ORIGINAL ARTICLE

Observational Study

Drinking plain water is associated with decreased risk of depression and anxiety in adults: Results from a large cross-sectional study

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Abstract

AIM
To investigate the relation between plain water drinking and risk of depression and anxiety among a large sample of Iranian adults.

METHODS
A total of 3327 Iranian general adults were included in this cross-sectional study. Validated Iranian version of the Hospital Anxiety and Depression Scale was used to assess anxiety and depression. Water consumption was assessed by asking about the number of glasses of water that consumed daily. Water consumption was categorized into < 2, 2-5, and ⩾ 5 glasses of water/d.

RESULTS
In the crude model, the lowest level of water drinking (< 2 glasses/d) compared with reference group (⩾ 5 glasses/d) doubled the risk of depression and anxiety ($P < 0.0001$). After adjusting potential confounders, this inverse link remained significant for depression (OR: 1.79; 95%CI: 1.32, 2.42; $P < 0.0001$), but not for anxiety (OR: 1.49; 95%CI: 0.98, 2.25; $P = 0.109$). In stratified analyses by sex, after controlling for potential confounders, water drinking < 2 glasses/d was associated with 73% and 54% increment in the risk of depression in men and women, respectively ($P < 0.05$), whilst no significant association was observed for anxiety either in men or in women.

CONCLUSION
We found inverse associations between plain water consumption and depression. Also, these findings showed a tended risky association, but not statistically significant, between lower levels of water consumption and anxiety. These findings warrant evaluation in prospective and clinical trials studies to establish the plausible role of water in mental health status.

Key words: Water; Anxiety; Depression; Psychological disorders; Iranian

Core tip: Evidence supports the relation between water consumption and health outcomes. Validated Iranian version of the Hospital Anxiety and Depression Scale was used to assess anxiety and depression.

Water consumption was assessed by asking about the number of glasses of water that consumed daily. After adjusting potential confounders, an inverse link was observed between water and depression, but not for anxiety, though in the crude model both disorders were inversely related to water drinking. These findings warrant evaluation in prospective studies to establish the plausible role of water in mental health status.

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INTRODUCTION

The prevalence of common psychological disorders has been increasing over recent decades[1,2]. Approximately, 29.2% of people are suffering from one of the common mental disorders worldwide[3]. Brain disorders, including both mental and neurologic disorders account for one-third of the economic cost of all diseases[4].

Drinking plenty of water is publicly believed to be useful for health and has been recommended in various dietary guidelines. Findings from a systematic review revealed that increased water consumption had a weight-reduction effect[5], and it has widely been known as an approach in weight-loss programs[6]. In addition, several studies have reported a bidirectional link between excess body weight[7,8] or diabetes[9] and mental disorders. It has been indicated that pathogenic substrates are the same in both metabolic and brain disorders; and therefore, the term of "metabolic-mood syndrome" has been suggested[10]. Lifestyle changes may to some extent explain the concurrency of obesity and mental disorders. Replacing water with sugar sweetened beverages might be the reason for inverse link between water consumption and obesity[11,12]. There is also evidence indicating the higher risk for mental disorders especially depression with higher consumption of sugar sweetened beverages[13], as well as higher glycaemic index diets[14,15].

Overall, accumulating evidence suggests that the beneficial relation between water ingestion and mental disorders is possible. However, the knowledge regarding beneficial effects of water consumption in mental health is rare. Water facilitates signaling pathway and nutrients delivery to the brain, removes toxins and inflammatory markers and provides energy sources for brain, and thereby improves brain function. Although several studies have shown that water insecurity is associated with psychological distress and anxiety[16,17], to the best of our knowledge, there is no study assessing the association between the water quantity and common

mental disorders including depression and anxiety. In the current study, therefore, we aimed to evaluate whether decreased plain water intake is associated with higher risk of mental disorders and whether it is gender-specific.

MATERIALS AND METHODS

Subjects

This cross-sectional study was carried out within the framework of the cross- sectional study on the Epidemiology of psychological, Alimentary health and Nutrition (SEPAHAN) project. The main aim of this project was to investigate the relationship between functional gastrointestinal disorders and lifestyle, nutritional factors and psychological profiles. The details of the project have been provided in Alibi *et al*[18] (2012). Briefly, the participants of the study were selected using multistage cluster and convenience sampling method amongst non-academic Isfahanian adults working at Isfahan University of Medical Sciences (IUMS) in 20 cities across Isfahan province. Each city was consider as a first stage's cluster and health centers affiliated to IUMS in each city were considered as second stage clusters and among them, considering the full coverage of geographic regions, some centers were selected randomly and those participants who were willing to participate in SEPAHAN study were recruited. In order to increase the participation rate and the data collection accuracy, the project was conducted in two phases. In the first phase, 10087 questionnaires were distributed to the participants, collecting information about anthropometric measures, demographic profile, lifestyle, nutritional factors and physical activity. 8691 completed questionnaires were returned in the first phase (response rate: 86.16%). In the second phase, psychological data were collected (response rate: 64.6%). Finally, after matching returned questionnaires in phase 2 with their equivalents in phase 1, we reached 4763 questionnaires. Of these, 2904 persons had complete information about both water consumption and psychological profile which were included in the statistical analysis. The study protocol was reviewed and approved by the ethical committee of Isfahan University of Medical Sciences.

Water consumption was assessed by asking about the average number of glasses of plain water that usually consumed in a day by each participant. The possible items to answer were < 2 glasses/d, 2-5 glasses/d and ⩾ 5 glasses/d.

Mental disorders assessment

A validated Iranian version of the Hospital Anxiety and Depression scale (HADS) was used to assess anxiety and depression[19]. HADS is a simple psychological questionnaire includes two separate parts to screen the severity of anxiety and depression. Each part includes 7 questions with a four-point rating scale (0-3); higher scores indicate greater degree of anxiety or depression.

For both disorders, the score range is from 0 to 21. To identify the presence of either disorder, score 8 was considered as the cut point. Therefore, score 8 or greater were considered to have depression or anxiety and scores ⩽ 7 were considered normal[20].

Covariates assessment

Dietary intakes of participants were assessed using a valid and reliable 106-item dish-based food frequency questionnaire[21]. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). The current level of participants' physical activity was assessed using General Practice Physical Activity Questionnaire[22] and participants were categorized as physically moderately active, active, moderately inactive and inactive. Because of close relation between gastrointestinal disorders and psychological health, we considered functional gastrointestinal disorders (FGID) as an important covariate in our analysis. Suffering from gastrointestinal disorders was assessed using a valid and modified Iranian version of ROME Ⅲ questionnaire[23]. FGID was defined as suffering from at least one of the following main gastrointestinal disorders: gastroesophageal reflux, dyspepsia, irritable bowel syndrome and constipation.

Statistical analysis

General characteristics in categories of plain water intake were reported as means and standard error (SE) or percentage for continuous variables and categorical variables, respectively. To examine the differences across plain water categories, analysis of variance (ANOVA) for continuous variables and χ^2 test for categorical variables were used. All dietary intakes were adjusted for age (yr) and weight (kg) by analysis of covariance (ANCOVA). Multiple logistic regression was used to estimate odds ratios (OR) (95%CI) for the presence of depression and anxiety across categories of plain water intake in crude and multivariable-adjusted models. In adjusted models, we controlled confounding impacts of age, sex, marital status (married, single, divorced, widowed), educational level (less than 12 years, 12-16 years and more than 16 years), BMI (continuous), smoking (non- and ex-smokers vs. current smokers), physical activity (moderately active and active vs. moderately inactive and inactive), FGIDs (Yes/No), intake of anti-psychotic medicines (Yes/No), and dietary intakes which play role in mental health [magnesium, riboflavin, pyridoxine, folate, cobalamin, Docosahexaenoic acid (DHA), Eicosa pentaenoic acid (EPA), energy, fibre and caffeine]. All confounders, including energy intake, were included in the statistical analysis as covariates. We performed stratified analyses, applying the above-mentioned models, by sex to evaluate potential modifying effect of sex related to mental health status. The adjusted models were also controlled for the same potential confounders, mentioned above. In all logistic regression analyses, *P* for linear trends was determined by Mantel-Haenszel

Variables	Plain water drinking			*P* value[1]
	< 2 glasses/d	2-5 glasses/d	≥ 5 glasses/d	
Participants (*n*)	854	1764	709	
Age (yr)[2]	37.2 ± 0.3	36.1 ± 0.2	34.8 ± 0.3	< 0.0001
BMI (kg/m^{2})[2]	24.7 ± 0.1	24.7 ± 0.10	25.5 ± 0.2	< 0.0001
Anxiety score[2]	4.0 ± 0.1	3.5 ± 0.10	3.0 ± 0.1	< 0.0001
Depression score[2] *n* (%)	6.8 ± 0.1	6.1 ± 0.09	5.3 ± 0.1	< 0.0001
Anxious	136 (16.2)	244 (14.1)	61 (8.7)	< 0.0001
Depressed	303 (36.0)	478 (27.7)	151 (21.6)	< 0.0001
Male	242 (28.3)	757 (42.9)	387 (54.6)	< 0.0001
Marital status				0.035
Married	680 (81.4)	1431 (82.9)	549 (78.8)	
Single	135 (16.2)	271 (15.7)	139 (19.9)	
Other	20 (2.4)	25 (1.4)	9 (1.3)	
Anti-psychotic medicines use	56 (6.6)	91 (5.2)	39 (5.5)	0.342
Current smokers	147 (17.2)	243 (13.8)	70 (9.9)	< 0.0001
Moderately active and active	303 (39.6)	729 (45.7)	350 (56.1)	< 0.0001
Educational level				0.005
≤ 12 yr	333 (39.8)	633 (36.9)	301 (43.1)	
12-16 yr	438 (52.4)	956 (55.6)	347 (49.7)	
≥ 16 yr	65 (7.8)	129 (7.5)	50 (7.2)	
FGID[3] (%)	488 (57.1)	892 (50.6)	321 (45.3)	< 0.0001
Nutrients[4]				
Energy (kcal/d)	2306.1 ± 30.1	2385.8 ± 20.7	2487.9 ± 34.7	0.001
Protein (% of total calorie)	84.3 ± 1.2	88.5 ± 0.8	93.2 ± 1.4	< 0.0001
Fat (% of total calorie)	95.5 ± 1.3	98.7 ± 0.9	103.1 ± 1.5	0.001
Carbohydrate (g/d)	285.3 ± 4.2	294.5 ± 2.9	306.3 ± 4.9	0.006
Fibre (g/d)	22.0 ± 0.2	22.5 ± 0.1	23.0 ± 0.2	0.003
Caffeine (mg/d)	106.7 ± 3.1	96.7 ± 2.2	96.0 ± 3.7	0.022
Magnesium (mg/d)	314.1 ± 4.3	327.2 ± 3.0	349.6 ± 5.0	< 0.0001
Thiamin (mg/d)	1.8 ± 0.03	1.8 ± 0.02	1.9 ± 0.03	0.062
Riboflavin (mg/d)	1.8 ± 0.03	1.9 ± 0.02	2.0 ± 0.03	< 0.0001
Pyridoxine (mg/d)	1.9 ± 0.03	2.0 ± 0.02	2.1 ± 0.03	< 0.0001
Folate (mg/d)	562.4 ± 5.8	573.8 ± 4.0	600.2 ± 6.7	0.801
Cobalamine (mg/d)	2.8 ± 0.05	3.0 ± 0.03	3.1 ± 0.05	< 0.0001
DHA (g/d)[3]	0.2 ± 0.01	0.2 ± 01	0.2 ± 0.01	< 0.0001
EPA (g/d)[3]	0.06 ± 0.003	0.1 ± 0.002	0.1 ± 0.003	< 0.0001
Food groups				
Fruits (g/d)	285.8 ± 8.7	322.4 ± 6.0	351.1 ± 10.1	< 0.0001
Vegetables (g/d)	215.4 ± 4.8	241.4 ± 3.3	264.7 ± 5.5	< 0.0001
Nuts, legumes and soy (g/d)	55.5 ± 1.5	56.8 ± 1.0	60.9 ± 1.7	0.047
White meat (g/d)	59.4 ± 1.8	64.03 ± 1.2	67.5 ± 2.02	0.009
Red meat (g/d)	75.4 ± 1.8	78.4 ± 1.2	84.5 ± 2.06	0.004
Refined grains (g/d)	401.6 ± 7.1	390.7 ± 5.4	389.4 ± 9.11	0.473
Whole grains (g/d)	39.5 ± 2.9	40.8 ± 1.1	52.1 ± 3.40	0.007

Table 1 General characteristic of participants across categories of plain water consumption

[1]Derived from one way ANOVA and chi-square test for continuous and categorical variables, respectively and analysis of covariance (ANCOVA) for nutrients and food groups; [2]Values are means ± SEs; [3]FGID defined as suffering from at least one of the following gastrointestinal disorders: Gastroesophageal Reflux, dyspepsia, irritable bowel syndrome and constipation; [4]The nutrients were adjusted for age and body weight. DHA: Docosahexaenoic acid; EPA: Eicosa pentaenoic acid.

extension chi-square test. All statistical analyses were done using Statistical Package for Social Sciences (SPSS, Inc., Chicago IL, United States; version 20). *P* < 0.05 was considered significant in all statistical analyses.

RESULTS

In terms of water intake, participants were categorized into three major classes (< 2 glasses, 2-5 glasses, ≥ 5 glasses/d). Those consumed more water had higher BMI (*P* < 0.0001) and were more probably to be younger, male, physically active (all *P* < 0.0001) and single (*P* < 0.05), but less educated compared with those who consumed less water (*P* = 0.005). Greater plain water drinking was associated with lower prevalence of smoking, anxiety, depression (*P* < 0.0001). Consistently, those consumed greater plain water had lower anxiety and depression score compared with those in the lowest category of plain water intake (< 2 glasses/d) (*P* < 0.0001). Water consumption was strongly associated with increased risk of FGID (*P* < 0.0001) (Table 1). Greater plain water consumption was associated with higher intakes of energy, protein, fat, carbohydrate, fibre, magnesium, riboflavin, pyridoxine, cobalamin, docosahexaenoic acid (DHA), eicosa pentaenoic acid (EPA), fruits, vegetables and red meat (*P* for all <

Table 2 General characteristics of participants based on categories of anxiety and depression _n_ (%)

	Depression		P value[1]	Anxiety		P value[1]
	Yes (28%)	No (72%)		Yes (13.1%)	No (86.9%)	
Age (yr)[2]	36.3 ± 0.3	36.1 ± 0.2	0.562	35.4 ± 0.2	36.3 ± 0.3	0.020
BMI (kg/m²)[2]	24.8 ± 0.1	24.9 ± 0.1	0.712	25.0 ± 0.2	24.9 ± 0.1	0.636
Male	285 (30.2)	1082 (46.0)	< 0.0001	117 (26.1)	1251 (43.9)	< 0.0001
Anti-psychotic medicines	106 (11.2)	76 (3.2)	< 0.0001	70 (15.6)	113 (4.0)	< 0.0001
Current smokers	164 (17.4)	290 (12.3)	< 0.0001	84 (18.8)	370 (13.0)	0.001
Moderately active and active	338 (39.7)	1028 (48.8)	< 0.0001	155 (38.5)	1212 (47.4)	0.001
Educational level			< 0.0001			< 0.0001
< 12 yr	153 (16.7)	236 (10.2)		84 (19.3)	306 (11.0)	
12-16 yr	715 (78.1)	1876 (81.4)		337 (77.5)	2255 (80.9)	
⩾ 16 yr	48 (5.2)	194 (8.4)		14 (3.2)	228 (8.2)	
Marital status			0.001			0.001
Married	733 (79.4)	1901 (82.4)		361 (83.2)	2274 (81.3)	
Single	163 (17.7)	380 (16.5)		58 (13.4)	486 (17.4)	
Other	27 (2.9)	26 (1.1)		15 (3.5)	38 (1.4)	
FGID[3]	665 (70.5)	1022 (43.4)	< 0.0001	357 (79.7)	1329 (46.6)	< 0.0001
Water drinking			< 0.0001			< 0.0001
< 2 glasses/d	303 (32.5)	539 (23.1)		136 (30.8)	706 (25.0)	
2-5 glasses/d	478 (51.3)	1246 (53.4)		244 (55.3)	1481 (52.4)	
⩾ 5 glasses/d	151 (16.2)	548 (23.5)		61 (13.8)	639 (22.6)	

[1]Derived from independent t-test and chi-square test for continuous and categorical variables, respectively; [2]Values are means ± SEs or percent; [3]FGID defined as suffering from at least one of the following gastrointestinal disorders: Gastroesophageal Reflux, dyspepsia, irritable bowel syndrome and constipation.

0.01). Tiamin, folate, white meat, refined grains, whole grains, nuts, legumes and soy consumptions were not significantly different across the categories of plain water intake.

Table 2 presents the general characteristics of study population stratified by the status of anxiety or depression. Individuals, who were anxious, but not depressed, were younger than healthy subjects. The prevalence of both depression and anxiety was higher among women, anti-psychotic medicines users, smokers and individuals who suffered from FGID. Conversely, healthy subjects were more probably to be physically active or moderately active, have higher education levels and drink more glasses of water. Whilst depression was less prevalent among married individuals, anxiety was more prevalent.

Crude and multivariable-adjusted ORs (95%CIs) of depression and anxiety across the categories of plain water intake are illustrated in Table 3. Compared with the reference group (⩾ 5 glasses/d), lower levels of water consumption (< 2 glasses/d) was associated with a greater chance of having depression (OR: 2.04; 95%CI: 1.62, 2.56; P < 0.0001) and anxiety (OR: 2.02; 95%CI: 1.46, 2.78; P < 0.0001) in crude model. Adjustment for multiple potential confounders slightly weakened these associations, but remained strongly significant for depression (P < 0.0001). However, after adjustment for dietary intakes, the lower levels of plain water consumption was a risk factor for anxiety however the significant link disappeared (for < 2 glasses/d: OR: 1.49; 95%CI: 0.98, 2.25, and for 2-5 glasses/d: OR: 1.58, 95%CI: 1.08, 2.30; P = 0.109; *vs* ⩾ 5 glasses/d).

In all crude and adjusted models, lower levels of water consumption (< 2 glasses/d) compared with the reference group (⩾ 5 glasses/d) was associated with a greater chance of having depression either in men or in women not only in crude but also in fully adjusted models (2-5 glasses/d: OR: 1.54; 95%CI: 1.00, 2.36 and < 2 glasses/d: OR: 1.73; 95%CI: 1.02, 2.93; P = 0.04) for men and in women (2-5 glasses/d: OR: 1.18 ; 95%CI: 0.86, 1.63 and < 2 glasses/d: OR: 1.54; 95%CI: 1.09, 2.15; P = 0.007). In the crude model drinking lower levels of water was associated with increased risk of anxiety in men (2-5 glasses/d: OR: 2.01; 95%CI: 1.20, 3.34 and < 2 glasses/d: OR: 1.83; 95%CI: 0.97, 3.43; P = 0.041) and in women (2-5 glasses/d: OR: 1.42 ; 95%CI: 0.98, 2.05 and < 2 glasses/d: OR: 1.59; 95%CI: 1.08, 2.34; P = 0.026); nevertheless, after adjustment for various confounders the significance associations disappeared in both genders.

DISCUSSION

In this analysis of a large cross-sectional study of general adults, lower daily plain water intake was associated with increased risk of depression and anxiety in the crude model. Although controlling for potential confounders attenuated these associations, the inverse link for depression remained strongly significant, whilst anxiety risk tended to be higher for lower water intake in the final model.

To our knowledge, this was the first investigation to examine the association of plain water consumption and common mental disorders, although the linkage of water/fluid consumption with obesity[6,12,24], coronary diseases[25], hyperglycaemia or diabetes[26,27], cancer[28] and mortality[29,30] has been examined in earlier studies. Some of these studies[6,12,24,25], but not all[26-30], confirm

Table 3 Multivariable-adjusted ORs (and 95%CIs) for depression and anxiety across categories of plain water consumption in the whole population and stratified by sex

	Plain water drinking			P trend[1]
	< 2 glasses/d	2-5 glasses/d	≥ 5 glasses/d	
Depression				
Crude model	2.04 (1.62, 2.56)	1.39 (1.13, 1.71)	1 (reference)	< 0.0001
Model 1[2]	1.75 (1.35, 2.26)	1.30 (1.02, 1.64)	1 (reference)	< 0.0001
Model 2[2]	1.84 (1.37, 2.45)	1.39 (1.07, 1.80)	1 (reference)	< 0.0001
Model 3[2]	1.84 (1.40, 2.49)	1.41 (1.07, 1.84)	1 (reference)	< 0.0001
Model 4[2]	1.79 (1.32, 2.42)	1.37 (1.04, 1.80)	1 (reference)	< 0.0001
Anxiety				
Crude model	2.02 (1.46, 2.78)	1.73 (1.29, 2.32)	1 (reference)	< 0.0001
Model 1[2]	1.53 (1.07, 2.17)	1.44 (1.04, 1.99)	1 (reference)	0.026
Model 2[2]	1.58 (1.06, 2.36)	1.60 (1.11, 2.30)	1 (reference)	0.029
Model 3[2]	1.56 (1.03, 2.35)	1.63 (1.12, 2.40)	1 (reference)	0.066
Model 4[2]	1.49 (0.98, 2.25)	1.58 (1.08, 2.30)	1 (reference)	0.109
Men (n = 1386)				
Depression				
Crude model	1.77 (1.19, 2.63)	1.37 (0.99, 1.90)	1 (reference)	0.004
Model 1[2]	2.00 (1.26, 3.20)	1.45 (0.98, 2.13)	1 (reference)	0.003
Model 2[2]	1.95 (1.18, 3.21)	1.59 (1.06, 2.38)	1 (reference)	0.008
Model 3[2]	1.73 (1.02, 2.92)	1.54 (1.01, 2.36)	1 (reference)	0.037
Model 4[2]	1.73 (1.02, 2.93)	1.54 (1.00, 2.36)	1 (reference)	0.040
Anxiety				
Crude model	1.83 (0.97, 3.43)	2.01 (1.20, 3.34)	1 (reference)	0.041
Model 1[2]	2.36 (1.17, 4.74)	1.55 (0.87, 2.78)	1 (reference)	0.016
Model 2[2]	2.15 (1.02, 4.54)	1.59 (0.86, 2.95)	1 (reference)	0.042
Model 3[2]	1.76 (0.81, 3.84)	1.55 (0.82, 2.94)	1 (reference)	0.147
Model 4[2]	1.74 (0.80, 3.80)	1.52 (0.80, 2.88)	1 (reference)	0.161
Women (n = 1941)				
Depression				
Crude model	1.75 (1.30, 2.35)	1.26 (0.95, 1.67)	1 (reference)	<0.0001
Model 1[2]	1.61 (1.17, 2.21)	1.21 (0.90, 1.63)	1 (reference)	0.001
Model 2[2]	1.61 (1.16, 2.23)	1.21 (0.89, 1.65)	1 (reference)	0.002
Model 3[2]	1.61 (1.15, 2.26)	1.22 (0.89, 1.67)	1 (reference)	0.003
Model 4[2]	1.54 (1.09, 2.15)	1.18 (0.86, 1.63)	1 (reference)	0.007
Anxiety				
Crude model	1.59 (1.08, 2.34)	1.42 (0.98, 2.05)	1 (reference)	0.026
Model 1[2]	1.35 (0.89, 2.05)	1.41 (0.95, 2.07)	1 (reference)	0.264
Model 2[2]	1.39 (0.91, 2.13)	1.44 (0.97, 2.15)	1 (reference)	0.233
Model 3[2]	1.37 (0.88, 2.13)	1.44 (0.95, 2.18)	1 (reference)	0.288
Model 4[2]	1.30 (0.83, 2.02)	1.40 (0.92, 2.12)	1 (reference)	0.420

[1]Derived from a Mantel-Haenszel extension chi-square test; [2]Model 1: Adjusted for age, sex (in the whole population), marital status, educational level, model 2: Further adjustment for BMI, smoking, physical activity, model 3: Additional control for functional gastrointestinal disorders (FGID) and anti-psychotic medicines, model 4: Further control for magnesium, riboflavin, pyridoxine, folate, cobalamin, DHA and EPA, energy, fibre and caffeine. DHA: Docosahexaenoic acid; EPA: Eicosa pentaenoic acid.

the beneficial effects of water drinking in reducing diseases' risk. Therefore, due to bidirectional link between metabolic status and mental health[10], it might be concluded that water consumption can affect mental disorders risk *via* affecting metabolic status.

The bidirectional link between obesity and mental disorders is based on some shared peripheral and central pathological pathways, as well as genetic and environmental risk factors[10]. However, in line with some studies[26,31-33], we found that higher water consumption was associated with greater BMI. Therefore, some other plausible mechanisms may explain this inverse link. Our results indicate that higher water intake is associated with various healthy behaviours such as being more physically active and consuming greater amounts of nutrients particularly those involved in the

nervous system (*e.g.*, riboflavin, magnesium, pyridoxine and cobalamin), which is consistent with previous studies[31,34]. Beneficial effects of these nutrients in neurotransmitters synthesis and transportation, as well as activity of many enzymes in the nervous system have been shown earlier[35,36]. Nevertheless, even after controlling for dietary intakes, depression was significantly related to water consumption, and anxiety tended to be higher in those who drank less water. A possible reason for the inverse link between water consumption and the risk of depression might be the decreased activity of the sympathetic nervous system by drinking water which reduces plasma levels of norepinephrine[37]. Elevated level of norepinephrine is a characteristic of psychosomatic depression[38] which may induce noradrenergic-vasopressinergic activation,

and consequently the activation of the hypothalamic-pituitary-adrenal (HPA) axis. Increased vasopressinergic activation of the HPA axis has been suggested as a plausible mechanism in all depressive disorders[38], which can be involved in mental symptoms production. In spite of similar link between water drinking and depression risk in men and women, the linkage for anxiety was stronger in men than women, though adjustment for antipsychotic medicines and FGIDs eliminated it. This difference between men and women might be related to sex-differences in the use of coping strategies[39]. However, the reasons for this difference are not clear and require further investigation.

In the current analysis, water consumption was evaluated using a direct question regarding the average amount of daily consumption of water, and data regarding other beverages intake and moisture contents of food were not considered. In addition, we provided predefined categories of plain water intake for participants. These factors may lead to misclassification of participants and decrease the reliability of our findings. However, it should be taken into account that noncalorically sweetened beverages are not public among Iranians and they are not used generally. Moreover, tea and coffee are mostly consumed with sugar. Therefore, since all other beverages, which consumed by this population, had calorie and we controlled the confounding effect of energy in our analysis, it could be concluded that our findings have enough precise. The consistence between our study's results and available evidence regarding the health beneficial of water intake might be further reason to confirm the accuracy of our findings.

The limitations of the current study are using self-administered questionnaires for evaluating the study variables. However, the validity of all used instruments has been approved among Iranians. Although using self-reported tools of habitual fluid/water intake is a common limitation in this area of research, the validity of self-reported measures has been approved in earlier studies[40,41]. In addition, no ideal method has been determined to assess beverage consumption and applying 24-h recall or frequency questionnaire beside a computer program on food composition is the existing recommend method in this regard[42]. The cross-sectional design is another limitation that does not allow causal inferences. Indeed, it is possible that individuals with mental disorders tend to drink less water. Nevertheless, such changes would have weakened the associations identified. Therefore, the true estimates are probably even stronger than those we found. Moreover, since we studied the participants who are staffs of IUMS, although they were not academic and medical experts, this sample may not be representative of the entire general population and therefore the results of our study may not be generalizable to other individuals in our society. The strengths of this study are the large sample size and controlling various confounders' effects.

In conclusion, we found inverse associations between plain water consumption and common psycho-

logical disorders. After controlling for various potential confounders, this association was stronger for depression, whilst for anxiety tended to be higher. These findings warrant evaluation in prospective studies to establish the plausible role of water in the mental health status.

ARTICLE HIGHLIGHTS

Research background
Drinking a plenty of plain water has been known as a healthy behavior.

Research motivation
The association between drinking water and mental disorders has not been investigated.

Research objectives
We aimed to assess whether drinking water is associated with mental disorders, and also examine the sex-specific associations.

Research methods
Three thousand three hundred and twenty-seven adults in a cross-sectional study were categorized into three groups according the amount of water drinking (< 2, 2-5, and ≥ 5 glasses of water/d). The risk of depression and anxiety was evaluated across different categories.

Research results
After controlling for various potential confounders, we found inverse associations between plain water consumption and depression, whilst for anxiety tended to be significant. These findings warrant evaluation in prospective studies to establish the plausible role of water in the mental health status.

Research conclusions
There were inverse associations between plain water consumption and common psychological disorders.

Research perspectives
Prospective studies to establish the plausible role of water consumption levels in the mental health status are needed.

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