Higher dietary fat quality is associated with lower anxiety score in women: a cross-sectional study

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Abstract
Background: The relationship between anxiety and dietary fat quality (DFQ) has not been well studied. The aim of this study was to investigate the relationship between anxiety disorder and fatty acids’ intake in women.

Methods: This cross-sectional study included 300 women aged 18–49 attending healthcare centers. Dietary exposure was measured by a 168-item semi-quantitative food frequency questionnaire (FFQ). To determine the status of anxiety, the Depression, Anxiety, and Stress Scale (DASS) questionnaire was used. Based on the total score of anxiety, the participants were divided into two groups of without anxiety (< 8) and with anxiety (≥ 8). The relationship between fatty acids intake and odd ratio (OR) for anxiety was analyzed by simple logistic regression.

Results: About 37.7% of individuals reported anxiety. After adjustment for covariates, an increase in the OR for anxiety was observed across the quintuples of saturated fatty acids (SFAs) (OR 3.17; 95% CI 1.43–7.00; p-trend = 0.005). In addition, higher intakes of monounsaturated fatty acids (MUFAs) (OR 0.15; 95% CI 0.05–0.44; p-trend = 0.001), oleic acid (OR 0.25; 95% CI 0.09–0.67; p-trend = 0.002), alpha-linolenic acid (ALA) (OR 0.07; 95% CI 0.02–0.23; p-trend < 0.001), and n-3:n-6 poly unsaturated fatty acids (PUFAs) (OR 0.56; 95% CI 0.24–1.03; p-trend = 0.02) were found to be related with lower OR of anxiety.

Conclusion: Intake of SFAs was positively related to anxiety disorder, whereas MUFAs, oleic acid, ALA, and n-3:n-6 PUFAs intake were inversely related to anxiety score. For investigating the association of fat intake and anxiety disorder, DFQ may be a useful measure.

Keywords: Anxiety disorder, Dietary fat quality, Fatty acids

Introduction
According to the World Health Organization’s (WHO) report, anxiety is one of the most common psychiatric disorders [1]. The global prevalence of anxiety has been reported 11.4% [2]. This disorder is more common in women than men [3]. The prevalence of anxiety in individuals with more than 14 years of age in Iran has been reported 15.2% (18.3% in women and 10.8% in men) [4]. Anxiety disorders are significantly related to poor social relationships [5] and physical conditions such as heart disease [6], gastrointestinal disease [7], migraine headache [8], thyroid disease [9], depression, and stress [10, 11].

Lipids play an important role in the function of neurons in the brain [12]. Neuronal cell membranes have high content of polyunsaturated fatty acids (PUFAs), especially docosahexaenoic acid (DHA), which are important for development, maintenance, and function...
of the nervous system. These fatty acids are involved in 
membrane fluidity, which is important for synaptic trans-
mittance and function of membrane proteins and neuro-
transmitters such as serotonin and dopamine [13–15]. 
Lack of n-3 PUFAs in the brain may lead to depression-
and anxiety-associated behaviors [12]. A meta-analysis 
found that, compared with the control group, subjects 
with social anxiety disorders had lower blood levels of 
n-3 PUFAs, eicosapentaenoic acid (EPA) and DHA, and/or 
higher levels of n-6 PUFAs, arachidonic acid (ARA) 
[16]. Lower n-3:n-6 PUFAs ratio and higher saturated 
fatty acids (SFAs):monounsaturated fatty acids (MUFAs) 
ratio may have adverse effects on the membrane fluidity 
[17, 18]. In mice, a reduction of MUFAs in the hippocam-
pus resulted in alterations in cell membrane fluidity and 
loss of memory, learning disability, and Alzheimer’s dis-
ease that causes behavioral disturbances [19, 20]. SFAs 
negatively affects the brain functions and increases the 
risk of neurological diseases [21].

Few studies have investigated the association between 
dietary fat quality (DFQ) and anxiety disorder. Some 
studies have focused on the consumption of n-3 PUFAs 
such as docosapentaenoic acid (DPA), EPA, DHA, alphal-
inolenic acid (ALA), and their association with anxiety 
disorder. The results showed an inverse association 
between intake of these fatty acids and anxiety in adults 
[22–25]. In addition, higher consumption of fish, which 
is an important source of n-3 PUFAs, was associated 
with lower psychological disorders such as anxiety [24]. 
Due to the limitations of available cross-sectional stud-
ies, including the inherent weaknesses of design, age, and 
sex-specific differences and location differences, dispa-
rate results were reported. For instance, a prospective 
study on university graduates showed that dietary intake 
of n-3 PUFAs was not associated with anxiety disorder 
[26]. Another cross-sectional study in women reported 
no relationship between the intake of n-6 PUFAs and anxiety disorder [24]. Moreover, a cross-sectional study 
on subjects with current pure anxiety disorder did not 
find any association between blood n-6 PUFAs levels and 
anxiety disorders [27]. Pure anxiety is generalized anxiety 
disorder without depression and stress [28]. The results of 
experimental studies on the effects of n-3 PUFAs on anx-
xiety are not also consistent. The results change depend-
ing on the administered doses and the type of fatty acids uti-
lized in the trial. For instance, in an experimental study, 
consumption of 3 g/day of EPA and DHA in patients with 
current obsessive–compulsive disorder reduced anxiety 
disorder [29]. Another experimental study reported that 
consumption of at least 2000 mg/day n-3 PUFAs in adults 
reduced anxiety disorder [30]. However, a meta-analysis 
did not show beneficial effects of omega-3 supplementa-
tion on the prevention of anxiety symptoms [31].

Dietary intake may differ between countries that 
makes region and population-specific research of fatty 
acids’ intake and anxiety disorder important. The vari-
ability in fat and fatty acids’ intakes in various coun-
tries has been reported [32]. For instance, mean intake 
of total fat ranges from 11.1 to 46.2% E worldwide [33]. 
These percentages for SFAs and PUFAs are 2.9–20.9%E, 
and 2.8–11.3%E, respectively [33]. Even great differ-
ences in regional fat intakes have been reported in Africa, 
America, Asia, and Europe [32]. In Iran, consumption of 
total fat is approximately 22%E, with about 11.3%E com-
ing from SFAs [34]. The proportions of MUFAs (6.8%E) 
and PUFAs (2.1%E) are low. Since consumption of fish is 
very low, vegetable oils represent the major source of n-3 
PUFAs intake. Furthermore, due to high consumption of 
hydrogenated cooking fats, the intake of transfatty acids 
is much higher compared with many Western countries 
[35].

To the best of our knowledge, the relationship between 
three different anxiety and some fatty acids’ intake such as 
MUFAs has not been investigated in human so far. As 
it was mentioned before, anxiety is more common in 
women than men. Since women are the major group of 
people attending healthcare centers and the sample size 
was not large, we restricted the study to women. There-
fore, we aimed to evaluate the association between anxiety 
score and the DFQ in women.

Materials and methods
Participants
This cross-sectional study was conducted on 326 Iranian 
women attending healthcare centers of Amol city, from 
December 2017 to June 2018. Using random sampling 
method, 5 centers from 17 centers were selected. The 
frequency of women aged 18–49 years in each center 
was obtained. Simple sampling method was employed 
to select the study participants from each health center, 
using the proportion-to-size approach. The inclusion 
criteria were having 18 to 49 years of age and body mass 
index (BMI) 18.5–34.9 kg/m². The exclusion criteria were 
menopause and pregnancy or lactation. Participants with 
diagnosed diabetes, heart disease, cancer, liver and kid-
ney disease, hypertension, thyroid disorders, epilepsy, 
multiple sclerosis, depression, anxiety or stress, or drug 
use were excluded from the study. In addition, subjects 
who experienced stressful events in the last 6 months, 
such as divorce, love failure, loss of family, or close 
friends, adhering to certain diets in the past year, and 
smoking were not included in the study. The aim of the 
study was explained to the women, and written informed 
consent was obtained from all participants. Data were 
collected from each individual by face-to-face inter-
view. General data including age, marriage status, parity,
education level, job, family size, and dietary supplement intake were obtained using interview. The study was ethically approved by Ethics Committee of Tehran University of Medical Sciences.

**Anthropometric assessment**

Weight was measured with the participant wearing light clothes to the nearest 0.1 kg. Height was measured in standing position, shoulders, and barefoot touching the wall to the nearest 0.5 cm [36]. Waist circumference (WC) was measured to the nearest 0.5 cm at the midpoint between the lowest rib and the top of the iliac crest in standing position [37]. Body mass index (BMI) was calculated by dividing weight in kilograms by height in squared meters (kg/m²).

**Physical activity assessment**

Physical activity (PA) was measured using the short form of International Physical Activity Questionnaire (IPAQ) [38]. The reliability and validity of this questionnaire was assessed across 12 countries. The Spearman’s ρ for the reliability of IPAQ questionnaires has been reported around 0.8. The criterion validity had a median ρ of about 0.30, which was similar to other validation studies [39]. Participants reported times spent on strenuous, moderate, and mild physical activity over the past 7 days, and then, the values were multiplied by their metabolic equivalent (MET) quantities and the obtained numbers were summed together to calculate MET/mint/week value.

**Anxiety score assessment**

To determine the status of depression, anxiety and stress, the DASS [21 items] questionnaire was used. DASS questionnaire was provided by Lovibond in 1995 [40]. The questionnaire of DASS was validated by Jafari et al. [41] in 783 Iranian medical students in 2017. The Cronbach’s alpha for depression, anxiety, and stress scales have been reported 0.86, 0.76, and 0.79, respectively. In the short form of the DASS questionnaire, for each subscale of depression, anxiety, and stress, seven questions have been presented. Participants were asked to respond to each question based on to what extent that item applied to them during the last week (from 0 to 3: not at all, to some degree, to a considerable degree, and very much, respectively). At the end, the scores on the DASS-21 were multiplied by two to calculate the final score. Based on the total score of anxiety, the subjects were divided into five groups of without anxiety (0–7), mild (8–9), moderate (10–14), severe (15–19), and very severe (>20) anxiety [40]. However, due to the limited number of cases in some groups, similar to another study [42], we simply divided participants into two groups of without anxiety (<8) and with anxiety (≥8).

**Dietary intake assessment**

Dietary exposure was measured by a validated 168-item semi-quantitative food frequency questionnaire (FFQ). This questionnaire was validated in Iran. The mean energy-adjusted reliability coefficient for nutrient intake was reported 0.6 for women. The ranges of questionnaire validity coefficients were 0.21–0.56 for protein, 0.37–0.61 for potassium, 0.38–0.50 for beta carotene, 0.31–0.95 for cholesterol, 0.21–0.55 for retinol, and 0.28–0.38 for alpha tocopherol [43].

Participants were asked to report their frequency of consumption of a given serving of each food item during the previous year, on a daily (e.g., bread), weekly (e.g., rice, meat), or monthly (e.g., fish) basis. The reported frequency for each food was converted to daily intake and was analyzed for energy and nutrient intake using the US Department of Agriculture’s (USDA) food composition tables [44]. All food intakes were analyzed for energy intake, macronutrients, and micronutrients using Nutritionist 4 software modified for Iranian foods [45].

Participants with energy intake out of predefined limits (500 kcal/day or 3500 kcal/day) were excluded (n = 26) [46]. We used healthy eating index (HEI-2015) for examining the adherence to the healthy eating guidelines [47]. In this guideline, food is divided into 13 groups: whole fruit, whole fruits without juices, whole vegetables, beans and green vegetables, whole grains, dairy, whole protein foods, seafood dishes and vegetable proteins, fatty acids, refined grains, sodium, added sugars, and SFA. Each component is based on 1000 cal. Each component was scored on a scale of 0–5 or 0–10. We excluded fatty acids and SFA when calculating the HEI score.

**Statistical analysis**

Data analysis was done by Statistical Package for Social Sciences (SPSS) version 22 (SPSS Inc, Chicago). The Kolmogorov–Smirnov test was used to examine the normal distribution of variables. To compare the means of normally distributed variables between participants without anxiety and with anxiety, independent samples t test was used. Chi-square and ANOVA tests were used to determine the relationship between anxiety and qualitative and quantitative variables, respectively. All fatty acids’ intake was adjusted for energy intake using the residual method [48]. The relationship between fatty acids’ intake and odd ratio (OR) of anxiety was analyzed by simple logistic regression. In addition to the unadjusted analysis (model 1), we used multivariable models to assess the relationship between fatty acids’ intake and anxiety (model 2). In model 2, we adjusted for age, parity, job, physical activity [22], and total energy intake. These covariates have been associated with anxiety in the
In our study, a higher intake of MUFAs and oleic acid was associated with increased anxiety score. In addition, the inverse associations between anxiety and intake of total fat (OR 1.46; 95% CI 0.67–3.15; p-trend = 0.1), dietary cholesterol (OR 2.04; 95% CI 0.96–4.32; p-trend = 0.1), DHA (OR 0.47; 95% CI 0.22–1.02; p-trend = 0.2), EPA (OR 0.52; 95% CI 0.24–1.11; p-trend = 0.2), and n-6 PUFAs (OR 1.15; 95% CI 0.54–2.45; p-trend = 0.4) (Table 2, Model 1). After adjustment for age, parity, job, physical activity, BMI, and total energy intake, the positive association between anxiety and SFAs remained significant (OR 3.17; 95% CI 1.43–7.00; p-trend = 0.005, Model 3). In addition, the inverse associations between anxiety and intake of MUFAs (OR 0.15; 95% CI 0.05–0.44; p-trend = 0.001, Model 4), oleic acid (OR 0.25; 95% CI 0.09–0.67; p-trend = 0.002, Model 4), ALA (OR 0.07; 95% CI 0.02–0.23; p-trend < 0.001, Model 7), and n-3: n-6 PUFAs ratio (OR 0.56; 95% CI 0.24–1.03; p-trend = 0.02, Model 5) remained significant.

Furthermore, those participants who were included in the third quintile of n-3 PUFAs presented lower OR for anxiety (OR 0.37; 95% CI 0.15–0.94; p = 0.03) as compared with participants in the first quintile. After adjustment for covariates, we found no association between anxiety and intake of total fat (OR 1.20; 95% CI 0.56–2.66; p-trend = 0.4; Model 2), PUFAs (OR 1.49; 95% CI 0.53–4.14; p-trend = 0.1; Model 5), dietary cholesterol (OR 0.98; 95% CI 0.39–2.50; p-trend = 0.4; Model 6), DHA (OR 0.59; 95% CI 0.25–1.40; p-trend = 0.6; Model 7), EPA (OR 0.62; 95% CI 0.26–1.48; p-trend = 0.4; Model 7), and n-6 PUFAs (OR 1.24; 95% CI 0.38–4.08; p-trend = 0.3; Model 8) (Table 2).

**Fig. 1 Flowchart of participants**

**Discussion**

In the present study, we investigated the relationship between anxiety disorder and DFQ in women. The result of this study suggested that higher intake of SFAs was associated with increased anxiety score. In addition, intake of MUFAs, oleic acid, ALA, and n-3: n-6 PUFAs ratio was associated with lower odds of anxiety. Our study showed no significant association between intake of DHA, EPA, n-6 PUFAs, cholesterol, and total fat with anxiety disorder.

Our study showed that higher SFAs intake was associated with higher anxiety score. Similarly, a randomized crossover-design study in university students showed that SFAs intake is positively related to anxiety score [49]. In our study, a higher intake of MUFAs and oleic acid was
### Table 1 Characteristics of participants across anxiety status

| Variable                          | With anxiety (score ≥ 8) | Without anxiety (score < 8) | P-value<sup>a</sup> |
|-----------------------------------|--------------------------|-----------------------------|---------------------|
|                                   | N = 113                  | N = 187                     |                     |
| Age (year)<sup>b</sup>            | 30.63 ± 9.47 (18–49)     | 31.71 ± 8.56 (28–49)        | 0.3                 |
| Educational status<sup>c</sup>    |                          |                             | 0.9                 |
| Less than diploma                 | 20 (17.7)                | 34 (18.2)                   |                     |
| Diploma and higher                | 93 (82.3)                | 153 (81.8)                  |                     |
| Marital status<sup>c</sup>        |                          |                             | 0.058               |
| Single                            | 42 (37.2)                | 50 (26.7)                   |                     |
| Married                           | 71 (62.8)                | 137 (73.3)                  |                     |
| Job<sup>c</sup>                   |                          |                             | 0.005               |
| House wife                        | 59 (52.2)                | 128 (68.4)                  |                     |
| Employed                          | 54 (47.8)                | 59 (31.6)                   |                     |
| Dietary supplement intake<sup>c</sup> |                      |                             | 0.6                 |
| Yes                               | 54 (47.8)                | 84 (44.9)                   |                     |
| No                                | 59 (52.2)                | 103 (55.1)                  |                     |
| Total PA<sup>c</sup> (MET/min/week)|                          |                             | 0.06                |
| Low                               | 63 (55.8)                | 116 (62)                    |                     |
| Moderate                          | 23 (20.4)                | 46 (24.6)                   |                     |
| High                              | 27 (23.9)                | 25 (13.4)                   |                     |
| Family size<sup>b</sup>           | 3.69 ± 0.93              | 3.58 ± 0.95                 | 0.3                 |
| Parity<sup>b</sup>                | 0.98 ± 1.14              | 1.21 ± 1.21                 | 0.04                |
| Total energy intake<sup>b</sup> (kcal/day) | 2509 ± 589               | 2481 ± 518                  | 0.6                 |
| HEI<sup>b</sup>                   | 46.92 ± 5.95             | 46.93 ± 7.16                | 0.9                 |
| Anthropometric measures           |                          |                             |                     |
| Height<sup>b</sup>                | 161.38 ± 5.65            | 161.10 ± 11.96              | 0.8                 |
| Body weight (kg)                  | 66.38 ± 10.88            | 68.84 ± 10.45               | 0.053               |
| WC (cm)                           | 84.09 ± 11.54            | 85.63 ± 10.68               | 0.2                 |
| BMI (kg/m<sup>2</sup>)            | 26.43 ± 6.92             | 26.59 ± 3.82                | 0.7                 |
| Energy-adjusted dietary intake/d<sup>d</sup> |                           |                             |                     |
| Total fat (g)                     | 84.69 ± 17.36            | 82.77 ± 13.24               | 0.2                 |
| SFAs (g)                          | 27.34 ± 6.34             | 24.69 ± 4.48                | <0.001              |
| MUFAs (g)                         | 25.19 ± 4.40             | 26.45 ± 4.48                | 0.01                |
| Oleic acid (g)                    | 22.34 ± 4.13             | 24.00 ± 4.32                | 0.001               |
| PUFAs (g)                         | 15.26 ± 3.74             | 16.12 ± 4.39                | 0.08                |
| Dietary cholesterol (mg)          | 274.8 ± 71.8             | 265.2 ± 66.7                | 0.2                 |
| n-3 PUFAs (g)                     | 0.90 ± 0.35              | 0.89 ± 0.32                 | 0.8                 |
| ALA (g)                           | 1.04 ± 0.35              | 1.39 ± 0.51                 | <0.001              |
| DHA (g)                           | 0.09 ± 0.10              | 0.10 ± 0.11                 | 0.3                 |
| EPA (g)                           | 0.02 ± 0.03              | 0.03 ± 0.03                 | 0.3                 |
| n-6 PUFAs (g)                     | 8.82 ± 4.01              | 8.46 ± 3.82                 | 0.4                 |
| n-3:n-6 PUFAs                     | 0.10 ± 0.02              | 0.11 ± 0.03                 | 0.3                 |

Physical activity: low (less than 600 MET/min/week), moderate (600–3000 MET/min/week), and high (more than 3000 MET/min/week)

HEI: Healthy eating index, WC: Waist circumference, BMI: Body mass index, PA: Physical activity, MET: Metabolic equivalent, SFAs: Saturated fatty acids, MUFAs: Monounsaturated fatty acids, PUFAs: Polyunsaturated fatty acids, ALA: Alpha-linolenic acid, DHA: Docosahexaenoic acid, EPA: Eicosapentaenoic acid

<sup>a</sup> Chi-square test

<sup>b</sup> Mean and standard deviation for quantitative variables

<sup>c</sup> Number (%) for qualitative variables

<sup>d</sup> Independent t test
Table 2  Odds ratio (OR) and 95% confidence intervals (CIs) for anxiety across the quintuples (Q) of energy-adjusted dietary fatty acid intake

|                          | Q1   | Q2   | Q3   | Q4   | Q5   | p-trend |
|--------------------------|------|------|------|------|------|---------|
|                          | (n = 60) | (n = 60) | (n = 60) | (n = 60) | (n = 60) |         |
| Total fat (non-case/case) | (43/17) | (39/21) | (35/25) | (32/28) | (38/22) |         |
| Model 1                  | 1.00 | 1.36 (0.62–2.94) | 1.80 (0.84–3.86) | 2.21 (1.03–4.71) | 1.46 (0.67–3.15) | 0.1      |
| P-value                  | 0.4  | 0.1  | 0.1  | 0.4  | 0.4  |         |
| Model 2                  | 1.00 | 1.23 (0.55–2.73) | 1.77 (0.79–3.96) | 1.81 (0.82–3.98) | 1.20 (0.56–2.66) | 0.4      |
| P-value                  | 0.6  | 0.1  | 0.1  | 0.6  | 0.6  |         |
| SFAs (non-case/case)     | (44/16) | (43/17) | (35/25) | (37/33) | (28/32) |         |
| Model 1                  | 1.00 | 1.08 (0.48–2.42) | 1.96 (0.91–4.23) | 1.66 (0.79–3.60) | 3.25 (1.51–7.02) | 0.001    |
| P-value                  | 0.8  | 0.08 | 0.01 | 0.003 | 0.003 |         |
| Model 3: model 2 + MUFAs, PUFAs, Trans | 1.00 | 1.36 (0.59–3.12) | 2.12 (0.96–4.69) | 1.66 (0.75–3.70) | 3.17 (1.43–7.00) | 0.005    |
| P-value                  | 0.4  | 0.2  | 0.04 | 0.004 | 0.004 |         |
| MUFAs (non-case/case)    | (29/31) | (38/22) | (39/21) | (39/22) | (28/32) |         |
| Model 1                  | 1.00 | 0.54 (0.26–1.12) | 0.50 (0.24–1.04) | 0.52 (0.25–1.09) | 0.37 (0.17–0.80) | 0.02     |
| P-value                  | 0.06 | 0.06 | 0.002 | 0.002 | 0.002 |         |
| Model 4: model 2 + SFAs, PUFAs, Trans | 1.00 | 0.43 (0.20–0.92) | 0.33 (0.15–0.72) | 0.28 (0.12–0.64) | 0.25 (0.09–0.67) | 0.002    |
| P-value                  | 0.43 | 0.02 | 0.005 | 0.004 | 0.004 |         |
| Oleic acid (non-case/case) | (25/35) | (38/22) | (40/20) | (41/19) | (43/17) |         |
| Model 1                  | 1.00 | 0.42 (0.20–0.88) | 0.34 (0.16–0.73) | 0.33 (0.15–0.69) | 0.28 (0.13–0.60) | 0.001    |
| P-value                  | 0.8  | 0.02 | 0.005 | 0.004 | 0.004 |         |
| Model 4: model 2 + SFAs, PUFAs, Trans | 1.00 | 0.96 (0.41–2.23) | 1.71 (0.72–4.05) | 2.35 (0.99–5.58) | 1.49 (0.53–4.14) | 0.1      |
| P-value                  | 0.9  | 0.2  | 0.052 | 0.04  | 0.04  |         |
| Dietary cholesterol (non-case/case) | (42/18) | (34/26) | (41/19) | (38/22) | (32/28) |         |
| Model 1                  | 1.00 | 1.78 (0.84–3.78) | 1.08 (0.49–2.34) | 1.35 (0.63–2.89) | 2.04 (0.96–4.32) | 0.1      |
| P-value                  | 0.1  | 0.8  | 0.4  | 0.06  | 0.06  |         |
| Model 6: model 2 + SFAs, PUFAs, MUFAs, Trans | 1.00 | 1.91 (0.83–4.41) | 0.92 (0.38–2.22) | 0.93 (0.38–2.20) | 0.98 (0.39–2.50) | 0.4      |
| P-value                  | 0.2  | 0.05 | 0.7  | 0.06  | 0.4   |         |
| n-3 PUFAs (non-case/case) | (36/24) | (35/25) | (47/13) | (32/28) | (37/23) |         |
| Model 1                  | 1.00 | 1.07 (0.51–2.21) | 0.41 (0.18–0.92) | 1.31 (0.63–2.70) | 0.93 (0.44–1.94) | 0.9      |
| P-value                  | 0.8  | 0.03 | 0.4  | 0.8   | 0.8   |         |
| Model 7: model 2 + SFAs, MUFAs, n-6 | 1.00 | 1.05 (0.46–2.40) | 0.37 (0.15–0.94) | 0.92 (0.38–2.26) | 0.66 (0.21–2.04) | 0.4      |
| P-value                  | 0.8  | 0.03 | 0.8  | 0.4   | 0.4   |         |
| ALA (non-case/case)      | (24/36) | (35/25) | (28/32) | (46/14) | (54/6)  |         |
| Model 1                  | 1.00 | 0.44 (0.21–0.92) | 0.73 (0.35–1.51) | 0.18 (0.08–0.40) | 0.08 (0.03–0.21) | <0.001   |
| P-value                  | 0.02 | 0.02 | <0.001 | <0.001 | <0.001 |         |
| Model 7: model 2 + SFAs, MUFAs, Trans, n-6 | 1.00 | 0.34 (0.15–0.79) | 0.59 (0.25–1.39) | 0.14 (0.05–0.37) | 0.07 (0.02–0.23) | <0.001   |
| P-value                  | 0.6  | 0.6  | 0.1  | <0.001 | <0.001 |         |
| DHA (non-case/case)      | (34/26) | (38/22) | (39/21) | (32/28) | (44/16) |         |
| Model 1                  | 1.00 | 0.75 (0.36–1.57) | 0.70 (0.33–1.47) | 1.14 (0.55–2.35) | 0.47 (0.22–1.02) | 0.2      |
| P-value                  | 0.4  | 0.3  | 0.7  | 0.05  | 0.05  |         |
| Model 7: model 2 + SFAs, MUFAs, Trans, n-6 | 1.00 | 0.77 (0.34–1.73) | 0.94 (0.41–2.15) | 1.29 (0.57–2.90) | 0.59 (0.25–1.40) | 0.6      |
| P-value                  | 0.5  | 0.8  | 0.5  | 0.2   | 0.2   |         |
| EPA (non-case/case)      | (33/27) | (39/21) | (37/23) | (36/24) | (42/18) |         |
| Model 1                  | 1.00 | 0.65 (0.31–1.37) | 0.76 (0.36–1.57) | 0.81 (0.39–1.68) | 0.52 (0.24–1.11) | 0.2      |
| P-value                  | 0.2  | 0.4  | 0.5  | 0.09  | 0.09  |         |
related to lower anxiety score. To the best of our knowledge, no study has reported the association of MUFAs with anxiety disorder. In addition, we showed an inverse association between n-3:n-6 PUFAs ratio and anxiety score. Similar to our study results, a prospective cohort study showed a positive significant association between lower ratio of n-3: n-6 PUFAs and anxiety disorder [50]. Although no association was found between DHA, EPA, and n-6 PUFAs with anxiety score in the present study, the data from some cross-sectional studies have shown an inverse relationship between intake of DHA and EPA with anxiety in adults [22–24]. In addition, some experimental studies have shown that intake of EPA and DHA reduces anxiety disorder [29, 51]. However, a prospective study did not find any relationship between intake of n-3 PUFAs and anxiety disorder [26]. In addition, a cross-sectional study showed that dietary intake of n-6 PUFAs is not related with anxiety [24]. Contrary to our findings, an experimental study on adults showed beneficial effect of low-fat diet in comparison with a high-fat diet on psychological mood states [52]. The disparity between the findings might be explained by the differences in study design, sample size, characteristics of study participants, and geographic differences. Some biological mechanisms explain the effect of fatty acids in psychiatric disorders; these include regulation of corticotropin-releasing factor, the hypothalamic-pituitary-adrenocortical axis, increased serotonergic neurotransmission, alterations in dopaminergic function, and improved cerebral blood flow [53–55]. In addition, fatty acids have an effect on receptor function, signal transmission, and neurotransmitter reuptake [26]. A few studies have examined the relationship between fatty acids’ intake and anxiety, especially in a general population. The current study was adjusted for several important confounders that are known to affect anxiety disorder and DFQ. In addition, women in our study were not informed of their anxiety status. When individuals are aware of their anxiety disorder, they might change their food intake or dietary intake report. However, the study has some limitations. First, FFQ has a potential recall bias. Respondents are requested to report their intake retrospectively, which may affect their reporting. Recall bias increases with recall periods longer than 7 days [56]. The FFQ used in the present study was excessively long and required recall of up to 1 year, which may affect the report of dietary intake in the participants. In addition, it is difficult for respondents to answer the questions regarding usual frequency of intake and usual portion size, and are thus prone to measurement error [56]. Second, the study design was cross-sectional, which cannot interpret a cause-and-effect relationship. Third, it is possible that experiencing anxiety might have resulted in lifestyle modification including lower dietary intake or altered dietary choices, which could result in potential bias. Fourth, regardless of adjusting for many confounding variables in the analysis, residual confounding together with unmeasured confounders may have affected the results. Fifth, as the study population was women who attended the healthcare centers, we cannot generalize our results to all women in this age group. In addition, the findings might not be generalized to men and populations with ethnic and cultural differences.

| Model 7: model 2 + SFAs, MUFAs, Trans, n-6 | Q1 (n = 60) | Q2 (n = 60) | Q3 (n = 60) | Q4 (n = 60) | Q5 (n = 60) | p-trend |
|------------------------------------------|-------------|-------------|-------------|-------------|-------------|---------|
| Model 1                                 | 1.00        | 0.63 (0.27–1.44) | 0.93 (0.41–2.12) | 0.78 (0.35–1.75) | 0.62 (0.26–1.48) | 0.4     |
| P-value                                 | 0.2         | 0.8         | 0.5         | 0.2         |             |         |
| n-6 PUFAs (non-case/case)               |             |             |             |             |             |         |
| (40/20)                                 | (40/20)     | (35/25)     | (34/26)     | (38/22)     |             |         |
| Model 1                                 | 1.00        | 1.00 (0.46–2.13) | 1.42 (0.68–3.00) | 1.52 (0.72–3.20) | 1.15 (0.54–2.45) | 0.4     |
| P-value                                 | 1.0         | 0.3         | 0.2         | 0.7         |             |         |
| Model 8: model 2 + SFAs, MUFAs, Trans, n-3 | 1.00        | 0.89 (0.37–2.10) | 1.56 (0.65–3.71) | 1.61 (0.65–4.00) | 1.24 (0.38–4.08) | 0.3     |
| P-value                                 | 0.7         | 0.3         | 0.2         | 0.7         |             |         |
| n-3: n-6 (non-case/case)                |             |             |             |             |             |         |
| (34/26)                                 | (33/27)     | (33/27)     | (47/13)     | (40/20)     |             |         |
| Model 1                                 | 1.00        | 1.07 (0.5–2.2) | 1.07 (0.5–2.2) | 0.3 (0.16–0.80) | 0.6 (0.31–1.37) | 0.02    |
| P-value                                 | 0.85        | 0.85        | 0.01        | 0.26        |             |         |
| Model 5: model 2 + SFAs, MUFAs, Trans   | 1.00        | 0.97 (0.42–2.23) | 0.94 (0.41–2.17) | 0.36 (0.15–0.88) | 0.56 (0.24–1.03) | 0.02    |
| P-value                                 | 0.9         | 0.9         | 0.02        | 0.1         |             |         |

Model 1: Crude
Model 2 Adjusted for age, physical activity, total energy intake, job, body mass index, and parity
SFAs saturated fatty acids, MUFAs monounsaturated fatty acids, PUFAs polyunsaturated fatty acids, ALA alpha-linolenic acid, DHA docosahexaenoic acid, EPA eicosapentaenoic acid

Table 2 (continued)
Conclusion

Based on the results of the present study, an inverse association was found between intakes of MUFAs, oleic acid, ALA, and n-3:n-6 PUFA ratios with odds of anxiety. In addition, higher intake of SFAs was associated with higher anxiety score. The study analysis showed that overall DFQ may be important in anxiety disorder. These results may help to develop nutritional interventions and dietary guidelines to prevent or reduce anxiety in women. Nevertheless, experimental studies are required to evaluate the effect of DFQ on anxiety disorder.

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Authors’ contributions

SBS has made substantial contributions to conception and design, and has been involved in drafting of the manuscript. GS has made substantial contributions to the design, revised the manuscript critically, and given the final approval of the version to be submitted. MS has made substantial contributions to conception and design. ARF has contributed greatly in offering advice on statistical design and analysis. All authors read and approved the final manuscript.

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Data availability statement

The data used to support the findings of this study are available from the corresponding author.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran (IR.TUMS.VCR.REC.1397.146). The aim of the study was explained to the women, and written informed consent was obtained from all participants.

Competing interests

The authors declare that they have no competing interests.

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