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Association of Dietary Acid Load and Depression among Iranian Women: A Case-Control Study

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ABSTRACT

Background: The present study aimed to investigate the association between dietary acid load and depression among Iranian women. **Methods:** This case–control study was conducted on 110 women with depression and 220 healthy controls recruited from two psychiatric clinics in Tehran, Iran. Dietary intake over the previous 12 months was assessed using a validated semi-quantitative food frequency questionnaire (FFQ) consisting of 168 items. Dietary acid load was calculated using two established indices: Potential Renal Acid Load (PRAL) and Net Endogenous Acid Production (NEAP). The association between dietary acid load and depression was evaluated using multivariate logistic regression models in crude and adjusted analyses. The adjusted model was controlled for potential confounders, including energy, physical activity, history of depression, smoking status, periods of unemployment, occupational status, and body mass index (BMI). **Results**: Participants in the highest quartile of PRAL and NEAP had significantly higher odds of depression compared to those in the lowest quartile. In the fully adjusted model, the odds ratio (OR) for depression was 3.52 (95% CI: 1.64–7.54; *P* for trend <0.001) for PRAL and 4.07 (95% CI: 1.86–8.89; *P* for trend <0.001) for NEAP. **Conclusion:** Higher dietary acid load, as measured by PRAL and NEAP, was associated with increased odds of depression in women. However, due to the case–control design, causal inferences cannot be established. Further prospective studies are warranted to confirm these findings.

Introduction

Psychological disorders, particularly depression, have increased at an alarming rate worldwide in recent years (Depression, 2017). It is estimated that approximately 4.4% of the global population (5.1% of females and 3.6% of males) are affected by depressive disorders, with a notably

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higher prevalence of approximately 21% reported among the adult population in Iran (Depression, 2017, Noorbala *et al.*, 2004).

The etiology of mental disorders is multifactorial, involving genetic predisposition as well as environmental and social determinants (Lange *et al.*, 2017, Sarris *et al.*, 2016, Saveanu and Nemeroff, 2012). Recently, growing evidence has highlighted the critical role of nutrition and overall dietary patterns in the prevention and management of mental health disorders (Abshirini *et al.*, 2019, Murakami and Sasaki, 2010, Rao *et al.*, 2008). Notably, examining dietary patterns rather than isolated food items provides more robust and reliable insights, as it accounts for the synergistic and interactive effects of various dietary components (Mozaffari *et al.*, 2018). Dietary acid load has emerged as a comprehensive indicator for evaluating the acidifying or alkalizing potential of an individual's diet (Scialla and Anderson, 2013). Established indices such as net endogenous acid production (NEAP) and potential renal acid load (PRAL) are widely used, valid, and practical approaches for estimating dietary acid load based on nutrient composition (Frassetto *et al.*, 1998, Remer and Manz, 1994).

A growing body of literature suggests that diets characterized by a high acid load - typically rich in animal-based products - may be associated with an increased risk of mental health disorders, including depression (Bahari *et al.*, 2023). In contrast, dietary patterns rich in fruits and vegetables, such as Mediterranean and plant-based diets, which exert a more alkalizing effect, have been associated with a reduced risk of these conditions (Molendijk *et al.*, 2018, Rahmani *et al.*, 2018, Saghafian *et al.*, 2018)**.**

From a mechanistic perspective, it has been proposed that a high dietary acid load may stimulate the secretion of glucocorticoids, particularly cortisol, thereby influencing psychological well-being (Buehlmeier *et al.*, 2016, Esche *et al.*, 2016). Elevated glucocorticoid levels can induce structural and functional alterations in key regions of the limbic system, including the hippocampus and amygdala, ultimately contributing to changes in emotional regulation and behavior (Dedovic *et al.*, 2009, Mora *et al.*, 2012). Given these inconsistencies, further well-designed studies are warranted, particularly in regions such as West Asia and North Africa, where the intake of alkalizing foods is low and the prevalence of psychological disorders is high. Therefore, the present study was designed to comprehensively investigate the association between dietary acid load and depression.

Materials and Methods

Study population

This case-control study was conducted among 110 depressed women and 220 control participants. Patients with depression were diagnosed by psychiatrists according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (Gonçalves *et al.*, 2008), validated for the Iranian population. Participants were recruited from two psychiatric clinics in Tehran using a convenience sampling method (Shooshtari *et al.*, 2007). The control group had no evidence of major depressive disorder based on the Beck Depression Inventory-II (BDI-II) (Whisman *et al.*, 2000) validated for the Iranian population (Ghassemzadeh *et al.*, 2005). In addition, participants in both groups had no history of depression during the previous year. Cases and controls were individually matched according to sex, age, and residential area. Each patient with depression was matched with two control subjects within a 10-year age range. Moreover, eligible control subjects were recruited from the patients' residential areas by trained interviewers. The inclusion criteria included age 18–65 years, residence in Tehran, Iran, and a diagnosis of major depressive disorder; only recent-onset cases were included. The exclusion criteria included the presence of cognitive or psychotic disorders diagnosed by a psychiatrist, current use of antidepressant medications or other psychiatric treatments, hormonal disorders, chronic diseases such as diabetes, cardiovascular diseases, and cancer, history of trauma resulting in unconsciousness or hospitalization within the past 3 months, acute or chronic infectious diseases,

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alcohol or drug use at the time of the study or within the past 3 months, body mass index (BMI) ≥ 40 kg/m², pregnancy or lactation at the time of the study or within the past year, adherence to any special diet within the past year, and unwillingness to participate in the study (FÚart *et al.*, 2009, Samieri *et al.*, 2008). A written informed consent form was completed by the subjects. This study has been approved by the Ethics Committee of Tehran University of Medical Sciences.

Sample size calculation

The sample size was calculated using OpenEpi software for an unmatched case–control study with a case-to-control ratio of 1:2 (110 depressed women and 220 healthy controls). The calculation was based on a two-sided 95% confidence level, 80% statistical power, and the expected proportion of exposure in controls and odds ratio from previous studies.

Assessment of dietary intake

A validated semi-quantitative food frequency questionnaire consisting of 168 items was used to assess food consumption in the previous 12 months (Mirmiran *et al.*, 2010). Data from the questionnaire was converted into grams per day. The conversion of food portion sizes to grams was also conducted via household measures (Ghaffarpour *et al.*, 1999). Then, the registered foods were assessed using the upgraded Nutritionist IV software (First Databank, San Bruno, CA, USA) specifically designed for Iranian foods. Finally, the FFQs were administered by an expert dietitian.

Calculation of dietary acid load indices

The dietary acid load was calculated using the relevant data with 2 validated methods: PRAL and NEAP. PRAL was calculated using the method explained by Remer and Manz (Remer and Manz, 1994):

PRAL (mEq/day) = (0.4888 × protein intake [g/day]) + (0.0366 × phosphorus [mg/day]) − (0.0205 × potassium [mg/day]) − (0.0125 × calcium [mg/day]) − (0.0263 × magnesium [mg/day]).

NEAP was computed by the algorithm illustrated by Frassetto *et al*. (Frassetto *et al.*, 1998) as follows:

NEAP (mEq/day) = (54.5 × protein intake [g/day]/potassium intake [mEq/day]) − 10.2.

Assessment of other variables

General information and data on drug use were collected through a general questionnaire. For all participants, weight and height were measured, and BMI was calculated. A categorized physical activity questionnaire, based on the metabolic equivalent hours per day (MET-h/day), was applied. This questionnaire includes nine levels of activity, from rest and sleep (MET=0.9) to severe activity (MET ≥6). The validity and reliability of this questionnaire have been affirmed by Kelishadi *et al.* in Iran (Kelishadi *et al.*, 2001).

Ethical considerations

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects/patients were approved by the Shahid Sadoughi University of Medical Sciences (IR.SSU.SPH.REC.1405.028). Written informed consent was obtained from all subjects/patients.

Data analysis

Qualitative and quantitative variables were compared between the case and control groups using a chi-square test and independent t-test, respectively. Also, the comparison of quantitative variables and dietary intakes of the participants across quartiles of PRAL was made using a one-way ANOVA test. The association between depression and PRAL and NEAP was investigated using multivariate logistic regression in crude and adjusted models. Model I was adjusted for energy intake. In model II, physical activity, history of depression, smoking status, periods of unemployment, job, and BMI were additionally adjusted. Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 26.0). P-values<0.05 were considered statistically significant.

Results

General characteristics of the study population

The general characteristics of women with and without depression, as well as across PRAL quartiles, are presented in **Table 1**. As shown in the table, physical activity, history of depression, periods of unemployment, and job differed

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significantly between the case and control groups (*P*<0.05). With increasing PRAL scores, the number of smokers and individuals with a history of depression also increased significantly (*P*<0.05).

Table 1. Characteristics of study participants according to the patients and controls and quartiles of the PRAL score.

Variables	Health status			PRAL quartiles				
	Control	Case	P-value[a]	Q1	Q2	Q3	Q4	P-value[b]
Body mass index (kg/m^2)	26.43±5.51	26.45±5.13	0.98	27.25±5.72	27.14±6.02	25.69±4.71	25.63±4.79	0.08
Physical activity (MET-h/week)	38.58±4.93	36.94±5.45	0.006	38.75±4.38	37.72±5.57	38.81±6.02	38.88±4.28	0.05
Years of education	12.20±4.56	11.24±4.27	0.070	12.16±4.32	11.37±4.61	11.95±4.68	12.07±4.34	0.67
History of depression	22(10)	33(30)	<0.001	22(10)	33(30)	22(10)	33(30)	<0.001
Marital status								
Single	67(30.3)	32(29.1)	0.24	21(26.5)	20(24.1)	26(31.3)	32(36.6)	0.45
Married	143(64.7)	67(60.9)		56(68.3)	58(69.9)	51(61.4)	45(54.2)	
Divorced or widowed	11(5)	11(10)		5(6.1)	5(6)	6(7.2)	6(7.2)	
Smoking status								
Non smoker	209(94.6)	98(89.9)	0.11	80(76.6)	79(95.2)	75(90.4)	73(89)	<0.001
Smoker	12(5.4)	11(10.1)		2(2.4)	4(4.8)	8(9.6)	9(11)	
Periods of unemployment								
House worker	98(44.3)	65(59.1)	0.007	44(53.7)	46(55.4	39(47)	34(41)	0.23
≤6 months in the last 5 years	104(47.1)	32(29.1)		6(7.3)	9(10.8)	5(6)	12(14.5)	
More than 6 months in the last 5 years	19(8.6)	13(11.8)		32(39)	28(33.7)	39(47)	37(44.6)	
Job								
Employee	42(19.4)	12(11.3)	0.014	18(22)	13(16.3)	11(13.6)	12(15.2)	0.10
Self-employed	32(14.8)	16(15.1)		8(9.8)	12(15)	11(13.6)	17(21.5)	
Students	38(17.6)	9(8.5)		7(8.5)	8(10)	17(21)	15(19)	
House worker & retired	104(48.1)	69(65.1)		49(59.8)	47(58.8)	42(51.9)	35(44.3)	

As characteristics are very similar according to the NEAP score, baseline characteristics are only presented according to the PRAL score quartiles; [a]: Obtained from Chi-squared test and independent t-test for categorical and continuous variables, respectively; [b]: Chi-squared test for qualitative variables and ANOVA test for quantitative variables. Continuous and categorical data are presented as mean ± SD and frequency (percentage), respectively.

Dietary intakes of participants

Table 2 presented the energy and dietary intakes of study participants based on PRAL quartiles. Individuals in the highest PRAL quartiles had significantly greater intakes of energy, protein, cholesterol, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, magnesium, zinc, and phosphorus (*P*<0.05), but significantly lower intakes of carbohydrates, fiber, calcium, potassium, vitamin A, vitamin C, vitamin B6, and vitamin B12 (*P*<0.05). Intake of fat (*P*=0.36) and sodium (*P*=0.13) did not differ significantly across PRAL quartiles. Based on food group intake, participants with higher PRAL scores had significantly lower intakes of fruits and vegetables (*P*<0.001), whereas they had higher intakes of red meat (*P*=0.008) and refined grains (*P*<0.001). There were no significant differences in the intake of fish (*P*=0.23), dairy products (*P*=0.08), whole grains (*P*=0.13), legumes and nuts (*P*=0.15), sugars (*P*=0.65), sugar-sweetened beverages (*P*=0.28), or tea and coffee (*P*=0.28) across PRAL quartiles.

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Table 2. Dietary daily intakes (mean±SD) of participants according to the PRAL quartiles.

Variables	Q1(N=82)	Q2(N=83)	Q3(N=83)	Q4(N=83)	P-value[a]
PRAL (mEq/d)	-49.73 ± 23.53	-19.45 ± 3.79	-7.49 ± 4.60	19.95 ± 25.29	<0.001
NEAP (mEq/d)	22.30 ± 5.15	29.70 ± 3.89	36.58 ± 3.44	51.20 ± 10.34	<0.001
Energy intake(kcal)	2872.6 ± 1209.5	2411.8 ± 843.5	2530 ± 953.6	3060.6 ± 1216.5	<0.001
Carbohydrate(g)	63.42 ± 0.08	61.57 ± 0.06	61.42 ± 0.07	58.85 ± 0.09	0.003
Protein(g)	13.70 ± 0.02	13.97 ± 0.02	14.35± 0.02	16.13± 0.09	0.01
Fat(g)	25.86 ± 0.07	26.87 ± 0.06	28.08 ± 0.07	27.78± 0.09	0.36
Fibre (g/d)	38.42 ± 14.72	24.98 ± 7.86	23.87 ± 8.14	26.02 ± 21.83	<0.001
Cholesterol (mg/d)	281.22 ± 171.87	258.84 ± 140.79	247.23 ± 116.19	327.09 ± 283.77	<0.001
SFA (mg/d)	24.48 ± 13.42	21.53 ± 8.97	22.04 ± 12.27	27.91 ± 17.57	0.009
MUFA (mg/d)	26.46 ± 16.19	23.49 ± 12.08	23.97 ± 13.51	29.56 ± 16.43	0.031
PUFA (mg/d)	21.97 ± 17.89	18.81 ± 10.84	18.97 ± 11.24	24.64 ± 15.54	0.024
Zinc (mg/d)	13.22 ± 5.39	11.24 ± 4.26	11.80 ± 4.23	16.10 ± 8.36	<0.001
Phosphorus (mg/d)	1774.75 ± 734.91	1498.32 ± 561.61	1559.73 ± 549.76	2050.12 ± 1008.65	<0.001
Potassium (mg/d)	6317.21 ± 2521.29	4374.48 ± 1343.74	4041.48 ± 1349.23	4084.45 ± 1608.45	<0.001
Calcium (mg/d)	1286.86 ± 463.54	1051.15 ± 390.96	1054.02 ± 435.91	1156.88 ± 483.75	0.002
Magnesium (mg/d)	508.32 ± 218.18	397.07 ± 137.06	403.56 ± 143.23	515.09 ± 364.49	<0.001
Sodium (mg/d)	3927.35 ± 1909.09	3801.80 ± 2013.87	3725.79 ± 2141.43	4444.20 ± 2542.79	0.13
Vitamin A (RAE/d)	2758.91± 2105.37	1523.93 ± 771.45	1536.64 ± 911.56	1349.35 ± 767.60	<0.001
Vitamin C (mg/d)	388.59± 196.43	218.65 ± 76.35	188.94 ± 91.10	146.90 ± 78.15	<0.001
Vitamin B6 (mg/d)	3.17 ± 2.02	2.16± 0.76	2.15 ± 0.75	2.42 ± 1.20	<0.001
Folate (µg/d)	710.06 ± 290.59	549.04 ± 204.30	559.02 ± 222.31	654.40 ± 307.98	<0.001
Vitamin B12 (mg/d)	8.57 ± 39.17	3.91 ± 3.18	3.80 ± 2.47	5.26 ± 5.29	0.37
Food groups (g/1000 kcal)					
Fruits	944.69 ± 448.73	520.66 ± 202.64	478.13 ± 258.63	362.74 ± 209.21	<0.001
Vegetables	537.38 ± 259.33	368.82 ± 166.08	313.59 ± 152.43	231.08 ± 128.01	<0.001
Red meat	24.66 ± 72.22	19.79 ± 17.54	25.17 ± 17.88	39.72 ± 65.03	0.008
Fish	8.45 ± 8.68	6.65 ± 9.70	10.13 ± 16.36	10.56 ± 17.10	0.23
Dairy	492.98 ± 249.22	408.29 ± 226.20	406.67 ± 297.79	405.43 ± 261.12	0.08
Legumes and nuts	81.17 ± 57.78	67.73 ± 49.17	65.94 ± 52.73	29.78 ± 25.53a	0.15
Whole grains	70.11 ± 97.49	64.05 ± 70.97	78.86 ± 107.67	102.34 ± 154.29	0.13
Refined grains	362.15 ± 28.76	380.67 ± 222.67	446.84 ± 244.37	608.40 ± 322.87	<0.001
Sugars	22.45 ± 66.25b	23.32 ± 19.02	22.36 ± 20.79	19.35 ± 15.72	0.65
Sugar-sweetened beverages (ml/day)	37.47 ± 61.09	66.46 ± 129.02	56.41 ± 120.89	62.16 ± 86.94	0.28
Tea and coffee	859.19 ± 510.70	887.20 ± 498	730.91 ± 598.87	656.59 ± 482.61	0.28

***PRAL**: Potential renal acid load; **NEAP**: net endogenous acid production; **SFA**: Saturated fatty acid; **MUFA**: Monounsaturated fatty acid; **PUFA**: Polyunsaturated fatty acid; As characteristics are very similar according to the NEAP score, baseline characteristics are only presented according to the PRAL score quartiles; [a]: ANOVA test was used.*

Association between PRAL and NEAP and odds of depression

Crude and multivariate-adjusted odds ratios for the association between PRAL, NEAP, and depression are presented in **Table 3**. In the crude model, participants in the highest quartiles of PRAL and NEAP had 4.11- and 4.43-times higher odds of depression, respectively, compared with those in the lowest quartiles. This association remained significant after adjustment for energy intake, physical activity, history of depression, smoking status, periods of unemployment, job, and BMI (Odds Ratio $(OR)_{PRAL}$: 3.52; 95%, CI:1.64 to 7.54, *P* for trend: <0.001) and OR_{NEAP}: 4.07; 95%, CI:1.86 to 8.89, *P* for trend: <0.001).

Discussion

The findings showed that higher dietary acid load indices (PRAL and NEAP) are associated with higher odds of depression in women. Furthermore, the authors observed that participants in the highest quartile of dietary acid load compared to the lowest quartile had a significantly

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higher intake of red meat and refined grains. Also, fruit and vegetable consumption were significantly lower in the highest quartile of dietary acid load versus the lowest quartile.

Table 3. The OR (95%CI) of depression across quartiles of PRAL and NEAP.

Dietary acid load score	Cases (N)	Crude	Model I	Model II
PRAL (mEq/day)				
<-27.2	27	1	1	1
-27.2 to -13.6	20	1.21 (0.58-2.52)	1.31 (0.62-2.77)	0.95 (0.42-2.14)
-13.5 to 1.61	30	2.16 (1.07-4.34)	2.30 (1.13-4.67)	2.59 (1.19-5.60)
≥2.21	43	4.11 (2.07-8.16)	4.03 (2.02-8.03)	3.52 (1.64-7.54)
P-trend		<0.001	<0.001	<0.001
NEAP (mEq/day)				
<27.2	16	1	1	1
27.2 to 27.9	20	1.31 (0.62-2.75)	1.33 (0.63-2.81)	1.14 (0.51-2.55)
34.4 to 37.7	31	2.45 (1.21-4.97)	2.38 (1.17-4.84)	2.12 (0.96-4.66)
≥42.9	43	4.43 (2.21-8.88)	4.23 (2.10-8.52)	4.07 (1.86-8.89)
P-trend		<0.001	<0.001	<0.001

***PRAL**: Potential renal acid load; **NEAP**: **OR**: Odds ratio; **NEAP**: Net endogenous acid production; **Model I**: Adjusted for energy intake; **Model II**: Model I + adjusted for physical activity**,** history of depression, smoking status, periods of unemployment, job and BMI; Logistic regression was used.*

Few studies have investigated the relationship between dietary acid load and depression. A cross-sectional study on women in the age range of 20-50 showed that individuals who had higher dietary acid load scores had greater odds for stress, anxiety, and depression compared to lower scores (Mozaffari *et al.*, 2020). Results from Ausimmune longitudinal study (AusLong study) with a 10-year follow-up indicated that a higher dietary acid load in multiple sclerosis patients increased depression levels but not anxiety (Saul *et al.*, 2023). Wu *et al.* in a longitudinal study among breast cancer survivors demonstrated that women in the highest quartile of PRAL had a greater risk of depression versus women in the lowest quartile (Wu *et al.*, 2020). Findings from a study on 4378 persons (1909 male and 2469 female) reported that subjects in the highest category of the dietary acid load had a higher risk of anxiety and depression compared to those in the lowest (Milajerdi *et al.*, 2020). However, another research did not show a significant relationship between the intake of acidic foods and the risk of depression (Jans *et al.*, 2018). The results from a cohort study demonstrated that adherence to a high-protein diet might be a protective factor against depression in men while having a detrimental role in women (Wolfe *et al.*, 2011). The fact was that these disagreement results were related to differences in the sources of consumed proteins. It is suggested that a higher intake of animal proteins, as opposed to plant-based protein sources, is a major contributor to psychological disorders such as depression (Hosseinzadeh *et al.*, 2016).

The results demonstrated that women in the highest quartile of dietary acid load versus the lowest quartile had a significantly higher intake of red meat and refined grains. In a cross-sectional study on 3172 adults (18–55 years old), women in the highest quartile of refined grains intake compared with the first quartile, had higher odds of anxiety and depression (Sadeghi *et al.*, 2019). In a study by Mofrad *et al.* women in the highest quartile of red meat consumption compared with those in the lowest quartile had the highest prevalence of depressive symptoms, anxiety and stress (Mofrad *et al.*, 2021). In contrast, the results of a study published in 2021, showed no association between red meat consumption and mental disorders in women (Kazemi *et al.*, 2021). Moreover, Chi *et al.* in a prospective study, did not find any relationship between red meat and poultry consumption and the risk of depression in postmenopausal women (Chi *et al.*, 2016). Also,

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the authors observed that fruit and vegetable consumption were significantly lower in the highest quartile of dietary acid load compared to the lowest quartile. Findings from the Taiwan Longitudinal Survey on Aging (TLSA) showed that fruit and vegetable consumption combined with physical activity was inversely related to the risk of depression (Fann *et al.*, 2022). Grases *et al.* in an observational retrospective study indicated no consumption of legumes, and low intake of fruit and vegetable were significantly correlated with depression (Grases *et al.*, 2019). Results of a study on women by 15 years of follow up showed that a higher consumption of fruit (≥ 4 servings) and vegetable (≥ 5 servings) was associated with lower odds of depression symptoms (Dharmayani *et al.*, 2022). The Australian Diabetes, Obesity and Lifestyle Study (AusDiab study) after 12 years of follow up, demonstrated that a diet rich in fruits and vegetables, especially yellow/orange/red and leafy green vegetables, lowered the odds of depressive symptoms (Radavelli-Bagatini *et al.*, 2021). Moreover, other cross-sectional studies on Finnish population and university students from 16 countries found no association between fruit and vegetable intake and depression (Allgöwer *et al.*, 2001, Hintikka *et al.*, 2005). Different findings might be due to diversity in the study population, using different measurement tools for the evaluation of psychopathy, and lack of adjusting some special dietary intakes (such as fiber and omega-3) as confounders (Crichton *et al.*, 2013, Jacka *et al.*, 2010).

Several pathways have been suggested to describe the positive association between dietary acid load and psychopathy: First, there is an acid-sensing ion channel-1a (ASIC1a) expressed in the nervous system, especially in the amygdala, which has a central role in the regulation of mood (Coryell *et al.*, 2007, Rauch *et al.*, 2003). Overexpression of ASIC1a in mice caused the fear condition, while ASIC1a inhibition had anti-anxiety and anti-depressant effects (Wemmie *et al.*, 2008). Therefore, a high dietary acid load produces high PH which might motivate ASIC1a and result in psychological disorders. Second, metabolic acidosis can elevate the secretion of cortisol (Maurer *et al.*, 2002, Perez *et al.*, 1979). A large number of researches supported a direct relationship between cortisol and psychological disorders (Heinze *et al.*, 2016, Vives *et al.*, 2015, Zorn *et al.*, 2017). In addition, metabolic acidosis can increase the inflammatory parameters level (de Nadai *et al.*, 2013), so oxidative stress might result in higher risk of psychological disorders (Najjar *et al.*, 2013).

Consumption of refined grains augments the risk of inflammation, as a risk factor for psychopathy (Lopez-Garcia *et al.*, 2004). Moreover, refined grains lead to postprandial hyperglycemia and hyperinsulinemia (Bao *et al.*, 2011, Seaquist *et al.*, 2013) and this might reduce blood glucose concentrations to a level that is a threshold for the release of autonomic hormones such as cortisol, adrenaline, growth hormone and glucagon (Ludwig, 2002). Red meat contains a high amount of dietary fat which has contributed to causing depression in animals. In one study conducted on rats, those who had a high-fat diet were more likely to have depression (Abildgaard *et al.*, 2011). Arachidonic acid which is abundant in red meat, produces the inflammatory mediators named eicosanoids. In contrast, eicosapentaenoic acid (EPA) and docosahexaenoic acid (Dharmayani *et al.*) are known due to their anti-inflammatory effects. Therefore, the level of inflammation ascertains through the balance between Arachidonic acid and DHA or EPA. High consumption of red meat by changing the balance toward Arachidonic acid results in inflammation and finally depression (Shibata *et al.*, 2018). In addition, animal protein consumption caused an increase in some gut microbiota like Bacteroides entero, which are deemed to have a role in developing depression via the link between the gut and brain (Dash *et al.*, 2015).

The existing findings are focused on the particular nutrients within fruit and vegetables, which affect psychological health (Rooney *et al.*, 2013). B vitamins have effects on single-carbon metabolism and synthesis of neurotransmitters, including serotonin, catecholamines and other

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monoamine neurotransmitters (Kennedy, 2016, Stough *et al.*, 2011). Moreover, the vital role of B vitamins in brain function is ascertained via a number of neuropsychiatric signs related to deficiencies in each of the B vitamins, like folate and vitamin B12 (Kennedy, 2016, Rao *et al.*, 2008). A recent investigation showed that the association between dietary patterns and depression is mediated by folate and vitamin B12 serum concentrations. This study reported that an increase in serum folate and vitamin B12 in healthy dietary pattern and a decrease in these two vitamins in unhealthy dietary pattern were associated with depression (Khosravi *et al.*, 2020). Also, fruits and vegetables are rich in antioxidants components and have a promising relationship with psychological well-being (Islam *et al.*, 2020). They lead to decrease oxidative stress and inflammation, potentially via the activation of transcription factors, including nuclear factor erythroid 2-related factor 2 (Nrf2) or nuclear factor κB (NFκB) (Kaulmann and Bohn, 2014).

Although this was the first case-control study that examined the relation of dietary acid load scores (PRAL and NEAP) among women, and results were adjusted for energy intake, physical activity, history of depression, smoking status, periods of unemployment, job and BMI; however, this study had some limitations. First, because this study only included women, the results cannot be generalized to both genders. Furthermore, the use of the FFQ questionnaire for participants 'dietary assessment is inevitably subject to error. Due to the subjective nature of this method, over-or under-reporting of food intake cannot be predicted, therefore more detailed studies are required.

Conclusion

The results revealed that there is a significant inverse association between dietary acid load scores (PRAL and NEAP) and the odds of depression in women. However, more studies are needed to support these findings in the future.

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Authors' contributions

Darand M, Hosseinzadeh M and Khosravi M designed the study. Darand M, Ghorbani M, Arabi V and Hosseinzadeh M contributed to the statistical analysis, data interpretation and manuscript drafting. The final version of manuscript for submission was approved by all authors for submission.

Conflicts of interest

There were not any conflicts of interest.

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