

## Original Article

# Association between Inflammatory Potential of Diet and Stress Levels in Adolescent Women in Iran

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## Abstract

**Background:** The relation between diet and stress has not been widely explored. In this study, we examined the association between the inflammatory potential of diet and levels of stress among adolescent girls in Iran.

**Methods:** A total of 299 adolescent girls aged 15–18 years were recruited during 2014–2015. Stress was assessed using the Depression, Anxiety and Stress Scale (DASS)-21 scale. Data were analyzed as continuous DASS scores and as a dichotomous outcome with a cut-off value of 9. The dietary inflammatory index (DII) is a literature-derived population-based dietary. DII scores were index computed from dietary intake assessed using a validated food frequency questionnaire. Multivariable linear and logistic regressions were used to calculate beta estimates and odds ratios adjusting for potential confounding factors.

**Results:** In total, 84 girls (28% of the entire study sample) had at least a moderate level of stress symptoms (DASS > 9). Girls with the most pro-inflammatory diet (tertile 3) had higher DASS stress scores ( $\beta = 2.75$ ; 95% CI = 1.05, 4.46) and were at 3.48 times (95% CI = 1.33, 9.09) risk of having at least moderate level of stress compared to girls with the most anti-inflammatory diets (tertile 1).

**Conclusion:** These data suggest that Iranian adolescent girls with a pro-inflammatory diet, as shown by higher DII scores, had higher levels of stress and greater odds of having at least a moderate level of stress symptoms.

**Keywords:** Dietary inflammatory index, diet, Iran, inflammation, stress, adolescent health

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## Introduction

Stress, along with depression and anxiety, are common mental disorders.<sup>1</sup> Stress, which can seriously influence development and performance, may be particularly damaging to adolescents.<sup>2</sup> There is strong evidence that stress is linked to various lifestyle factors, the most important of which is diet.<sup>3,4</sup> Mental stress can lead to certain biological changes such as decrease in overall quality of diet<sup>5,6</sup> and delay in gastric emptying.<sup>7</sup> All of these effects may in turn lead to increased consumption of high-energy and high-fat foods<sup>8</sup> and reduced consumption of fruits and vegetables.<sup>9</sup> There have been reports showing increased intake of food among people with stress while several reports have also shown food intake to be decreased in this population; notwithstanding, some other studies have observed no difference in dietary intake between different levels of stress.<sup>10</sup> The association between stress and diet is complex and the results from studies are thus inconsistent. Despite a large literature on inflammation, there is no study on the inflammatory potential of diet in relation to stress levels or *vice versa*. Mental stress has been shown to be associated with increased levels of inflammatory

markers.<sup>11–14</sup> Results from a study conducted in the United Kingdom suggest that moderate inflammation and immune activation may be associated with increased stress levels.<sup>14</sup> Another report suggests levels of inflammatory markers to be high among people with acute mental stress.<sup>13</sup> To our knowledge, to date there has been only one study conducted in Iran in relation to diet and stress and this was carried out among adults; i.e. >18 years of age.<sup>15</sup> Stress levels are particularly important among adolescents who experience varying levels of emotional and/or psychological distress in their secondary school years and while in transition to universities.<sup>16</sup>

The literature-derived, population-based dietary inflammatory index (DII) was developed to assess the inflammatory potential of an individual's diet.<sup>17</sup> The DII also has been previously construct validated with several inflammatory markers<sup>18–21</sup> and has been found to be associated with a variety of chronic inflammation-related outcomes<sup>22–29</sup> including mental disorders, such as depression, among Spanish college students.<sup>30</sup> The DII has been examined in Iran with respect to various outcomes including bone mineral density<sup>31</sup> and esophageal squamous cell cancer.<sup>32</sup> Our aim was to assess the association between the inflammatory potential of diet of adolescent Iranian girls, as indicated by higher DII scores, and dimensions of stress as measured by Depression Anxiety Stress Scale-21 (DASS-21).<sup>33</sup>

## Materials and Methods

### Study population

This cross-sectional study of 299 adolescent girls aged 15 to 18 years was carried out in Tehran (capital of Iran) from 2014

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to 2015. Participants were randomly chosen by stratified cluster sampling. We first stratified high schools based on socioeconomic status of the districts (low, intermediate and high). Then, we randomly selected 8 high schools from each stratum. Finally, subjects were chosen from a registration list (in each selected high school) by simple random sampling to fulfill the sample size requirement ( $n = 299$ ). We did not include participants who reported major depression and anxiety disorders, use of any antidepressant or sedative medication or those who were pursuing a distinct diet. The study protocol was approved by the research council of the National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences. Written informed consent was obtained from each subject prior to the interviews, and anonymity was preserved.

#### Assessment of dietary intake

Food consumption was based on a reliable and valid Food Frequency Questionnaire (FFQ) consisting of 168 food items typically used in Iran with standard serving sizes (of validated FFQ).<sup>34</sup> Participants reported their daily, weekly, monthly or yearly of intake frequency for each food item. Daily frequencies were computed for each item. Then, by applying the manual for household measures, the daily grams of food intake were calculated.<sup>35</sup> Because the Iranian food composition table (IFCT) is incomplete and contains information on a limited number of raw materials and few nutrients, we used the USDA food composition data included in the Nutritionist 4 software (First Databank; Hearst, San Bruno, CA, USA) to calculate the energy and nutrient content of foods. However, for Iranian food items not included in Nutritionist 4, such as *kashk* (a dairy product), the IFCT was used.<sup>36</sup>

#### Anthropometric measurement

Body weight was assessed to the nearest 0.1 kilogram using digital scales (Seca 881<sup>®</sup> Germany) while participants were barefoot and with light clothing. Height was evaluated using a stadiometer in the standing position and was recorded to the nearest 0.1 cm. Body Mass Index (BMI) was computed as weight divided by height squared ( $\text{kg}/\text{m}^2$ ).

#### Socio-demographic information

Characteristics including age (years), ethnicity (Persian, Azerbaijani, Mazandarani, Gilaki, and others), parents' occupation (Unemployed, grade 3 (e.g., laborers), grade 2 (e.g., clerks), grade 1 (e.g., managers and higher), parents' education (<diploma, diploma, university education), marital status of parents (married, unmarried), salary (USD), diet supplement (yes, no) and smoking status (never, previous, current) were collected with a general questionnaire for all subjects.

#### Physical Activity Assessment

Physical activity was assessed using a valid self-reported questionnaire<sup>37</sup> that has been used previously in a sample of Iranian women and demonstrated consistent outcomes.<sup>38</sup> Participants were asked to check the activities in which they had participated during the last year. From these reports, the total time spent in particular activities was summed and mean durations were calculated. Total physical activity was expressed as metabolic equivalent-hours per day (METs/d).

#### Other variables

Further information on body image was collected using the 28-item eating disorder examination questionnaire (EDE-Q-28).<sup>39</sup> The Persian version of EDE-Q-28 was used in this study.<sup>40</sup>

#### Dietary Inflammatory Index (DII)

The development and validation of the DII are described in detail elsewhere.<sup>17</sup> Briefly, developing the DII involved reviewing and scoring nearly 2000 scientific articles representing cell culture and laboratory animal experiments, and a variety of human studies on diet and six inflammatory markers [i.e., CRP, interleukin (IL)-1b, IL-4, IL-6, IL-10, tumor necrosis factor (TNF)- $\alpha$ ]. Developing the DII also entailed creation of a world standard database that involved obtaining 11 datasets from around the world to which individuals' intakes of 45 food parameters (consisting of nutrients, spices and whole foods) on which the DII is based, could be compared.

FFQ-derived dietary data were used to calculate DII scores for all participants. Dietary data were first linked to the previously described regionally representative world database that provided a robust estimate of a mean and standard deviation for each parameter.<sup>17</sup> These then became the multipliers to express an individual's exposure relative to the "standard global mean" as a z-score. This score was computed by subtracting the "standard global mean" from the amount reported and dividing this value by the "global standard deviation" of the world population as represented by the 11 datasets used for comparative purposes.<sup>17</sup> To minimize the effect of "right skewing," this value was then converted to a centered (on zero) percentile score by computing the percentile equivalent of the z-score, multiplying by 2 and subtracting 1.

For each individual food parameter, this score was multiplied by the respective food parameter effect score, derived from the literature review, in order to obtain a food parameter-specific DII score.<sup>17</sup> All of the food parameter-specific DII scores were then summed to create the overall DII score for each study participant,  $\text{DII} = b_1 * n_1 + b_2 * n_2 + \dots + b_{31} * n_{31}$ , where  $b$  indicates the literature-derived inflammatory effect score for each of the evaluable food parameters and  $n$  indicates the food parameter-specific centered percentiles, which were derived from the FFQ-derived dietary data.

For the current study, data on 31 of the 45 DII food parameters could be derived from the FFQ and were thus used for DII calculation. These include: pro-inflammatory components (energy, carbohydrate, protein, fat, saturated fat, iron, cholesterol, trans-fat, vitamin B12) and anti-inflammatory components (alcohol, fiber, mono-unsaturated fat, poly-unsaturated fat, omega-3, omega-6, niacin, thiamin, riboflavin, magnesium, zinc, vitamin A, vitamin C, vitamin E, vitamin D, vitamin B6, folic acid, beta-carotene, tea, turmeric, garlic and onions).

#### Psychological assessment of stress

The Persian version of Depression, Anxiety, Stress Scale-21 (DASS-21), which is based on the version by Lovibond,<sup>41</sup> was used to determine the level of depression, anxiety and stress in our sample population. This questionnaire has three subscales, each of which consists of seven items. The score of each subscale is obtained by adding the scores of relevant questions. The Persian version of the DASS-21 was found to be a reliable and valid tool to examine the level of stress among Iranian adolescents.<sup>42</sup>

### Statistical analysis

Study characteristics were described for adolescents according to reporting of stress levels and by tertiles of the DII. Formal comparisons are based on *t*-tests, ANOVA or chi-square tests. Multiple linear and logistic regression analyses were then used to calculate adjusted beta estimates and odds ratios (ORs) and 95% confidence intervals (CIs) for stress scores as both a continuous and a categorical variable (DASS-21>9) in relation to DII in 2 separate models. Model 1 adjusted for total energy intake and age; model 2 additionally adjusted for physical activity, marital status, income, smoking, BMI and presence of chronic disease. Covariates were chosen *a priori* based on previous research conducted on stress. All analyses were carried out using SAS 9.4.

## Results

Table 1 describes distribution of characteristics across categories of stress levels based on DASS-21 scores. Girls with at least moderate level of stress included a higher percentage of girls who were either

past/current smokers and with the most pro-inflammatory diet (tertile 3 of DII); however, significance was observed only for smoking. Table 2 shows distribution of characteristics across tertiles of DII scores. The only significant relationship was observed for BMI (girls in tertile 3 had higher BMI compared to girls in tertile 1). Table 3 describes the results for depression as a continuous score and as a dichotomous outcome where the scores were dichotomized based on having at least a moderate level of stress symptoms (DASS-21 > 9). Significant associations were observed for both types of outcomes in both models. Results are described for the full model, girls in third tertile had significantly higher stress scores ( $\beta = 2.75$ , 95% C.I. 1.05, 4.46) and greater odds of having at least moderate level of stress (DASS-21 > 9) (OR = 3.48, 95% CI 1.33, 9.09) compared to girls in tertile 1 (Table 3).

## Discussion

In this study, we report a significant positive association between increasing inflammatory potential of diet, measured by DII scores,

**Table 1.** Characteristics of participants according to different categories of stress levels.

Characteristics <sup>a,b</sup>	Normal or mild level of stress (DASS ≤ 9)	At least moderate level of stress levels (DASS > 9)	P-value
	N = 215	N = 84	
Age (mean ± SD)	16.2 ± 1.0	16.3 ± 1.0	0.226
Physical Activity (METs hr/d) (mean ± SD)	36.1±5.7	35.6±5.3	0.474
BMI (kg/m <sup>2</sup> ) (mean ± SD)	22.5 ± 4.8	21.9 ± 4.3	0.391
Smoking (%)			<0.001
Never	98.6	89.3	
Current/Past	1.4	10.7	
Chronic disease (%)			0.547
Yes	2.3	3.6	
No	97.7	96.4	
Diet Supplement use (%)			0.202
Yes	32.6	40.5	
No	67.4	59.5	
Marital status (%)			0.774
No	94.9	94.1	
Yes	5.1	5.9	

<sup>a</sup>t- test was used for continuous variables; <sup>b</sup>Chi-square test was used for categorical variables.

**Table 2.** Participant characteristics by level of dietary inflammatory index (DII).

Characteristics <sup>a,b</sup>	Tertile 1	Tertile 2	Tertile 3	P-value
Age (mean ± SD)	16.1 ± 1.0	16.3 ± 1.0	16.2 ± 0.9	0.826
Physical Activity (METs hr/d) (mean ± SD)	36.3 ± 5.9	36.2 ± 5.0	35.4 ± 5.9	0.284
BMI (kg/m <sup>2</sup> ) (mean ± SD)	21.4 ± 4.8	22.7 ± 4.4	23.0 ± 4.6	0.020
Smoking (%)				0.393
Never	97.0	97.0	93.0	
Current/Past	3.0	3.0	7.0	
Chronic disease (%)				0.589
Yes	2.0	4.0	2.0	
No	98.0	96.0	98.0	
Diet supplement use (%)				0.174
Yes	42.0	30.3	32.0	
No	58.0	69.0	68.0	
Marital status (%)				0.286
No	95.0	97.0	92.0	
Yes	5.0	3.0	8.0	

<sup>a</sup>ANOVA test was used for continuous variables; <sup>b</sup>Chi-square test was used for categorical variables.

**Table 3.** Beta estimates and odds ratios and confidence intervals for the association between DII and stress levels among 299 Iranian female adolescents.

DII	Beta Estimates for stress symptoms expressed as continuous DASS-21 score				Odds Ratios for at least moderate level of stress (DASS-21>9)			
	Tertile 1	Tertile 2	Tertile 3	P-Value	Tertile 1	Tertile 2	Tertile 3	P-Value
Model 1 <sup>a</sup>	0	2.50 (1.03, 3.97)	2.85 (1.13, 4.57)	0.003	1	2.82 (1.31, 6.08)	3.51 (1.42, 8.67)	0.001
Model 2 <sup>b</sup>	0	2.72 (1.29, 4.15)	2.75 (1.05, 4.46)	0.005	1	3.16 (1.43, 7.00)	3.48 (1.33, 0.09)	0.002

<sup>a</sup> Adjusted for age and energy. <sup>b</sup> Model 1+physical activity, BMI, smoking, presence of chronic disease, diet supplement use, salary and marital status.

and stress levels as measured by DASS-21, among adolescent girls in Iran. This is the first study to examine the association between DII scores and stress among adolescent girls. Previously, in a cross-sectional study conducted in Iran, a positive association was observed between stress and consumption of saturated oils (OR: 1.17; 95% CI: 1.08 – 1.28) and inverse associations were observed between stress and intake of unsaturated oils (OR: 0.84 ; 95% CI: 0.77 – 0.91), fruits and vegetables (OR: 0.83; 95% CI: 0.76 – 0.90), meat (OR: 0.88; 95% CI: 0.82 – 0.97), and dairy products (OR: 0.88 ; 95% CI: 0.81 – 0.96).<sup>15</sup> In another study conducted among Australians  $\geq 18$  years, men who experienced mild to moderate levels of stress were two to three times more likely to eat cereals ( $P < 0.01$ ), fish/seafood ( $P < 0.001$ ), and protein powder ( $P < 0.05$ ). They also tended to eat more meat alternatives ( $P < 0.05$ ), and highly processed foods ( $P < 0.05$ ), and to drink more alcohol ( $P < 0.05$ ) than unstressed male students. However, they were less likely to consume vegetables and fruits ( $P < 0.05$ ) compared with their unstressed counterparts.<sup>43</sup> Female students who experienced mild to moderate stress were 2.22 times more likely to eat processed food ( $P < 0.01$ ) than unstressed female students.<sup>43</sup>

A significant inverse dose–response trend was found between stress levels and consumption of vegetables and fruits.<sup>43</sup> Fruits and vegetable are rich in vitamins, minerals and flavonoids, which contribute to lower DII scores.<sup>19</sup> In another study conducted in Puerto Rico, students with at least moderate levels of perceived stress, had diets that were below the dietary recommendations for grains, fruits, vegetables, dairy products, and protein, whereas fat consumption was adequate.<sup>44</sup> Regarding the robustness of the DII, scores have been validated with various inflammatory markers, including C-reactive protein,<sup>19,45</sup> interleukin-6,<sup>21</sup> tumor necrosis factor-alpha<sup>20</sup> and homocysteine.<sup>22</sup> The exact mechanism for this association is not known; this is the first study to explore this association between DII and stress, and more studies should be conducted to identify the exact association; however, it is shown that levels of inflammatory markers were increased in people with stress,<sup>14</sup> and various dietary factors were shown to have an effect on inflammation.<sup>19,45</sup>

Our study had some limitations, which should also be considered when interpreting the results. First, the validity and reliability of FFQ have not been established in adolescents with stress. Second, we could not determine causality due to the cross-sectional nature of the study. Reverse causation is plausible; e.g., girls with stress may be choosing unhealthier-inflammatory foods. Other limitations include the small sample size, possibility of recall bias, including under/over reporting of specific foods. Additionally, in this study, data are available only on 31 of the 45 food parameters. No data was available on inflammatory markers; hence, we could not carry out these analyses, which may be considered as

a limitation.

In conclusion, female adolescents with a pro-inflammatory diet, as indicated by higher DII scores, were more likely to experience at least a moderate level of stress. Thus, it appears that promoting diets with higher concentrations of anti-inflammatory foods such as vegetables and fruits, may be protective against development of stress in young girls. This is sound dietary advice from a number of other perspectives. However, further studies analyzing the link between diet, inflammation and stress are warranted among both men and women to deepen our understanding of the causal role of diet in development of stress and other mental disorders.

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