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Comparison between Macro & Micro Nutrient Intake in Depressed Patients with Healthy People

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ABSTRACT

Background: In recent years, the prevalence of depression has grown dramatically in the world. According to WHO reports, about 350 million people suffer from depression. In addition to the side effects of antidepressants, many patients are resistant to treatment with these drugs. One of the most important effective factors in the pathology of depression is the role of nutrition in controlling and preventing this disease. Therefore, the aim of this study was to investigate the macronutrient and micronutrient status in depressed patients and compare them with healthy people. **Methods:** In this case-control study, 110 depressed patients were matched with 220 healthy controls based on their age, gender, and area of residence. Patients were selected by simple sampling method. In the case group, unipolar major depressive disorder was diagnosed by a psychiatrist using the DSM-IV criteria. Food intakes of all participants were obtained using reliable semi-quantitative food frequency questionnaires and analyzed with Nutritionist4 software. Anthropometric measurements including height, weight, and waist circumference were calculated for all participants. **Results:** The participants included 260 women and 71 men. The two groups had a statistically significant difference in terms of occupation, history of depression, childhood traumatic experiences, and family history of depression ($P < 0.05$). Regarding the macronutrients and micronutrients, a significant difference was observed between the case and control groups in terms of vitamin C, vitamin K, and dietary fiber intake, which were lower in depressed patients. **Conclusion:** The results of this study indicated that intake of some micronutrients such as vitamins C, K, and dietary fiber may be associated with an increased risk of depression. Consumption of some micronutrients, mainly fruits and vegetables may be effective to control or prevent the risk of depression.

Keywords: *Depression; Micronutrient; Macronutrient; Nutrition.*

Introduction

Prevalence of depression in the world has grown dramatically. According to the World Health Organization, about 350 million people are suffering from depression (World health organization, 2018).

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Depression has several risk factors including: disability, progression of an illness, unhealthy lifestyle, poor health status, history of depression, deprivation, sleep disorders, and female gender (Cole and Dendukuri, 2003). Scientists have recently suggested more psychological and physical effects for depression. For example, Karina Davidson and colleagues observed that depression had a relationship with premature hypertension or even early coronary artery disease (Davidson *et al.*, 2000).

Different drug groups are applied to treat depression including selective serotonin re-uptake inhibitor like monoamine oxidase, but these drugs have their own side effects and sometimes do not respond to treatment (Hodgson, 2015). Recently, studies were conducted to assess the impact of lifestyle changes (diet and exercise) on the prevention and control of depression, as a better solution. Some studies found that various nutrients are associated with the risk of depression in adults; folate, omega-3, increase in omega-3/omega-6 ratio, olive oil, and moderate alcohol consumption are associated with lower risk of depression, in contrast, trans fats, fast foods, and industrial breads are associated with higher risk of depression (Beydoun *et al.*, 2015, Gea, 2012, Kyrozis *et al.*, 2009, Sanchez-Villegas *et al.*, 2012). Robio-Lopez et al. (Rubio-Lopez *et al.*, 2016) found that intake of thiamine, vitamin K, and bromine had a positive correlation with the improvement of depression symptoms. However, protein, carbohydrate, pantothenic acid, biotin, vitamin B-12, vitamin E, zinc, manganese, cobalt, and aluminum intake had a negative correlation with depression symptoms in children.

Severity of depression symptoms can also be related to the diet. For example, a higher consumption of fiber in vegetables and fruits can reduce the symptoms (Miki *et al.*, 2016). Therefore, the aim of this study was to compare the status of macronutrients and micronutrients between the depressed patients and healthy individuals. The effect of many confounding factors was also controlled or moderated in this study.

Materials and Methods

Study design and participants: In this case-control study, sampling was easy and non-random. Participants were within the age range of 18-65 years old. The case group consisted of 110 depressed patients and the control group had 220 non-depressed members. Major depressive disorder was diagnosed by a psychiatrist according to the 4th Edition DSM criteria. This method was developed by the American Psychological Association (Goncalves *et al.*, 2008) and was standardized in Iran (Barnes, 1994). The control group consisted of the individuals with no depression in the past year based on the Beck Depression Inventory. Interviewers went to each patient's home and invited the qualified individuals to participate in this study. Patients and control group members were matched according to their age, gender, and region of residence. Age groups were matched in the ranges of 30- 18, 40-31, 50- 41, and 65 -51 years. Participants were selected from two (Baharlou Hospital and Imam Hossein Hospital) hospitals in 7 and 15 districts in Tehran. The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences and written consent forms were obtained from all participants.

Inclusion criteria were being in the age range of 18-65 years old, living in Tehran, having unipolar MDD diagnosed by a psychiatrist according to the DSM-IV criteria (in the case group), having the symptoms of the disease for a maximum of three months before participating in the study, and attaining a score under 15 on the Beck Depression questionnaire (for the control group).

Exclusion criteria: Individuals with cognitive impairments or other psychiatric diseases based on the psychiatrist diagnosis, those with severe depression so that the patient is unable to cooperate in the study and answer the questions, individuals who were consuming any kind of medications or antidepressant therapy, and people with hormonal disorders such as Addison, Cushing, hyperparathyroidism, hypothyroidism or hyperthyroidism based on the physician's diagnosis or drugs' taken were not involved in this study. In addition, people with chronic diseases such as

cancer, CVD, diabetes, stroke, fibromyalgia, kidney failure or liver failure, multiple sclerosis, and Parkinson based on physician's diagnosis, those who took medications, and had a history of injury, contusion, cuts, fractures, bleeding, burn, accident, and other similar situations in the past three months leading to anesthesia and hospitalization were also excluded. Moreover, development of acute and infectious diseases in the last two weeks including AIDS, mononucleosis, tuberculosis, viral hepatitis, and pneumonia based on a physician's diagnosis or consumption of the related drugs were among the other exclusion criteria. People with alcohol and drug addiction at the enrollment time or within the past three months according to the participant's self-statement were also excluded. The history of grief experience within the past six months, pregnancy and lactation at the enrollment or in the last year, BM I≥ 40, any particular diet in the past two months, or history of having any particular diet for more than two months in the past year led the researchers to exclude the individual.

*Measurements***:** Food Frequency Questionnaire (FFQ) was administered to all participants one day after diagnosis. The FFQ has 148 food items and its reliability was confirmed in the Tehran Lipid and Glucose Study (Mirmiran *et al.*, 2010). This questionnaire surveys the consumption of food in the last year before diagnosis of the depression.

A questionnaire was developed and administered to collect the participants' demographic information, the study's confounding variables, and drug usage to find out about other diseases.

Anthropometric measurements for all participants included height, weight, and waist circumference. Height was measured in standing upright position without shoes using a height-measuring device with the precision of 0.5 cm. Weight was measured in minimal clothing with the precision of 0.1 kg and BMI was calculated by dividing the weight (kg) by the square of height (m^2). Waist circumference was measured with the precision 0.5 cm at the intermediate boundary of the lower ribs and the iliac crest in standing upright position, with normal breathing and without clothes.

Physical activity measurements were performed according to the metabolic equivalent (MET) classification of physical activity with nine activity levels ranging from sleep and rest (MET = 0.9) to severe activity (MET ≥ 6). This questionnaire was prepared in a previous study in Europe and its validity was confirmed by the Daily Physical Activity Inventory and the CSA Accelerometer (Model 7164 Ambulatory Monitor) (Aadahl and Jorgensen, 2003). Validity and reliability of this questionnaire in Iran was confirmed by Kelishadi et al. in a study on adolescents (Kelishadi *et al.*, 2004). Physical activity of individuals in this questionnaire is calculated in terms of metabolic equivalent per hour on the MET-h / day.

Data analysis: T-test was applied for covariates with normal distribution and Mann-Whitney was run for independent covariates without normal distribution. Moreover, we used $\chi 2$ qualitative variables. All variables in case and control groups were compared by applying the mentioned methods**.** Simple logistic regression was used to compare the quantitative and qualitative variables between the case and control groups and OR was also calculated. Multivariate logistic regression model was developed to adjust some important confounding variables. To validate the model, the Hosmer-Lemeshow test (P > 0.05) was used and the existence of logical confidence interval was investigated.

Results

Independent quantitative and qualitative variables in the case and control groups are described and compared in **Tables 1** and **2**, respectively. The study included 260 women and 70 men. The comparison of macronutrient intake and some of its components between the case and control groups are shown in **Table 3**.

The relationship between macronutrient intake and depression before and after adjustment for the effects of the confounding variables was also investigated. No significant difference was found with regard to the intake of macronutrients such as carbohydrates (P = 0.1 and P = 0.4), fat (P = 0.1 and P = 0.7), and protein (P = 0.09 and P = 0.7) before

and after adjustment for the effects of confounding variables between the two groups.

The fiber intake in the case group was significantly lower than that of the control group ($P < 0.05$), and the daily energy intake ($P = 0.04$) was significantly higher in the case group than the control group. However, this result became insignificant after adjusting for the effect of the confounding variables. The average intakes of vitamins and minerals were compared between the case and control groups and their relationship with depression before and after adjustment for the effect of the confounding variables is reported in **Tables 4** and **5**, respectively.

Based on the Recommended Dietary Allowances (RDAs), the intake of vitamin C ($P = 0.001$) and vitamin K ($P = 0.002$) was significantly lower in the case group than in the control group. Even after adjustment for the effect of the confounding variables, the difference remained significant. A significant difference was also observed in niacin intake ($P = 0.02$) between the two groups, but the difference became *in*significant after adjusting the effect of confounding variables.

No significant difference was observed between the two groups regarding minerals of zinc, magnesium, calcium, potassium, phosphorus, iron, and copper, whereas, selenium intake was significantly different between the two groups ($P = 0.001$). This rate became insignificant after the effect of the confounding variables was adjusted.

Table 1. Comparison of mean of quantitative independent variables between case and control groups

Quantitative variables	N	Case group	Control group	P-value[a]
Age (year)	۳۲۷	35.85 ± 1.04[b]	53.96 ± 0.72	0.8
Birth order	۳۳۰	3.70 ± 0.19	2.9 ± 0.12	0.4
Number of family members	۳۳۱	3.7 ± 0.15	3.8 ± 0.08	0.6
Number of education years	۳۲۷	11.2 ± 0.42	21.2 ± 0.3	0.07
Weight (kg)	۳۲۹	96.7 ± 1.3	7.1 ± 0.96	0.8
Height (cm)	۳۲۷	261.8 ± 0.79	361.4 ± 0.59	0.5
Body mass index (kg/m^2)	۳۲۱	62.4 ± 0.49	62.4 ± 0.37	0.9
Waist circumference (cm)	۳۲۷	98.1 ± 1.24	88.2 ± 0.92	0.5
Physical activity (METhr/d)	۳۲۵	36.9 ± 0.52	38.6 ± 0.33	0.007

[a]: *t*-test for normal covariates & Mann-Whitney for without normal covariates ; [b]: Mean ± SE

Table 2. Comparison of qualitative independent variables between case and control groups

Qualitative variables	Case N (%)	Control N (%)	P-value[a]
Job			
Housewife	66 (60.6)	99 (45.2)	0.03
Clerk	12 (11.0)	42 (19.2)	
Self-employed	6 (5.5)	8 (3.7)	
Retired	16 (14.7)	32 (14.6)	
Student	9 (8.3)	38 (17.4)	
Depression history			
No	77 (70.0)	199 (90.0)	0.001
Yes	33 (30.0)	22 (10.0)	
Childhood traumatic experiences			
No	70 (64.0)	171 (77.0)	< 0.001
Yes	50 (23.0)	39 (36.0)	
Family predisposition to depression			
No	80 (73.0)	196 (89.0)	0.001
Yes	30 (27.0)	25 (11.0)	
Number of children			
0	40 (36.4)	88 (39.8)	0.04
1	23 (20.9)	44 (19.9)	
2	20 (18.2)	60 (27.2)	
3<	27 (24.5)	29 (13.1)	

[a]: $\chi 2$ test

Table 3. Comparison of the mean (**±SE**) of daily intake of macronutrients and some of their components

Variables	Groups		P-value[a]	P-value[b]	Adjusted model	
	Case	Control			P-value[c]	OR(95%CI)
Energy (Kcal)	2887 ± 112	2634 ± 69	-	0.04	0.70	1.07 (0.72-1.6)
Carbohydrate(g)	439 ± 19	402 ± 10	-	0.10	0.40	1.0 (0.9- 1.0)
Energy from carbohydrate(%)	60.6 ± 0.7	61.6 ± 0.5	0.06	-	0.80	0.99 (0.96-1.0)
Protein (g)	101 ± 4	94 ± 3	-	0.09	0.70	1 (0.9-1.0)
Energy from protein (%)	14.8 ± 0.2	14.6 ± 0.4	0.60	-	0.90	0.9 (0.9-1.0)
Fat (g)	86 ± 4	79 ± 3	-	0.10	0.70	0.9 (0.9-1.0)
Energy from fat (%)	62 ±0.7	62 ±0.5	0.30	-	0.60	0.9 (0.9-1.0)
Fiber (g)	26 ± 1	29 ± 1	-	0.03	0.04	0.6 (0.4-0.9)
Tryptophan (g)	821 ± 32	845 ± 75	0.08	-	0.49	1.2 (0.6-2.2)
SFA (g)	26 ± 1	22 ± 0.8	-	0.05	0.60	1.0 (0.9-1.0)
MUFA (g)	28 ± 1	24 ± 0.9	-	0.03	0.80	1.0 (0.9-1.0)
PUFA (g)	21 ± 1	20 ± 1	-	0.10	0.40	0.9 (0.9-1.0)

[a:] Mann Whitney test; [b:] Independent *t*-test for logarithm or to the power 2 or cube root of variables; [c] : Multiple logistic regression to adjust for the effects of confounding variables including education level, occupation, physical activity, body mass index, and dietary patterns

Table 4. Comparison of the mean (**±SE**) daily intake of vitamins as micronutrients

Variables	Groups		P-value[a]	Adjusted model	
	Case	Control		P-value[b]	OR(95%CI)
B1 (mg)[d]	2.77 ± 0.11	2.45 ± 0.09	0.60	0.50	1.06 (0.87-1.28)
B2 (mg) [d]	2.31 ± 0.08	2.61 ± 0.06	0.60	0.49	0.89 (0.65-1.22)
B3 (mg) [d]	82.6 ± 1.2	52.8 ± 0.9	0.02	0.60	1.00 (0.98-1.03)
B5 (mg) [d]	8.10 ± 0.33	7.17 ± 0.2	0.60	0.50	1.03 (0.93-1.13)
B6 (mg) [d]	2.24 ± 0.09	2.5 ± 0.1	0.60	0.40	0.92 (0.75-1.13)
Folate(mcg) [d]	623.8 ± 27.5	614.9 ± 17.3	0.90	0.70	1.1 (0.60-1.93)
B12 (mcg) [d]	4.86 ± 0.44	5.37 ± 1.6	0.70	0.40	0.99 (0.97-1.01
C (mg) [d]	212.4 ± 13.9	246.7 ± 10.3	0.001	0.04	0.5 (0.26-0.97)
K (mcg) [d]	178.4 ± 10.0	259.0 ± 2.9	0.002	0.01	0.99 (0.99-0.99)
A (RE) [d]	1669 ± 118	1848 ± 96	0.19	0.60	1.15 (0.61-2.15)
D (mcg) [e]	1.73 ± 0.14	2.51 ± 0.74	0.30	0.40	0.80 (0.48-1.36)
E (mg) [f]	14.9 ± 1.0	15.4 ± 0.8	0.70	0.30	0.98 (0.96-1.01)

[a:] Mann Whitney test; [b:] Independent *t*-test for logarithm or to the power 2 or cube root of variables; [c:] Multiple logistic regression to adjust for the effects of confounding variables including education level, occupation, physical activity, body mass index, and dietary patterns; [d]: More than the Recommended Dietary Allowances (RDA) for men and women; [e]: The RDA for vitamin D for men and women is 15 mcg; [f]: The RDA for vitamin E for men and women is 15 mcg.

Table 5. Comparison of the mean (**±SE)** daily intake of minerals as micronutrients

Variables	Groups		P-value[a]	P- value[b]	Adjusted model	
	Case	Control			P-value[c]	OR(95%CI)
Zn (mg/day) [d]	13.6 ± 0.52	12.9 ± 0.43	-	0.16	0.9	0.99 (0.95-1.04)
Mg (mg/day) [d]	449.4 ± 17.4	459.1 ± 17.7	-	0.90	0.3	0.99 (0.99-1.00)
Ca (mg/day) [e]	1158 ± 46	1125 ± 29	-	0.68	0.3	1.29 (0.74-2.28)
Potassium (mg/day)[f]	4455 ± 167	4820 ± 141	-	0.10	0.5	0.87 (0.57-1.33)
P (mg/day) [d]	1759 ± 65	1701 ± 0.53	-	0.27	0.8	1.07 (0.59-1.92)
Fe (mg/day) [d]	21.27 ± 0.9	21.3 ± 0.8	-	0.89	0.2	0.98 (0.95-1.01)
Cu(mg/day) [d]	2.2 ± 0.09	2.2 ± 0.07	-	0.80	0.2	0.80 (0.62-1.10)
Se (mg/day) [d]	0.124 ± 0.00	0.149 ± 0.03	0.001	-	0.3	0.52 (0.12-2.29)

[a:] Mann Whitney test; [b:] Independent *t*-test for logarithm or to the power 2 or cube root of variables; [c:] Multiple logistic regression to adjust for the effects of confounding variables including education level, occupation, physical activity, body mass index, and dietary patterns; [d]: More than the Recommended Dietary Allowances (RDA) for men and women; [e]: The RDA for calcium is 1000-1200 g/d for women and 1000 g/d for men; [f]: The RDA for potassium for men and women is 4.7 g/day.

Discussion

According to our findings, although the intake of carbohydrate, protein, and fats did not differ significantly between the two groups, the daily energy intake ($P = 0.04$) was significantly higher in patients than the control group. However, after the effect of confounding variables was adjusted, the difference became insignificant.

The intake of fiber, before and after adjusting for the effect of confounding variables, was significantly lower in the case group than in the control group ($P < 0.05$). Furthermore, the difference in calorie intake of two groups may result in the amount of fiber consumption. This argument is further supported by adjusting for the effects caused by the variety of food intake patterns (healthy and unhealthy), including dietary fiber intake. Similarly, in the cross-sectional population-based study by Park no significant difference was found in daily energy intake between the depressed and healthy groups (Payne *et al.*, 2009).

It should be noted that in the present study, depressed patients were selected from the cases of incidence rather than the cases of prevalence. Since the cases of incidence are newly infected people, the difference in dietary intake of the two groups needs more time to appear. This is probably the reason for lack of a significant difference in the BMI of the two groups. The slight difference in energy intake was eliminated after adjustment for the effect of confounding variables. However, consumption of dietary fibers that is related to the type of food consumption and food choices was lower in patients, which could be due to lack of incentives and reduced energy levels among the patients for preparation of fruits and vegetables as rich sources of fiber.

In the present study, B vitamins had no significant correlation with depression before and after adjusting for the effect of confounding variables. Payne et al. (Beydoun *et al.*, 2010) in a study in the United States showed that dietary folate was inversely correlated with depression. However, they reported that other types of folate, including total folate intake and folic acid supplementation were not related with depression. This can be explained by a possible difference with respect to folate deficiency between the study populations.

It should be noted that in our study, the average of folate intake was higher than the RDAs; in other words, our participants did not suffer from folate deficiency. The results of a study by Beydon et al. represented that people with the highest average folic acid intake had the highest levels of plasma folate concentration and the lowest score for depression symptoms (Beydoun *et al.*, 2010). In other studies, depression had a positive correlation with low serum levels of folate and B12 (Blunden *et al.*, 2012, Coppen and Bolander-Gouaille, 2005,

Kim *et al.*, 2018). The reason for these differences can be due to the different status of folate deficiency.

Some vitamins in B family contribute to the development of depression through the metabolism of neurotransmitters (Blunden *et al.*, 2012). One of the mechanisms by which folate and vitamin B12 are associated with depression is that 5 methyl-tetra-hydro-folic acid (5-MTHF), with the help of vitamin B12, donates its methyl group to homocysteine and converts it into methionine. In this way, the level of homocysteine -a toxic metabolite in the nervous system- is reduced; on the other hand, methionine also contributes to the synthesis of neurotransmitters such as serotonin after conversion to S-adenosyl methionine (Kuczmarski *et al.*). The results of a research indicated that decline in serotonergic function in the brain was an important risk factor for etiology of emotional disorders, especially depression (Solfrizzi *et al.*, 2006).

In the present study, based on the comparison of the micronutrients in depressed and healthy people, niacin, selenium, vitamin C, and vitamin K before adjusting for the effect of the confounding variables, were significantly different between the two groups. After adjustment for education, occupation, physical activity, BMI, and dietary patterns, only intake of vitamin C and vitamin K was significantly higher in healthy people than the depressed patients.

This means that one or more of the confounders including education, occupation, physical activity, BMI, and dietary patterns are more likely to be associated with depression. So, by entering these variables into the model, the relationship between depression and consumed niacin and selenium removed.

In the study of Payne in the United States (Payne *et al.*, 2012), vitamin C intake was significantly lower in depressed patients than in healthy participants, with the difference remaining significant after adjustment for the effects of age, gender, education, vascular disease, BMI, fat, and vitamin C supplementation. However, no relationship was observed between depression and vitamin C supplementation. In the study of Prohan in Iran, vitamin C intake was significantly higher in healthy people than the depressed patients (Prohan *et al.*, 2014).

Based on the previous studies, antioxidants play important roles in preventing and treating depression because they help to reduce the oxidative stress and cellular degradation caused by free radicals (Frusciante *et al.*, 2007). Vitamin C is known as an important antioxidant in this field (Kaner *et al.*, 2015). To convert tryptophan to serotonin, it is first necessary to produce 5-hydroxytryptophan using a hydroxylase enzyme. Since vitamin C is a cofactor of this enzyme, the vitamin is probably associated with synthesis of serotonin and depression via this mechanism (Miller, 2008).

In the present study, intake of vitamin K in depressed people had a significant relationship after adjusting for the effect of confounding variables. In other words, non-adjustment of the confounding variables caused the relationship to be not observed, but the inclusion of these variables in the model revealed that this difference was significant. Moreover, an interaction was found between vitamin K and one of the confounders.

In the literature review, no study was found to confirm this association, but it was reported that some anticoagulants, such as the plasminogen activator, catalyze proteolysis of pro-brain-derived neurotrophic factor (pro BDNF) to BDNF and have antidepressant effects. The activity of some enzymes participating in the coagulation cascade, including serine protease present in the enzyme complex, depends on vitamin K (Hou *et al.*, 2009, Tsai, 2006, 2007).

In various studies, minerals such as zinc, calcium, iron, and selenium were observed to be effective in preventing and treating depression (Bourre, 2006, Duntas *et al.*, 2003). However, in our study, after adjusting for the effect of confounding variables, no significant relationship was found between depression and minerals. Therefore, a semi-quantitative questionnaire, i.e., FFQ is required.

In some studies, sufficient amounts of long chain polyunsaturated fatty acids, especially docosa hexaenoeic acid (DHA) were suggested to reduce the progression of depression (Stoll *et al.*, 1999).

Researchers found that an imbalance in essential fatty acids ratio, the ratio of n-6 to n-3, or n-3 deficiency may lead to symptoms of depression associated with reduced plasma cholesterol concentrations (Wells *et al.*, 1998). In the present study, no significant relationship was observed between the intake of fatty acids and depression. The probable cause of this observation is the limited dietary intake of n-3 fatty acids in our study population. The average consumption of seafood in the case group was 11.6 ± 1.6 g/day and in the control group 0.72 ± 7.6 g/day. A significant difference was seen between the two groups considering the consumption of seafood ($P < 0.05$) because intake of seafood was not investigated with respect to the content of n-3 fatty acids, particularly DHA. However, the difference in the content of the consumed ω-3 fatty acids was not significant between the two groups. Therefore, the reduction of the supply of seafood sources on the one hand and the lack of examination of the type of consumed seafood on the other hand, can be possible causes for the lack of observing the aforementioned relationship.

One of the strengths of this study was its large sample size compared to the previous studies and the adjustment for the effects of confounding variables, especially the dominant food patterns in the study population. The control group was also selected from healthy population rather than from inpatients in hospitals or other health centers. The healthy participants were also matched with the control group with regard to their age, gender, and district of residence. Limitation of the study was that information on the amount of nutrients consumed was based on a semi-quantitative questionnaire, not a quantitative instrument. Therefore, future researchers are recommended to apply the study methods that estimate food intake accurately, such as various versions of 24-hour Dietary Recall or food registries.

Future studies on the association between food intake and depression in different societies with different cultures and dietary patterns are also suggested. Identification of foods most closely associated with depression risk in all cultures and communities can help the researchers to make more comprehensive judgments about the micronutrients associated with the diseases.

Conclusions

The results of this study indicated that intake of some micronutrients such as vitamins C and K as well as dietary fibers were associated with an increased risk of depression. Since whole grain, fruits, and vegetables are good resources for micronutrients and dietary fibers, sufficient consumption of them may be helpful to control or prevent from the risk of depression. Given the importance of these issues, we recommend further studies on this subject.

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Conflict of interest

The authors declare no conflict of interest.

Authors' contributions

Khosravi M made substantial contribution in conceptualizing and designing the study, extracting the erythrocyte PUFA, analyzing and interpreting the data, and drafting the manuscript. Hosseinzadeh M made contribution in analyzing. Golzar M made substantial contribution in drafting the manuscript. Majdzadeh R made substantial contribution in conceptualizing and designing the study. Sotoudeh G made substantial contributions to conception and design. She also revised the manuscript critically. All authors approved the final version of the manuscript to submit.

References

Aadahl M & Jorgensen T 2003. Validation of a new self-report instrument for measuring physical activity. *Medicine & science in sports & exercise*. **35 (7)**: 1196-1202.

Barnes A 1994. Diagnostic and statistical manual mental of disorders: DSM-IV. Shahed university publications: Tehran.

Beydoun MA, et al. 2015. Associations of the Ratios of n-3 to n-6 Dietary Fatty Acids With Longitudinal Changes in Depressive Symptoms Among US Women. *American journal of epidemiology.* **181 (9)**: 691-705.

Beydoun MA, et al. 2010 .The sex-specific role of plasma folate in mediating the association of dietary quality with depressive symptoms. *Journal of nutrition.* **140 (2)**: 338-347.

Blunden CH, et al. 2012. Postpartum depressive symptoms: the B-vitamin link. *Mental health in family medicine.* **9 (1)**: 5-13.

Bourre JM 2006. Effects of nutrients (in food) on the structure and function of the nervous system: update on dietary requirements for brain. Part 1: micronutrients. *Journal of nutrition health and aging.* **10 (5)**: 377-385.

Cole MG & **Dendukuri N** 2003. Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. *American journal of psychiatry.* **160 (6)**: 1147-1156.

Coppen A & Bolander-Gouaille C 2005. Treatment of depression: time to consider folic acid and vitamin B12. *Journal of psychopharmacology.* **19 (1)**: 59-65.

Davidson K, Jonas BS, Dixon KE & Markovitz JH 2000. Do depression symptoms predict early hypertension incidence in young adults in the CARDIA study? Coronary Artery Risk Development in Young Adults. *Archives of internal medicine.* **160 (10)**: 1495-1500.

Duntas LH, Mantzou E & Koutras DA 2003. Effects of a six month treatment with selenomethionine in patients with autoimmune thyroiditis. *European journal of endocrinology.* **148 (4)**: 389-393.

Frusciante L, et al. 2007. Antioxidant nutritional quality of tomato. *Molecular nutrition & food research.* **51 (5)**: 609-617.

Gea A, Martinez-Gonzalez, M.A., Toledo, E., Sanchez-Villegas, A., Bes-Rastrollo, M., Nuñez-Cordoba, J.M., Sayon-Orea, C. and Beunza ,J.J., 2012. A longitudinal assessment of alcohol intake and incident depression: the SUN project. . *BMC public health.* **12 (1)**: 954.

Goncalves DM, Stein AT & Kapczinski F 2008. Performance of the Self-Reporting Questionnaire as a psychiatric screening questionnaire: a comparative study with Structured Clinical Interview for DSM-IV-TR. *Cadernos de saude publica.* **24 (2)**: 380-390.

Hodgson K, Tansey, K.E., Uher, R., Dernovšek, M.Z., Mors, O., Hauser, J., Souery, D., Maier, W., Henigsberg, N., Rietschel, M. and Placentino, A., 2015. Exploring the role of drug-metabolising enzymes in antidepressant side effects. *Psychopharmacology.* **232 (14)**: 2609-2617.

Hou SJ, Yen FC & Tsai SJ 2009. Is dysfunction of the tissue plasminogen activator (tPA)-plasmin pathway a link between major depression and cardiovascular disease? *Mededical hypotheses.* **72 (2)**: 166-168.

Kaner G, et al. 2015. Evaluation of nutritional status of patients with depression. *BioMed research international.* **2015**: 521481.

Kelishadi R, et al. 2004. Assessment of physical activity in adolescentsof Isfahan. *Sharekord University Of Medical Sciences Journal {persian}.* **3**: 55-65.

Kim NR, Kim KW, Kim HN & Song SW 2018. Associations Between Serum Zinc Levels and Mental Health: Findings from the 2010 Korean National Health and Nutrition Examination Survey. *Biological trace element research.* **181 (2)**: 192-198.

Kuczmarski MF, et al. Higher Healthy Eating Index-2005 scores associated with reduced symptoms of depression in an urban population: findings from the Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS) study. *Journal of the American dietetic association.* **110 (3)**: 383-389.

Kyrozis A, et al. 2009. Dietary lipids and geriatric depression scale score among elders: the EPIC-Greece cohort. *Journal of psychiatric research.* **43 (8)**: 763-769.

Miki T, et al. 2016. Dietary fiber intake and depressive symptoms in Japanese employees:

The Furukawa Nutrition and Health Study. *Nutrition (Burbank, Los Angeles County, Calif.).* **32 (5)**: 584-589.

Miller A 2008 .The methylation, neurotransmitter, and antioxidant connections between folate and depression. *Alternative medicine review*. **13 (3)**: 216-226.

Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M & Azizi F 2010. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. *Public health nutrition.* **13 (5)**: 654-662.

Payne ME, et al. 2009. Natural food folate and late-life depression. *Journal of nutrition for the elderly*. **28 (4)**: 348-358.

Payne ME, Steck SE, George RR & Steffens DC 2012. Fruit, vegetable, and antioxidant intakes are lower in older adults with depression. *Journal of the Academy of Nutrition and Dietetics*. **112 (12)**: 2022-2027.

Prohan M, Amani R, Nematpour S, Jomehzadeh N & Haghighizadeh MH 2014. Total antioxidant capacity of diet and serum, dietary antioxidant vitamins intake, and serum hs-CRP levels in relation to depression scales in university male students. *Redox Report.* **19 (3)**: 133-139.

Rubio-Lopez N, Morales-Suarez-Varela M, Pico Y, Livianos-Aldana L & Llopis-Gonzalez A 2016. Nutrient Intake and Depression Symptoms in Spanish Children: The ANIVA Study. *International journal of environmental research and public health.* **13 (3)**: 352=365.

Sanchez-Villegas A, et al. 2012. Fast-food and commercial baked goods consumption and the risk of depression. *Public health nutrition.* **15 (3)**: 424-432.

Solfrizzi V, et al. 2006. Dietary intake of unsaturated fatty acids and age-related cognitive decline: a 8.5-year follow-up of the Italian longitudinal study on aging. *Neurobiology of aging* **27 (11)**: 1694-1704.

Stoll AL, et al. 1999. Omega 3 fatty acids in bipolar disorder: a preliminary double-blind, placebo-controlled trial. *Archives of general psychiatry*. **56 (5)**: 407-412.

Tsai SJ 2006. The possible role of tissue-type plasminogen activator and the plasminogen system in the pathogenesis of major depression. *Medical hypotheses.* **66 (2)**: 319-322.

Tsai SJ 2007. The P11, tPA/plasminogen system and brain-derived neurotrophic factor: Implications for the pathogenesis of major depression and the therapeutic mechanism of antidepressants. *Medical hypotheses.* **68 (1)**: 180-183.

Wells AS, Read NW, Laugharne JD & Ahluwalia NS 1998. Alterations in mood after changing to a low-fat diet. *British journal nutrition.* **79 (1)**: 23-30.

World health organization 2018. Depression WHO: https://www.who.int/en/news-room/fact-sheets/detail/depression.