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Original article

Association between dietary inflammatory index and psychological profile in adults

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SUMMARY

Background & aims: Limited data are available on the association of inflammatory potential of the diet and odds of psychological disorders. We investigated the association between adherence to a pro-inflammatory diet, as measured by Dietary Inflammatory Index (DII), and odds of psychological disorders.

Methods: In this cross-sectional study, dietary intakes of 3363 Iranian adult participants were collected using a validated Dish-based 106-item Semi-quantitative Food Frequency Questionnaire (DS-FFQ). DII score was calculated based on participants' dietary intakes obtained from DS-FFQ. The Iranian validated version of Hospital Anxiety and Depression Scale (HADS) and General Health Questionnaire (GHQ) was used to assess psychological disorders. For depression and anxiety, scores of 8 or more on either subscale were considered as psychological disorders and scores of 0–7 were defined as "normal". In terms of psychological distress, the score of 4 or more was defined as psychological distress.

Results: Overall, 28% (n = 943) of study participants had depression, 13.3% (n = 448) were affected by anxiety and 22.6% (n = 760) by psychological distress. After controlling for potential confounders, individuals in the highest quintile of DII score had higher scores of depression (6.56 ± 0.16 vs. 5.48 ± 0.16; P < 0.001), anxiety (3.85 ± 0.17 vs. 3.09 ± 0.17; P = 0.006), and psychological distress (2.42 ± 0.13 vs. 1.77 ± 0.13; P = 0.001), compared with those in the lowest quintile. Participants in the top quintile of DII score had greater odds of depression (OR: 1.84, 95% CI: 1.30–2.60), anxiety (OR: 1.69, 95% CI: 1.07–2.67), and psychological distress (OR: 1.72, 95% CI: 1.20–2.46) than those in the bottom quintile.

Conclusions: We found that adherence to a pro-inflammatory diet was positively associated with psychological disorders.

1. Introduction

Common mental disorders are highly prevalent worldwide [1]. Mental disorders are linked with decreased quality of life and increased risk of mortality [2,3]. A national study revealed that 21% of Iranian adults are affected by these conditions in 1999 [4].

Inflammation has long been reported to be linked with psychological disorders [5]. In earlier studies, elevated levels of high sensitive C-reactive protein (hs-CRP) have been linked with increased risk of depression and anxiety [6,7]. Potential role of anti-

A list of abbreviations: DII, Dietary Inflammatory Index; OR, Odds Ratio; CI, Confidence Interval; DS-FFQ, Dish-based Semi-quantitative Food Frequency Questionnaire; HADS, Hospital Anxiety and Depression Scale; GHQ, General Health Questionnaire; SEPAHAN, Study on the Epidemiology of Psychological, Alimentary Health and Nutrition; FGIDs, Functional Gastrointestinal Disorders; GPPAQ, General Practice Physical Activity Questionnaire; BMI, Body Mass Index; WC, Waist Circumference; MUFA, mono-unsaturated fatty acids; PUFA, poly unsaturated fatty acids.

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inflammatory interventions in mood improvement has earlier been reported [8]. Therefore, dietary patterns with anti-inflammatory potential might be associated with psychological health. For instance, an inverse association was observed between diets rich in fruits, vegetables, whole grains and olive oil, all with anti-inflammatory properties, and depression [9]. Limited data are available on the association between inflammatory potential of the diet and mental health outcomes. It has been suggested that the association between dietary factors and depression may be mediated by inflammation [10,11]. To assess the inflammatory potential of the diet, recently Dietary Inflammatory Index (DII) has been developed. This index ranks people in terms of their diet's inflammatory potential varying from anti-inflammatory to pro-inflammatory levels [12]. Earlier studies have linked DII to obesity [13,14], cardiovascular disease [15,16], metabolic syndrome [16,17], and various types of cancers [18–23]. A longitudinal study reported that a pro-inflammatory diet was prospectively associated with higher risk of depression [24]. In a cross-sectional study among US adults, high DII score was associated with greater odds of frequent distress and depression [25]. Such findings were also reported from US and Ireland [26,27].

Most previous studies on the link of DII and chronic conditions have focused on metabolic abnormalities rather than non-metabolic conditions. Moreover, most information about the association of DII and relevant outcomes came from western countries and not much information is available in this regard from developing countries, including the understudy's region of the Middle East. Assessing the relation between DII and psychological disorders is particularly relevant for the Middle Eastern population due to the unique characteristics of their diet as well as the high prevalence of these conditions in this area. This study was therefore done to examine the association between the DII score and psychological disorders.

2. Methods and materials

2.1. Participants

This cross-sectional study was conducted within the framework of the Study on the Epidemiology of Psychological, Alimentary Health and Nutrition (SEPAHAN) project, a cross-sectional study that investigates the prevalence of functional gastrointestinal disorders (FGIDs) and their relationship with lifestyle factors and psychological disorders. Details about SEPAHAN project have been published elsewhere [28]. This study was performed among Iranian general adults working in 50 different healthcare centers affiliated to Isfahan University of Medical Sciences (IUMS) across Isfahan province. To calculate required sample size, we hypothesized the prevalence of FGDIs as 15%. Considering the study power of 80% and type 1 error of 5%, the minimum required sample size for the current analysis was 1387 subjects based on suggested formula for cross-sectional studies. In this project, data were collected in two main phases between April 2010 and May 2010. To collect information about anthropometric indices, demographic and lifestyle factors, including dietary intakes and physical activity, self-administered questionnaires distributed among 10,087 subjects in the first phase, and 8691 participants returned the completed questionnaires (response rate: 86.16%). In the second phase, data regarding psychological factors were collected for 6239 people (response rate: 64.6%). Finally, we were able to match 4763 questionnaires in the second phase with their equivalent questionnaires in the first phase. In the current study, we excluded subjects with total daily energy intakes outside the range of 800–4200 kcal/day (n = 787), as under-reports and over-reports of energy intakes, as well as those with missing data on psychological, demographic, anthropometric and dietary information (n = 130). Therefore, data from 3363 subjects, for whom complete information about both dietary intakes and psychological profiles were available, were included in the current analysis. General characteristics of individuals excluded from the study were not different from those remained in the analysis. All participants provided written inform consent forms. The study protocol was ethically approved by the Regional Bioethics Committee of Isfahan University of Medical Sciences.

2.2. Dietary intakes assessment

Dietary data were collected using a Willett-format dish-based 106-item semi-quantitative food frequency questionnaire (DS-FFQ) which was designed and validated specifically for Iranian adults. Detailed information about the design, foods included, and the validity of this questionnaire has been published elsewhere [29]. Briefly, the questionnaire contained five categories of foods and dishes: 1) mixed dishes (cooked or canned, 29 items); 2) grains (different types of bread, cakes, biscuits and potato, 10 items); 3) dairy products (dairies, butter, and cream, 9 items); 4) fruits and vegetables (22 items); and 5) miscellaneous food items and beverages (including sweets, fast foods, nuts, desserts and beverages, 36 items). For each food item, a commonly consumed portion size was defined. Participants were asked to report their dietary intakes of foods and mixed dishes based on nine multiple choice frequency response categories varying from “never or less than once a month” to “12 or more times per day”. The frequency response categories for the food list varied from six to nine choices. For foods consumed infrequently, we omitted the high-frequency categories, while for common foods with a high consumption, the number of multiple choice categories increased. For instance, the frequency response for tuna consumption included six categories, as follows: never or less than once/month, 1–3 times/month, 1 time per week, 2–4 times/week, 5–6 times/week, 1–2 times/day; and for tea consumption that is highly prevalent among Iranians, the frequency response included nine categories, as follows: never or less than 1 cup/month, 1–3 cups/month, 1–3 cups/week, 4–6 cups/week, 1 cup/day, 2–4 cups/day, 5–7 cups/day, 8–11 cups/day, ≥12 cups/day). Finally, to convert the food items into grams, we computed the amount of each portion size based on the booklet of “household measures” and then computed the amount of intake by considering the frequency of consumption of each food item. The validity of the DS-FFQ was examined in a subgroup of 200 randomly selected participants of SEPAHAN project. All participants in the validation study completed the DS-FFQ at study baseline and 6 months later. During this validation study, participants provided three detailed dietary records that were used as gold standard. As shown in earlier studies [29], it seems that this questionnaire provides reasonably valid measures of long-term dietary intakes.

2.3. Assessment of DII

Dietary data derived from DS-FFQ were used to calculate DII scores for all subjects. Earlier studies reported the development [12] and construct validation [30,31] of the DII. Shivappa et al. [12] found that a total of 45 specific foods and nutrients were associated with one or more of the inflammatory [Interleukin-1β (IL-1β), Interleukin-6 (IL-6), Tumor Necrosis Factor-α (TNF-α) or CRP] or anti-inflammatory biomarkers [Interleukin-4 (IL-4) and Interleukin-10 (IL-10)]. Then, they scored the inflammatory potential for each food parameter according to whether it increased inflammatory or decreased anti-inflammatory factors (+1), or it decreased inflammatory or increased anti-inflammatory factors (−1), or had no effect (0) on inflammatory or anti-inflammatory biomarkers. They calculated world mean and standard deviation for each of the 45 food

parameters based on 11 data sets from 11 countries in different parts of the world. Due to lack of consumption of some foods in Iranian dietary culture as well as missing some items (like polyphenols) in our nutrient database, in the current study we calculated DII score based on 29 food parameters (rather than 45). The food parameters we used in the current study were as follow: pro-inflammatory parameters included energy, carbohydrate, fat, protein, cholesterol, saturated fat, trans fat, vitamin B12 and iron and anti-inflammatory parameters included mono-unsaturated fatty acids (MUFA), poly unsaturated fatty acids (PUFA), fiber, vitamin B6, folic acid, niacin, riboflavin, thiamin, vitamin A, vitamin C, vitamin D, vitamin E, β-carotene, caffeine, pepper, onion, tea, zinc, selenium, and magnesium. First, we calculated energy-adjusted amounts of these nutrients using residual method [32]. Then, to calculate DII score for each participant, we calculated the *z* score for a given food parameter by subtracting the "standard global mean" from the amount consumed by each subject and dividing this value by the "global standard deviation". Global means and standard deviations were obtained from the study of Shivappa et al. [12]. We converted this value to a centered percentile score in order to reduce skewness, as earlier studies did [12]. For each participant, this score was then multiplied by the respective food parameter effect score derived from the study of Shivappa et al. [12]. Then, we calculated overall DII score for each participant by summing up all foods' DII score. A higher DII score (more positive) indicates a more inflammatory diet and a lower DII score (more negative) indicates a less inflammatory diet. For examining the association between DII score and psychological disorders, we classified individuals based on quintile cut-off points of DII score. This means that first we obtained cut-off points for quintiles (based on the distribution of DII score) in the whole study population. These cut-off points were as follow: −1.41, −0.47, +0.44, +1.38. Therefore, individuals with DII values of less than −1.41 were considered as quintile 1, those with values between −1.41 and <−0.47 as quintile 2, those with values between −0.47 and <+0.44 as quintile 3, participants with values between +0.44 and <+1.38 as quintile 4 and individuals with values equals to or greater than +1.38 as quintile 5.

2.4. Assessment of psychological profile

The Iranian validated version of Hospital Anxiety and Depression Scale (HADS) was used to screen for anxiety and depression [33]. HADS is a brief and useful questionnaire to assess psychological disorders and symptom severity of depression and anxiety disorders. The HADS contains 14 items and include two subscales: anxiety and depression. Each item includes a four-point scale; higher scores indicate an elevated level of anxious and depressive symptomatology. Maximum score is 21 for anxiety and depression. Scores of 8 or more on either subscale were considered as psychological disorders and scores of 0−7 were defined as "normal" in the current study. The convergent validation of translated version of HADS questionnaire was examined in 167 Iranian adults using the correlation of each item with its hypothesized scale. Pearson's correlation coefficients varied from 0.47 to 0.83 ($P < 0.0001$) for anxiety subscale and from 0.48 to 0.86 ($P < 0.0001$) for depression subscale, indicating that the questionnaire provides relatively valid measures of psychological health [33]. The Iranian validated version of General Health Questionnaire (GHQ) with 12-items was used to assess psychological distress [34]. GHQ-12 is a brief, simple, easy-to-complete instrument for measuring current and primary mental health that asks the respondents whether they have experienced a particular symptom of psychological distress or a change in their behavior recently. Each item consists of a four-point scale (less than usual, no more than usual, rather more than usual, or much more than usual). In this study, we used the bimodal (0-0-1-1) scoring method. This gives scores ranging from 0 to 12. Higher scores indicate a greater degree of psychological distress. In the current study, the score of 4 or more was defined as having psychological distress [35]. The convergent validity of GHQ-12 was examined in 748 Iranian young people. Significant inverse correlation was seen between the GHQ-12 and global quality of life scores ($r = -0.56$, $P < 0.0001$) [34].

2.5. Assessment of other variables

Required information on other variables including age, sex, marital status, smoking status, chronic conditions (diabetes, asthma, colitis, stroke, myocardial infarction, heart failure, and cancers), and antidepressant and supplements (vitamins, minerals, calcium and iron) use was obtained from demographic and medical history questionnaires. Physical activity was assessed using the General Practice Physical Activity Questionnaire (GPPAQ) [36], and participants were classified into two categories: physically active (≥1 h/week) and physically inactive (<1 h/week). Although this level of activity might seem low, but earlier publications have revealed that even 1 h per week of walking can reduce the risk of chronic conditions [37]. Anthropometric measures including weight, height, and waist circumference were assessed using a self-administered questionnaire. The validity of self-reported values of weight, height, and waist circumferences (WC) was examined in a pilot study on 200 participants from the same population. In the validation study, self-reported values of anthropometric indices were compared with actually measured values. The correlation coefficients for self-reported weight, height, and WC versus corresponding measured values were 0.95 ($P < 0.001$), 0.83 ($P < 0.001$), and 0.60 ($P < 0.001$), respectively. Body Mass Index (BMI) was calculated by dividing weight (kg) to height (m^2). The correlation coefficient for computed BMI from self-reported values, and the one from measured values was 0.70 ($P < 0.001$).

2.6. Statistical methods

First we classified participants based on quintile cut-off points of DII score. General characteristics of study participants across quintiles of DII score were expressed as means ±SDs for continuous variables and percentages for categorical variables. To examine the differences across quintiles, we used ANOVA with Tukey post-hoc comparisons for continuous variables and a chi-square test for categorical variables. Energy-adjusted dietary intakes of study participants across quintiles of DII score were compared using analysis of covariance (ANCOVA) with Bonferroni correction. The multivariable-adjusted means for scores of depression, anxiety and psychological distress across quintiles of DII score were computed and compared using ANCOVA with Bonferroni correction. We also used binary logistic regression to estimate ORs and 95% CIs for the presence of psychological disorders across quintiles of DII score in crude and multivariable-adjusted model. Age (continuous), sex (male/female), total energy intake (continuous), marital status (married/single/divorced and widowed), education (diploma or under-diploma/university graduate), family size (≤4/>4 members), home ownership (owner/non-owner), antidepressant use (yes/no), vitamin supplements use (yes/no), smoking (non-smoker/former smokers and current smokers), physical activity (<1 h/week/≥1 h/week), presence of chronic conditions (yes/no), and BMI were controlled for in the multivariable-adjusted model. P for trends was determined by considering quintiles of DII score as ordinal variables in the logistic regression analysis. All statistical analyses were done using the Statistical Package for Social Sciences (version 20; SPSS Inc.). $P < 0.05$ was considered as statistically significant.

3. Results

In the current study, the DII score ranged from −4.49 to +5.39. Median DII score across increasing quintiles were −2.05, −0.90, −0.029, +0.86 and + 2.06, respectively. In this study, 28% of study participants had depression (n = 943), 13.3% were affected by anxiety (n = 448) and 22.6% by psychological distress (n = 760). General characteristics of study participants in three phases of SEPAHAN project and across quintiles of DII score are presented in Table 1. Comparing individuals participated at first and those remained at final analysis, we did not find any significant differences in several variables of general characteristics, except for education. Slightly greater percentage of individuals remained for the current analysis was university graduated than those at first phase (61.9 vs. 54.7%). Compared with those in the bottom quintile, participants in the top quintile of DII score were younger, had lower BMI, were less likely to be physically active, females, overweight, and to have chronic conditions. No other significant differences were observed in terms of other variables across quintiles of DII score.

Dietary intakes of study participants across quintiles of DII score are presented in Table 2. A greater DII score was significantly associated with higher intakes of energy, carbohydrate, saturated fat, trans fat, niacin, thiamin and caffeine and lower intakes of fat, protein, dietary fiber, cholesterol, MUFA, PUFA, vitamin B12, vitamin B6, folic acid, riboflavin, vitamin A, vitamin C, vitamin D, vitamin E, β-carotene, pepper, onion, tea, zinc and magnesium.

Crude and multivariable-adjusted means for scores of depression, anxiety and psychological distress across quintiles of DII score are shown in Table 3. After controlling for potential confounders, individuals in the highest quintile of DII score had higher scores of depression, anxiety, and psychological distress compared with those in the lowest quintile.

Crude and multivariable-adjusted odds ratios (ORs) and 95% CIs for depression, anxiety and psychological distress across quintiles of DII score are provided in Table 4. After adjustment for potential confounders, participants in the top quintile of DII score had a greater odds of depression (OR: 1.84, 95% CI: 1.30–2.60), anxiety (OR: 1.69, 95% CI: 1.07–2.67), and psychological distress (OR: 1.72, 95% CI: 1.20–2.46) than those in the bottom quintile.

Crude and multivariable-adjusted odds ratios (ORs) and 95% CIs for psychological disorders across quintiles of DII score among men are provided in Table 5. We observed a significant positive association between DII score and depression in the crude model (OR: 1.56, 95% CI: 1.04–2.35); however, this association became non-significant after adjustment for potential confounders (OR: 1.68, 95% CI: 0.93–3.04). In addition, DII score was positively associated with anxiety (OR: 2.60, 95% CI: 1.36–5.00); however, this association also became non-significant in the multivariable-adjusted model (OR: 2.55, 95% CI: 0.94–6.88). A significant positive association was seen between DII score and psychological distress either before (OR: 1.98, 95% CI: 1.24–3.15) or after adjustment for covariates (OR: 2.09, 95% CI: 1.09–4.02).

The same associations for women are provided in Table 6. We found a significant positive association between DII score and depression among women in the crude (OR: 1.50, 95% CI: 1.11–2.03) and multivariable-adjusted models (OR: 1.92, 95% CI: 1.24–2.98). Neither in crude nor in adjusted model, no significant association was observed between DII score and anxiety. A significant direct association was seen between DII score and psychological distress before (OR: 1.84, 95% CI: 1.33–2.54) and after adjustment for covariates (OR: 1.61, 95% CI: 1.03–2.50).

In addition to DII, we found that female sex, antidepressant use, smoking status, and chronic conditions were positively and university education was inversely associated with the odds of depression. We also observed that female sex, antidepressant use, smoking status, and chronic conditions were positively and age and university education were inversely associated with the odds of anxiety. In terms of psychological distress, female sex, antidepressant use, smoking status, and chronic conditions were positively and university education was inversely linked to psychological distress (Table 7).

4. Discussion

In this study, examining the association between DII score and psychological disorders among a large group of Iranian adults, we found that a higher DII score was associated with greater odds of depression, anxiety and psychological distress. There was a significant positive association between DII score and depression among

Table 1
General characteristics of study participants in three phases of SEPAHAN project and across quintiles of DII score.[a]

Variables	Phase 1[d]	Phase 2[e]	Phase 3[f]	Quintiles of DII score					P-value[b]
	n = 8691	n = 4763	n = 3363	Q_1	Q_2	Q_3	Q_4	Q_5	
Age, y	37.1 ± 8.2	36.5 ± 8.1	36.3 ± 7.8	37.7 ± 7.9	37.1 ± 8.1	36.8 ± 7.7	34.7 ± 7.3	34.9 ± 7.6	<0.001
BMI, kg/m^2	25 ± 4.3	24.9 ± 3.8	24.9 ± 3.8	25.4 ± 3.9	25.1 ± 3.7	25.04 ± 3.7	24.6 ± 3.9	24.2 ± 3.6	<0.001
Female, %	54.9	57.1	58.3	61.3	60.3	57.7	59.9	52.1	0.005
Married, %	79.3	79.3	80	81.7	83.2	83.4	80.2	79.9	0.62
Physically active (≥1 h/week), %	31.2	34.8	33.6	39.9	36.2	31.8	29.9	30.1	<0.001
Overweight or obese, %	45.2	46.3	44.8	50.1	48.6	46.7	42.1	36.5	<0.001
Current smokers, %	4	3.5	3.1	3.7	2.7	3.2	2.3	3.8	0.51
Education (university graduate), %	54.7	57.2	61.9	58.6	59.3	59.8	64.5	67.3	0.003
Family size (>4 people), %	26.9	28.1	28.3	32.3	28.7	28.0	25.9	26.9	0.09
Home ownership (owner), %	56.8	58.9	58.3	74.1	71.1	70.3	66.3	63.2	0.001
Antidepressant use, %	4.7	4.9	4.9	6.4	6.2	4.6	5.1	5.5	0.56
Vitamin supplements[c], %	–	7.4	7.9	7.9	7.4	7.3	8.3	8.5	0.90
Chronic conditions, %	3.3	3	4.6	5.8	5.6	4.3	2.7	4.8	0.04
Depression[c], %	–	28.8	28	25.1	27.9	27.6	29.9	32.5	0.04
Anxiety[c], %	–	14.1	13.3	11.6	12.5	13.0	14.0	16.8	0.06
Psychological distress[c], %	–	23.1	22.6	18.5	21.8	21.1	25.6	28.7	<0.001

[a] Data are mean ± standard deviation (SD).
[b] Obtained from ANOVA or chi-square test, where appropriate.
[c] Not assessed in phase 1.
[d] Completed questionnaires regarding anthropometric indices, demographic and lifestyle factors, including dietary intakes and physical activity.
[e] With completed questionnaires regarding psychological factors.
[f] After exclusion those with missing data on psychological, demographic, anthropometric and dietary information.

Table 2
Dietary intakes of study participants across quintiles of DII score.

Variables	Quintiles of DII score					P-value[a]
	Q_1	Q_2	Q_3	Q_4	Q_5	
Subjects, n	673	673	672	673	672	
Energy (kcal/d)[b]	2316 ± 791	2271 ± 819	2243 ± 804	2330 ± 819	2732 ± 798	<0.001
Carbohydrate (g/d)	295.6 ± 1.85	288.2 ± 1.85	289.4 ± 1.85	292.1 ± 1.85	299.8 ± 1.88	<0.001
Fat (g/d)	97.7 ± 0.70	99.95 ± 0.70	99.93 ± 0.70	98.9 ± 0.70	96.4 ± 0.71	0.001
Protein (g/d)	91.9 ± 0.51	91.8 ± 0.51	89.2 ± 0.51	86.7 ± 0.51	81.6 ± 0.52	<0.001
Fiber (g/d)	27.8 ± 0.17	24.5 ± 0.17	22.7 ± 0.17	20.6 ± 0.17	16.8 ± 0.17	<0.001
Cholesterol (mg/d)	268.5 ± 3.7	269.1 ± 3.7	260.6 ± 3.7	251 ±0.1±3.7	229 ± 3.7	<0.001
MUFA (g/d)	38.4 ± 0.32	39.1 ± 0.32	39 ± 0.32	38.7 ± 0.32	37.6 ± 0.33	0.01
PUFA (g/d)	29.4 ± 0.25	29.5 ± 0.25	29.5 ± 0.25	28.9 ± 0.25	27.2 ± 0.25	<0.001
Saturated fat (g/d)	21.8 ± 0.22	23.3 ± 0.22	23.5 ± 0.22	23.6 ± 0.22	24.02 ± 0.22	<0.001
Trans fat (g/d)	0.19 ± 0.005	0.20 ± 0.005	0.22 ± 0.005	0.23 ± 0.005	0.24 ± 0.005	<0.001
Vitamin B12 (μg/d)	3.02 ± 0.04	3.14 ± 0.04	3.05 ± 0.04	2.90 ± 0.04	2.69 ± 0.04	<0.001
Vitamin B6 (mg/d)	2.31 ± 0.01	2.14 ± 0.01	2.00 ± 0.01	1.86 ± 0.01	1.58 ± 0.01	<0.001
Folic acid (μg/d)	615.05 ± 4.5	573.6 ± 4.5	567.5 ± 4.6	559.6 ± 4.5	547.4 ± 4.6	<0.001
Niacin (mg/d)	24.7 ± 0.16	24.8 ± 0.16	24.8 ± 0.16	25.1 ± 0.16	25.3 ± 0.16	0.08
Riboflavin (mg/d)	1.97 ± 0.01	1.94 ± 0.01	1.88 ± 0.01	1.80 ± 0.01	1.72 ± 0.01	<0.001
Thiamin (mg/d)	1.78 ± 0.02	1.78 ± 0.02	1.82 ± 0.02	1.86 ± 0.02	1.94 ± 0.02	<0.001
Vitamin A (RE)	693.06 ± 6.4	575.7 ± 6.4	505.9 ± 6.4	455.1 ± 6.4	358.7 ± 6.5	<0.001
Vitamin C (mg/d)	146.07 ± 1.67	116.8 ± 1.67	98.4 ± 1.67	83.7 ± 1.67	60.5 ± 1.7	<0.001
Vitamin D (μg/d)	0.98 ± 0.02	0.98 ± 0.02	0.96 ± 0.02	0.94 ± 0.02	0.93 ± 0.02	0.35
Vitamin E (mg/d)	23.5 ± 0.22	22.4 ± 0.22	21.7 ± 0.21	20.9 ± 0.22	18.8 ± 0.22	<0.001
β-Carotene (μg/d)	5577.2 ± 55.5	4099 ± 55.5	3372.7 ± 55.6	2839.9 ± 55.4	1882.4 ± 56.5	<0.001
Caffeine (g/d)	106.1 ± 3.49	93.5 ± 3.49	89.5 ± 3.49	93.5 ± 3.48	112.7 ± 3.55	<0.001
Pepper (g/d)	6.04 ± 0.15	5.49 ± 0.15	5.22 ± 0.15	4.78 ± 0.15	3.47 ± 0.15	<0.001
Onion (g/d)	59.01 ± 0.96	46.99 ± 0.96	40.44 ± 0.97	35 ± 0.96	23.9 ± 0.98	<0.001
Tea (g/d)	478.1 ± 10.8	390.9 ± 10.8	357.1 ± 10.8	328.7 ± 10.8	290.4 ± 10.9	<0.001
Zn (mg/d)	11.75 ± 0.06	11.55 ± 0.06	11.25 ± 0.06	10.7 ± 0.06	9.95 ± 0.06	<0.001
Se (μg/d)	106.6 ± 0.92	107.9 ± 0.92	109.02 ± 0.92	107.7 ± 0.92	105.7 ± 0.93	0.12
Mg (mg/d)	376.2 ± 1.66	346.9 ± 1.66	332.8 ± 1.66	307.2 ± 1.65	272.5 ± 1.69	<0.001
Fe (mg/d)	18.01 ± 0.12	17.42 ± 0.12	17.51 ± 0.12	17.47 ± 0.12	17.40 ± 0.12	0.002

Data are mean ± standard error (SE).
[a] Obtained from ANCOVA.
[b] Energy was not adjusted.

Table 3
Mean scores of psychological disorders across quintiles of DII score.

	Quintiles of DII score					P-value
	Q_1	Q_2	Q_3	Q_4	Q_5	
Median DII	−2.05	−0.90	−0.029	+0.86	+2.06	
DII range	−4.49 to −1.41	−1.41 to −0.47	−0.47 to +0.44	+0.44 to +1.38	+1.38 to +5.39	
Depression						
Crude	5.71 ± 0.13	5.93 ± 0.13	5.99 ± 0.13	6.32 ± 0.13	6.52 ± 0.13	<0.001
Multivariable-adjusted[a]	5.48 ± 0.16	5.64 ± 0.16	5.97 ± 0.15	6.29 ± 0.15	6.56 ± 0.16	<0.001
Anxiety						
Crude	3.14 ± 0.14	3.40 ± 0.14	3.40 ± 0.14	3.68 ± 0.14	3.87 ± 0.14	0.003
Multivariable-adjusted[a]	3.09 ± 0.17	3.14 ± 0.17	3.42 ± 0.17	3.72 ± 0.17	3.85 ± 0.17	0.006
Psychological distress						
Crude	1.74 ± 0.10	1.95 ± 0.10	1.93 ± 0.10	2.31 ± 0.10	2.43 ± 0.10	<0.001
Multivariable-adjusted[a]	1.77 ± 0.13	1.78 ± 0.13	2.05 ± 0.13	2.31 ± 0.13	2.42 ± 0.13	0.001

Data are mean ± standard error (SE).
[a] Adjusted for age, sex, energy intake, marital status, education, family size, home ownership, antidepressant use, vitamin supplements use, smoking status, physical activity, chronic conditions and BMI.

women. We also found a significant positive association between a pro-inflammatory diet and psychological distress in both genders. To our knowledge, the present study is among the first studies examining this association in a Middle Eastern country.

The range of DII score in this study differs from those in previous studies. For example, compared to the study of Phillips et al. [27], the range of DII score in our study was slightly higher (−4.49 to +5.39 in our study vs. −5.10 to +3.68 in their study). In other words, it seems that the dietary inflammatory potential in our study was slightly greater than that in the study of Phillips et al. [27]. It should be kept in mind that like our study, Phillips et al. used energy-adjusted DII; however, they included 26 food parameters to calculate DII. The range of DII score observed in our study (−4.49 to +5.39) was comparable to those reported by Bergmans et al. (−5.29 to +4.71), Akbaraly et al. (−3.35 to +4.23) and Adjibade et al. (−4.99 to +5.82) [25,40,41].

One of the interesting points we found was that mean BMI among those in the top DII category was lower than that those in the bottom category. It must be noted that the study design was cross-sectional and reverse causation is possible. In other words, overweight and obese people might take care of their dietary intakes in an attempt to lose weight. Moreover, individuals in the lowest quintile of DII score maybe over-reported their energy intake. We also found that adherence to pro-inflammatory diet was associated with university education. Due to doing the study among staffs of health centers, it might be assumed that many

Table 4
Crude and multivariable-adjusted odds ratios and 95% CIs for psychological disorders across quintiles of DII score.

	Quintiles of DII score					P-trend
	Q_1	Q_2	Q_3	Q_4	Q_5	
Median DII	−2.05	−0.90	−0.029	+0.86	+2.06	
DII range	−4.49 to −1.41	−1.41 to −0.47	−0.47 to +0.44	+0.44 to +1.38	+1.38 to +5.39	
Depression						
Crude	1.00	1.15 (0.90–1.47)	1.13 (0.88–1.45)	1.27 (0.99–1.62)	1.43 (1.13–1.82)	0.002
Multivariable-adjusted[a]	1.00	1.17 (0.83–1.66)	1.49 (1.06–2.10)	1.70 (1.21–2.40)	1.84 (1.30–2.60)	<0.001
Anxiety						
Crude	1.00	1.09 (0.78–1.52)	1.14 (0.82–1.59)	1.24 (0.90–1.72)	1.54 (1.12–2.10)	0.005
Multivariable-adjusted[a]	1.00	0.96 (0.60–1.55)	1.26 (0.80–2.00)	1.34 (0.85–2.10)	1.69 (1.07–2.67)	0.008
Psychological distress						
Crude	1.00	1.23 (0.93–1.61)	1.17 (0.89–1.54)	1.51 (1.16–1.97)	1.76 (1.36–2.29)	<0.001
Multivariable-adjusted[a]	1.00	1.04 (0.72–1.50)	1.18 (0.82–1.69)	1.44 (1.01–2.05)	1.72 (1.20–2.46)	0.001

Data are OR (95% CI).
[a] Adjusted for age, sex, energy intake, marital status, education, family size, home ownership, antidepressant use, vitamin supplements use, smoking status, physical activity, chronic conditions and BMI.

Table 5
Crude and multivariable-adjusted odds ratios and 95% CIs for psychological disorders across quintiles of DII score among men.

	Quintiles of DII score					P-trend
	Q_1	Q_2	Q_3	Q_4	Q_5	
Depression						
Crude	1.00	0.93 (0.59–1.46)	1.24 (0.81–1.91)	1.12 (0.72–1.73)	1.56 (1.04–2.35)	0.01
Multivariable-adjusted[a]	1.00	0.80 (0.41–1.55)	1.60 (0.88–2.90)	1.63 (0.88–3.02)	1.68 (0.93–3.04)	0.01
Anxiety						
Crude	1.00	0.96 (0.44–2.13)	1.90 (0.95–3.79)	2.00 (1.00–3.98)	2.60 (1.36–5.00)	<0.001
Multivariable-adjusted[a]	1.00	0.70 (0.19–2.48)	2.77 (1.02–7.50)	3.05 (1.10–8.49)	2.55 (0.94–6.88)	0.008
Psychological distress						
Crude	1.00	1.47 (0.90–2.42)	1.30 (0.79–2.14)	1.45 (0.88–2.39)	1.98 (1.24–3.15)	0.008
Multivariable-adjusted[a]	1.00	1.50 (0.75–3.01)	1.46 (0.74–2.89)	1.84 (0.92–3.66)	2.09 (1.09–4.02)	0.02

Data are OR (95% CI).
[a] Adjusted for age, energy intake, marital status, education, family size, home ownership, antidepressant use, vitamin supplements use, smoking status, physical activity, chronic conditions and BMI.

Table 6
Crude and multivariable-adjusted odds ratios and 95% CIs for psychological disorders across quintiles of DII score among women.

	Quintiles of DII score					P-trend
	Q_1	Q_2	Q_3	Q_4	Q_5	
Depression						
Crude	1.00	1.28 (0.95–1.73)	1.11 (0.82–1.51)	1.38 (1.02–1.85)	1.50 (1.11–2.03)	0.01
Multivariable-adjusted[a]	1.00	1.36 (0.89–2.07)	1.44 (0.94–2.20)	1.76 (1.16–2.68)	1.92 (1.24–2.98)	0.002
Anxiety						
Crude	1.00	1.14 (0.78–1.65)	1.00 (0.68–1.48)	1.09 (0.75–1.60)	1.41 (0.97–2.05)	0.12
Multivariable-adjusted[a]	1.00	1.03 (0.61–1.75)	1.02 (0.59–1.75)	1.14 (0.68–1.93)	1.57 (0.91–2.69)	0.11
Psychological distress						
Crude	1.00	1.14 (0.82–1.58)	1.16 (0.84–1.62)	1.57 (1.14–2.16)	1.84 (1.33–2.54)	<0.001
Multivariable-adjusted[a]	1.00	0.88 (0.57–1.37)	1.09 (0.71–1.69)	1.34 (0.88–2.04)	1.61 (1.03–2.50)	0.007

Data are OR (95% CI).
[a] Adjusted for age, energy intake, marital status, education, family size, home ownership, antidepressant use, vitamin supplements use, smoking status, physical activity, chronic conditions and BMI.

people with university education in this study were medical doctors. However, it should be considered that people studied in the current study were staffs of the health centers, not medical doctors. Therefore, they could be regarded as general adults in the community. Due to the availability of unhealthy foods in Iranian society, especially in work place, individuals with higher education, in particular those who are governmental staffs with a limited time to prepare food at home, might consume unhealthy and fast foods frequently than those with lower education.

The role of inflammatory potential of the diet and its relation with several chronic diseases has received great attention recently. To prevent psychological disorders, dietary modification is highly recommended [38]. We found a positive association between adherence to a pro-inflammatory diet and odds of depression. This finding was in line with earlier studies. A longitudinal study in Australia reported that a pro-inflammatory diet was prospectively associated with higher odds of depression in middle-aged Australian women [24]. Another study among US adults showed that higher DII score was associated with over two-fold greater odds of depression [25]. In another prospective study, adherence to a pro-inflammatory diet was linked with greater odds of depression [39]. Such finding was also seen in another cohort study that examined the association between DII and recurrence of depressive symptoms in middle-aged men. The investigators of the latter study found that for each standard deviation increment of DII score, the risk of recurrent depressive symptoms increased by 66% in

Table 7
Association between covariates in the model with psychological disorders.

Variables	Number	Depression	P-value	Anxiety	P-value	Psychological distress	P-value
Age (continuous)	3362	1.00 (0.99–1.02)	0.41	0.97 (0.94–0.99)	0.007	0.98 (0.97–1.00)	0.16
Sex[a] (female/male)	1959/1403	2.26 (1.77–2.90)	<0.001	2.65 (1.86–3.77)	<0.001	2.13 (1.64–2.76)	<0.001
Marital status	3293						
Married	2690	1.00		1.00		1.00	
Single	548	1.21 (0.87–1.68)	0.24	0.67 (0.42–1.08)	0.10	0.85 (0.59–1.20)	0.62
Divorced	55	1.53 (0.72–3.24)	0.26	1.63 (0.70–3.81)	0.23	0.78 (0.34–1.77)	0.83
Education[b] (university graduate/diploma or under diploma)	2081/1281	0.59 (0.47–0.74)	<0.001	0.53 (0.39–0.72)	<0.001	0.69 (0.55–0.88)	0.004
Family size[c] (≤4/>4 members)	2409/953	0.94 (0.72–1.21)	0.64	1.01 (0.71–1.43)	0.93	0.94 (0.72–1.24)	0.45
Home ownership[d] (owner/non-owner)	1959/882	0.88 (0.70–1.12)	0.31	0.94 (0.69–1.28)	0.71	0.84 (0.66–1.07)	0.08
Antidepressant use[e] (user/non-user)	187/3175	3.08 (2.02–4.67)	<0.001	2.87 (1.81–4.59)	<0.001	3.31 (2.19–5.00)	<0.001
Vitamin supplements use[f] (user/non-user)	265/3097	1.06 (0.74–1.52)	0.73	1.05 (0.65–1.69)	0.81	0.93 (0.63–1.36)	0.72
Smoking status[g] (current smoker/non-smoker)	94/2898	2.02 (1.09–3.74)	0.02	3.53 (1.70–7.32)	0.001	2.00 (1.06–3.77)	0.03
Physical activity[h] (≥1 h per week/<1 h per week)	1048/2073	0.77 (0.61–0.98)	0.03	0.81 (0.59–1.13)	0.23	0.91 (0.71–1.16)	0.45
Chronic conditions[i] (yes/no)	156/3206	2.13 (1.30–3.49)	0.003	3.09 (1.72–5.53)	<0.001	1.95 (1.17–3.25)	0.01
BMI (continuous)	3362	1.00 (0.97–1.03)	0.93	0.99 (0.96–1.03)	0.84	0.97 (0.94–1.00)	0.13

Data are OR (95% CI).
[a] Reference group: male.
[b] Reference group: diploma or under diploma.
[c] Reference group: >4 members.
[d] Reference group: non-ownership.
[e] Reference group: non-user.
[f] Reference group: non-user.
[g] Reference group: non-smoker.
[h] Reference group: <1 h/week.
[i] Reference group: no chronic conditions.

women, but not in men [40]. In opposite to these findings, some investigators failed to reach such associations. In a prospective study, it was observed that DII was not associated with depressive symptoms in the whole population, however; a marginally significant positive association was observed in men [41]. Given the available evidence, it seems that inflammatory nature of the diet is associated with depression, therefore, further prospective cohort studies; especially in developing countries are needed to confirm this finding.

We found a significant positive association between adherence to a pro-inflammatory diet and odds of anxiety. This study was one of the few investigations that examined this association. In line with our study, Phillips et al. observed a higher risk of anxiety among those with higher DII [27]. However, Bergmans et al. showed that higher DII was not associated with anxiety [25]. Differences in sample size and subject's characteristics might explain this dissimilarity. They examined dietary intakes using two 24-h dietary recalls, while we used a validated FFQ. In addition, while we applied validated HADS and GHQ-12 questionnaires to examine psychological disorders, Bergmans et al. used the Health-Related Quality of Life (HRQOL) questionnaire to measure frequent distress and anxiety. On the other hand, the components of DII were also different between these two studies. Bergmans et al. included alcohol, n-3 and n-6 fatty acids in their DII calculation, while we had no data on these parameters. It seems that data on the association between inflammatory potential of the diet and anxiety is limited and further studies are required.

We found a positive significant association between adherence to a pro-inflammatory diet and odds of psychological distress. In line with us, a study among US adults showed that higher DII score was associated with greater odds of frequent distress [25]. Combining these findings, it seems that adherence to a pro-inflammatory diet is associated with higher chance of psychological distress; therefore, to prevent psychological disorders, it should be advised to confine consumption of pro-inflammatory foods and nutrients.

The mechanisms through which a pro-inflammatory diet might influence psychological disorders are unknown. Pro-inflammatory diet is associated with high levels of circulating inflammation [42]. It has been suggested that inflammatory biomarkers such as cytokines may contribute to the development of depression through interacting with neurotransmitters metabolism, neuroendocrine function and neural plasticity [43]. Cytokines could also change the metabolism and function of neurotransmitters involved in brain function includes serotonin, norepinephrine, dopamine and glutamate; therefore, cytokines may play a potential role in the pathology of inflammation-induced depression [44]. A pro-inflammatory diet might also affect psychological health through its effects on relevant conditions. For instance, it has been indicated that individuals with greater adherence to the pro-inflammatory diet are at greater risk of obesity [13,14], which in turn is associated with depression [45,46]. Inflammation may also damage brain and nerve cells by oxidative stress [47].

This study has several strengths. Among others, having a large sample size and taking the role of potential confounders into account. Moreover, the study came from the understudied region of the Middle East. Considering the wide geographic area, the study population residing as well as various socioeconomic statuses of participants, a wide range of dietary intakes covered. Some limitations should also be considered. Due to cross-sectional nature of the present study, causal relationships between DII score and psychological disorders cannot be inferred. Therefore, prospective studies are needed to confirm our findings. Inverse causality must also be considered; such that psychological disorders might have an effect on the diet consumed. Although we controlled for several potential confounders, residual confounding cannot be excluded. It must also be noted that participants of this study were young people which might affect our findings. In the current study, we used a validated FFQ for dietary assessment and DII score calculation; however, measurement errors and misclassification of study participants cannot be avoided. Since, the study participants were working in health care system, it is possible that they choose healthy food items; therefore, generalizability of the findings must be done cautiously. Although we tried our best to control for several confounders, missing data, limited ability to adjust for participants' socioeconomic status and using a single dietary questionnaire to ascertain habitual dietary intake patterns are among limitations of

this study. In this study, data on 29 food parameters were available for DII score calculation and 16 food parameters were missing. The missing items include alcohol, eugenol, garlic, ginger, n-3 fatty acids, n-6 fatty acids, saffron, turmeric, flavan-3-ol, flavones, flavonols, flavonones, anthocyanidins, isoflavones, thyme/oregano and rosemary. In the Iranian food database, data regarding flavonoids are not available. Lack of information on these nutrients might influence our results and make our findings weaker or stronger; therefore, interpretation of our findings must be done cautiously. In a case-control study on patients with colitis in Iran, the investigators included 27 food parameters for DII calculation [48]. Another case-control study on multiple sclerosis also included 27 food parameter [49]. Moreover, no data on inflammatory biomarkers were available for DII validation. Although we controlled the analyses for large number of potential confounders, our results did not change so much. This might be explained by the greater role of diet in these conditions than that results from other factors.

In conclusion, we found that adherence to a pro-inflammatory diet was positively associated with depression, anxiety and psychological distress. Further studies, in particular of prospective nature, are required to confirm our findings.

Conflict of interest

None of the authors had any personal or financial conflicts of interest.

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