-	0.007 Reference	-

DED, dietary energy density; MRS, Menopause Rating Scale.

^aData presented as β (95% confidence interval).^bSomatic score; psychological score; urogenital score; and total MRS score were log 10-transformed.^cLinear regression was used.^dCrude model.^eAdjusted for age, time since menopause, marital status, educational level, socioeconomic status, body mass index, dietary tea and coffee, and dietary supplement use (yes, no).

observed in the association of DII and DED with psychological symptoms could be partially attributed to the difference in dietary fatty acid intake. Our results indicated that participants with a higher DED consumed more MUFA, overall PUFA and n-6 PUFA, while these unsaturated fatty acids had similar intakes across the tertiles of the DII. It is documented that higher intake of these unsaturated fatty acids, particularly n-6 fatty acids, concomitant with a lower intake of n-3 PUFA, has been associated with a decline in psychological health.^{50,51} Further studies are needed to confirm these results and determine to what extent intake of specific fatty acids may mediate the effect of DII and DED in relation to psychological symptoms.

No significant association was found between the DII score and DED with urogenital symptoms. Several factors including personal and cultural beliefs could affect sexual desire and function during this period⁵²; therefore, some unknown factors might have influenced our results.

In the present study, the DII score ranged from -4.33 to 4.21. The range of DII scores varies widely across populations; that is, it has been reported from -4.49 to 5.39 in Iran,⁵³ -6.14 to 5.80 in Australia,⁵⁴ and -5.14 to 3.97 in Spain.⁵⁵

We found a range of 0.45 to 1.82 (kcal/g) for DED. Values in this range have been reported in America 0.46 to 3.94 (kcal/g),⁵⁶ in Ireland 4.93 to 5.92 (kcal/g)⁵⁷ and in Spain 0.93 to 2.11 (kcal/g).⁵⁸ The difference in the range of DII score and DED may be attributed to the characteristics of study participants, their race, and culture which may affect food choices.

The main strength of the present study is that it is the first to examine the association of DII score and DED with menopausal symptoms. Other strengths of the current study are its relatively large sample size and measurement of a variety of covariates, with the concomitant ability to control for multiple covariates. Applying validated tools for assessing diet and menopausal symptoms is a strength of the present study. Our findings could, however, be limited by potential information bias, including errors in assessing dietary intake associated with the use of the FFQ, which we have observed in American women.^{59,60} In addition, the cross-sectional nature of the study limited our ability to infer causality. It is possible that experiencing menopausal symptoms may lead to consumption of more calorically dense comfort foods, which are strongly proinflammatory. Moreover, it must be considered that the results of this study may not be generalizable either to other populations with different ethnicities and cultures or to the average community-dwelling postmenopausal Iranian woman of similar age.

CONCLUSION

In conclusion, our results demonstrated increased somatic symptoms in women consuming more proinflammatory diets. We also found that eating high-DED diets was associated with increased menopausal symptoms, in particular somatic and psychological symptoms. Our results may help inform dietary guidelines for middle-aged women. Future studies are warranted to confirm our findings and evaluate the effect of

dietary modifications, specifically DII and DED, on menopausal symptoms.

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