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***Observational Study***

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

Haghighatdoost F *et al*. SEPAHAN project

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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/day.

***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

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**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]. BMI was calculated as weight (kg) divided by height squared (m2).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](https://www.ncbi.nlm.nih.gov/pubmed/28405322), 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](https://www.ncbi.nlm.nih.gov/pubmed/28302406) (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 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](https://www.ncbi.nlm.nih.gov/pubmed/28302406) (DHA), eicosa pentaenoic acid (EPA), fruits, vegetables and red meat (*P* for all < 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 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](https://www.ncbi.nlm.nih.gov/pubmed/28257896) (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 psychological 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/day). 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 in the mental health status.

**REFERENCES**

1 **Murphy JM**, Horton NJ, Laird NM, Monson RR, Sobol AM, Leighton AH. Anxiety and depression: a 40-year perspective on relationships regarding prevalence, distribution, and comorbidity. *Acta Psychiatr Scand* 2004; **109**: 355-375 [PMID: 15049772 DOI: 10.1111/j.1600-0447.2003.00286.x]

2 **Mojtabai R**. National trends in mental health disability, 1997-2009. *Am J Public Health* 2011; **101**: 2156-2163 [PMID: 21940913 DOI: 10.2105/AJPH.2011.300258]

3 **Berry CL**, Looker T, Germain J. The growth and development of the rat aorta. I. Morphological aspects. *J Anat* 1972; **113**: 1-16 [PMID: 4648481 DOI: 10.1093/ije/dyu038]

4 **Olesen J**, Leonardi M. The burden of brain diseases in Europe. *Eur J Neurol* 2003; **10**: 471-477 [PMID: 12940825 DOI: 10.1046/j.1468-1331.2003.00682.x]

5 **Muckelbauer R**, Sarganas G, Grüneis A, Müller-Nordhorn J. Association between water consumption and body weight outcomes: a systematic review. *Am J Clin Nutr* 2013; **98**: 282-299 [PMID: 23803882 DOI: 10.3945/ajcn.112.055061]

6 **Stookey JD**, Constant F, Popkin BM, Gardner CD. Drinking water is associated with weight loss in overweight dieting women independent of diet and activity. *Obesity* (Silver Spring) 2008; **16**: 2481-2488 [PMID: 18787524 DOI: 10.1038/oby.2008.409]

7 **Luppino FS**, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW, Zitman FG. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry* 2010; **67**: 220-229 [PMID: 20194822 DOI: 10.1001/archgenpsychiatry.2010.2]

8 **McElroy SL**, Kotwal R, Malhotra S, Nelson EB, Keck PE, Nemeroff CB. Are mood disorders and obesity related? A review for the mental health professional. *J Clin Psychiatry* 2004; **65**: 634-651, quiz 730 [PMID: 15163249 DOI: 10.4088/JCP.v65n0507]

9 **Hemmy Asamsama O**, Lee JW, Morton KR, Tonstad S. Bidirectional longitudinal study of type 2 diabetes and depression symptoms in black and white church going adults. *J Diabetes Metab Disord* 2015; **14**: 25 [PMID: 25897418 DOI: 10.1186/s40200-015-0150-5]

10 **Mansur RB**, Brietzke E, McIntyre RS. Is there a "metabolic-mood syndrome"? A review of the relationship between obesity and mood disorders. *Neurosci Biobehav Rev* 2015; **52**: 89-104 [PMID: 25579847 DOI: 10.1016/j.neubiorev.2014.12.017]

11 **Popkin BM**. Contemporary nutritional transition: determinants of diet and its impact on body composition. *Proc Nutr Soc* 2011; **70**: 82-91 [PMID: 21092363 DOI: 10.1017/S0029665110003903]

12 **Fresán U**, Gea A, Bes-Rastrollo M, Ruiz-Canela M, Martínez-Gonzalez MA. Substitution Models of Water for Other Beverages, and the Incidence of Obesity and Weight Gain in the SUN Cohort. *Nutrients* 2016; **8**: E688 [PMID: 27809239 DOI: 10.3390/nu8110688]

13 **Guo X**, Park Y, Freedman ND, Sinha R, Hollenbeck AR, Blair A, Chen H. Sweetened beverages, coffee, and tea and depression risk among older US adults. *PLoS One* 2014; **9**: e94715 [PMID: 24743309 DOI: 10.1371/journal.pone.0094715]

14 **Gangwisch JE**, Hale L, Garcia L, Malaspina D, Opler MG, Payne ME, Rossom RC, Lane D. High glycemic index diet as a risk factor for depression: analyses from the Women's Health Initiative. *Am J Clin Nutr* 2015; **102**: 454-463 [PMID: 26109579 DOI: 10.3945/ajcn.114.103846]

15 **Haghighatdoost F**, Azadbakht L, Keshteli AH, Feinle-Bisset C, Daghaghzadeh H, Afshar H, Feizi A, Esmaillzadeh A, Adibi P. Glycemic index, glycemic load, and common psychological disorders. *Am J Clin Nutr* 2016; **103**: 201-209 [PMID: 26607943 DOI: 10.3945/ajcn.114.105445]

16 **Stevenson EG**, Ambelu A, Caruso BA, Tesfaye Y, Freeman MC. Community Water Improvement, Household Water Insecurity, and Women's Psychological Distress: An Intervention and Control Study in Ethiopia. *PLoS One* 2016; **11**: e0153432 [PMID: 27124391 DOI: 10.1371/journal.pone.0153432]

17 **Aihara Y**, Shrestha S, Sharma J. Household water insecurity, depression and quality of life among postnatal women living in urban Nepal. *J Water Health* 2016; **14**: 317-324 [PMID: 27105416 DOI: 10.2166/wh.2015.166]

18 **Adibi P**, Keshteli AH, Esmaillzadeh A, Afshar H, Roohafza H, Bagherian-Sararoudi R, Daghaghzadeh H, Soltanian N, Feinle-Bisset C, Boyce P, Talley N. The study on the epidemiology of psychological, alimentary health and nutrition (SEPAHAN): Overview of methodology. *J Res Med Sci* 2012; **17**: S292-S298

19 **Montazeri A**, Vahdaninia M, Ebrahimi M, Jarvandi S. The Hospital Anxiety and Depression Scale (HADS): translation and validation study of the Iranian version. *Health Qual Life Outcomes* 2003; **1**: 14 [PMID: 12816545 DOI: 10.1186/1477-7525-1-14]

20 **Montazeri A**, Harirchi AM, Shariati M, Garmaroudi G, Ebadi M, Fateh A. The 12-item General Health Questionnaire (GHQ-12): translation and validation study of the Iranian version. *Health Qual Life Outcomes* 2003; **1**: 66 [PMID: 14614778 DOI: 10.1186/1477-7525-1-66]

21 **Keshteli A**, Esmaillzadeh A, Rajaie S, Askari G, Feinle-Bisset C, Adibi P. A Dish-based Semi-quantitative Food Frequency Questionnaire for Assessment of Dietary Intakes in Epidemiologic Studies in Iran: Design and Development. *Int J Prev Med* 2014; **5**: 29-36 [PMID: 24554989]

22 **NHS**. The General Practice Physical Activity Questionnaire (GPPAQ), 2008. Available from: URL: http://www.enhertsccg.nhs.uk/sites/default/files/pathways/General%20Practice%20Physical%20Activity%20Questionnaire%20%28GPPAQ%29.docx

23 **Gholamrezaei A**, Zolfaghari B, Farajzadegan Z, Nemati K, Daghaghzadeh H, Tavakkoli H, Emami MH. Linguistic validation of the Irritable Bowel Syndrome-Quality of Life Questionnaire for Iranian patients. *Acta Med Iran* 2011; **49**: 390-395 [PMID: 21874644]

24 **Vij VA**, Joshi AS. Effect of excessive water intake on body weight, body mass index, body fat, and appetite of overweight female participants. *J Nat Sci Biol Med* 2014; **5**: 340-344 [PMID: 25097411 DOI: 10.4103/0976-9668.136180]

25 **Chan J**, Knutsen SF, Blix GG, Lee JW, Fraser GE. Water, other fluids, and fatal coronary heart disease: the Adventist Health Study. *Am J Epidemiol* 2002; **155**: 827-833 [PMID: 11978586 DOI: 10.1093/aje/155.9.827]

26 **Pan A**, Malik VS, Schulze MB, Manson JE, Willett WC, Hu FB. Plain-water intake and risk of type 2 diabetes in young and middle-aged women. *Am J Clin Nutr* 2012; **95**: 1454-1460 [PMID: 22552035 DOI: 10.3945/ajcn.111.032698]

27 **Roussel R**, Fezeu L, Bouby N, Balkau B, Lantieri O, Alhenc-Gelas F, Marre M, Bankir L; D.E.S.I.R. Study Group. Low water intake and risk for new-onset hyperglycemia. *Diabetes Care* 2011; **34**: 2551-2554 [PMID: 21994426 DOI: 10.2337/dc11-0652]

28 **Di Maso M**, Bosetti C, Taborelli M, Montella M, Libra M, Zucchetto A, Turati F, Parpinel M, Negri E, Tavani A, Serraino D, Ferraroni M, La Vecchia C, Polesel J. Dietary water intake and bladder cancer risk: An Italian case-control study. *Cancer Epidemiol* 2016; **45**: 151-156 [PMID: 27821348 DOI: 10.1016/j.canep.2016.09.015]

29 **Kant AK**, Graubard BI. A prospective study of water intake and subsequent risk of all-cause mortality in a national cohort. *Am J Clin Nutr* 2017; **105**: 212-220 [PMID: 27903521 DOI: 10.3945/ajcn.116.143826]

30 **Palmer SC**, Wong G, Iff S, Yang J, Jayaswal V, Craig JC, Rochtchina E, Mitchell P, Wang JJ, Strippoli GF. Fluid intake and all-cause mortality, cardiovascular mortality and kidney function: a population-based longitudinal cohort study. *Nephrol Dial Transplant* 2014; **29**: 1377-1384 [PMID: 24398890 DOI: 10.1093/ndt/gft507]

31 **Yang M**, Chun OK. Consumptions of plain water, moisture in foods and beverages, and total water in relation to dietary micronutrient intakes and serum nutrient profiles among US adults. *Public Health Nutr* 2015; **18**: 1180-1186 [PMID: 24507693 DOI: 10.1017/S136898001400007X]

32 **Kant AK**, Graubard BI, Atchison EA. Intakes of plain water, moisture in foods and beverages, and total water in the adult US population--nutritional, meal pattern, and body weight correlates: National Health and Nutrition Examination Surveys 1999-2006. *Am J Clin Nutr* 2009; **90**: 655-663 [PMID: 19640962 DOI: 10.3945/ajcn.2009.27749]

33 **Langdon SW**, Dennee-Sommers B. Exploring the relationships between self-objectification, rationales, and use of water as a strategy for appetite suppression. *Psychol Health Med* 2010; **15**: 17-25 [PMID: 20391221 DOI: 10.1080/13548500903431519]

34 **Gazan R**, Sondey J, Maillot M, Guelinckx I, Lluch A. Drinking Water Intake Is Associated with Higher Diet Quality among French Adults. *Nutrients* 2016; **8**: [PMID: 27809236 DOI: 10.3390/nu8110689]

35 **Casper RC**. Diet and mental health: an up-to-date analysis. *World Rev Nutr Diet* 2011; **102**: 98-113 [PMID: 21865824 DOI: 10.1159/000327798]

36 **Ananth J**, Yassa R. Magnesium in mental illness. *Compr Psychiatry* 1979; **20**: 475-482 [PMID: 487803 DOI: 10.1016/0010-440X(79)90034-8]

37 **Jordan J**, Shannon JR, Grogan E, Biaggioni I, Robertson D. A potent pressor response elicited by drinking water. *Lancet* 1999; **353**: 723 [PMID: 10073520 DOI: 10.1016/S0140-6736(99)99015-3]

38 **Goekoop JG**, de Winter RF, Wolterbeek R, Van Kempen GM, Wiegant VM. Increased plasma norepinephrine concentration in psychotic depression. *Ther Adv Psychopharmacol* 2012; **2**: 51-63 [PMID: 23983957 DOI: 10.1177/2045125312436574]

39 **Kelly MM**, Tyrka AR, Price LH, Carpenter LL. Sex differences in the use of coping strategies: predictors of anxiety and depressive symptoms. *Depress Anxiety* 2008; **25**: 839-846 [PMID: 17603810 DOI: 10.1002/da.20341]

40 **Jimoh FO**, Bunn D, Hooper L. Assessment of a Self-Reported Drinks Diary for the Estimation of Drinks Intake by Care Home Residents: Fluid Intake Study in the Elderly (FISE). *J Nutr Health Aging* 2015; **19**: 491-496 [PMID: 25923476 DOI: 10.1007/s12603-015-0458-3]

41 **Nissensohn M**, López-Ufano M, Castro-Quezada I, Serra-Majem L. Assessment of beverage intake and hydration status. *Nutr Hosp* 2015; **31** Suppl 3: 62-69 [PMID: 25719773 DOI: 10.3305/nh.2015.31.sup3.8753]

42 **Sidossis LS**. Assessment of energy expenditure and energy intake in children: is it possible? *Curr Op Clin Nutr Metab Care* 2003; **6**: 499 [DOI: 10.1097/01.mco.0000087964.83880.e1]

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Plain water drinking** | | |  |
| **Variables** | **< 2 glasses/d** | **2-5 glasses/d** | **≥ 5 glasses/d** | ***P* value1** |
| Participants (*n*) | 854 | 1764 | 709 |  |
| Age (yr)2 | 37.2 ± 0.3 | 36.1 ± 0.2 | 34.8 ± 0.3 | < 0.0001 |
| BMI (kg/m2)2 | 24.7 ± 0.1 | 24.7 ± 0.10 | 25.5 ± 0.2 | < 0.0001 |
| Anxiety score2 | 4.0 ± 0.1 | 3.5 ± 0.10 | 3.0 ± 0.1 | < 0.0001 |
| Depression score2 | 6.8 ± 0.1 | 6.1 ± 0.09 | 5.3 ± 0.1 | < 0.0001 |
| *n* (%) |  |  |  |  |
| 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) |  |
| FGID3 (%) | 488 (57.1) | 892 (50.6) | 321 (45.3) | < 0.0001 |
| **Nutrients4** |  |  |  |  |
| 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 |

1Derived from one way ANOVA and chi-square test for continuous and categorical variables, respectively and analysis of covariance (ANCOVA) for nutrients and food groups; 2Values are means ± SEs; 3FGID defined as suffering from at least one of the following gastrointestinal disorders: [Gastroesophageal Reflux](https://www.ncbi.nlm.nih.gov/pubmed/28405322), dyspepsia, irritable bowel syndrome and constipation; 4The nutrients were adjusted for age and body weight. DHA: [Docosahexaenoic acid](https://www.ncbi.nlm.nih.gov/pubmed/28302406); EPA: Eicosa pentaenoic acid.

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

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Depression** | | ***P* value1** | **Anxiety** | | ***P* value1** |
|  | **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) |  |
| FGID3 | 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) |  |

1Derived from independent *t*-test and chi-square test for continuous and categorical variables, respectively; 2Values are means ± SEs or percent; 3FGID defined as suffering from at least one of the following gastrointestinal disorders: [Gastroesophageal Reflux](https://www.ncbi.nlm.nih.gov/pubmed/28405322), dyspepsia, irritable bowel syndrome and constipation.

**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** | | |  |
|  | **< 2 glasses/d** | **2-5 glasses/d** | **≥ 5 glasses/d** | ***P* trend1** |
| **Depression** |  |  |  |  |
| Crude model | 2.04 (1.62, 2.56) | 1.39 (1.13, 1.71) | 1 (reference) | < 0.0001 |
| Model 12 | 1.75 (1.35, 2.26) | 1.30 (1.02, 1.64) | 1 (reference) | < 0.0001 |
| Model 22 | 1.84 (1.37, 2.45) | 1.39 (1.07, 1.80) | 1 (reference) | < 0.0001 |
| Model 32 | 1.84 (1.40, 2.49) | 1.41 (1.07, 1.84) | 1 (reference) | < 0.0001 |
| Model 42 | 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 12 | 1.53 (1.07, 2.17) | 1.44 (1.04, 1.99) | 1 (reference) | 0.026 |
| Model 22 | 1.58 (1.06, 2.36) | 1.60 (1.11, 2.30) | 1 (reference) | 0.029 |
| Model 32 | 1.56 (1.03, 2.35) | 1.63 (1.12, 2.40) | 1 (reference) | 0.066 |
| Model 42 | 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 12 | 2.00 (1.26, 3.20) | 1.45 (0.98, 2.13) | 1 (reference) | 0.003 |
| Model 22 | 1.95 (1.18, 3.21) | 1.59 (1.06, 2.38) | 1 (reference) | 0.008 |
| Model 32 | 1.73 (1.02, 2.92) | 1.54 (1.01, 2.36) | 1 (reference) | 0.037 |
| Model 42 | 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 12 | 2.36 (1.17, 4.74) | 1.55 (0.87, 2.78) | 1 (reference) | 0.016 |
| Model 22 | 2.15 (1.02, 4.54) | 1.59 (0.86, 2.95) | 1 (reference) | 0.042 |
| Model 32 | 1.76 (0.81, 3.84) | 1.55 (0.82, 2.94) | 1 (reference) | 0.147 |
| Model 42 | 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 12 | 1.61 (1.17, 2.21) | 1.21 (0.90, 1.63) | 1 (reference) | 0.001 |
| Model 22 | 1.61 (1.16, 2.23) | 1.21 (0.89, 1.65) | 1 (reference) | 0.002 |
| Model 32 | 1.61 (1.15, 2.26) | 1.22 (0.89, 1.67) | 1 (reference) | 0.003 |
| Model 42 | 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 12 | 1.35 (0.89, 2.05) | 1.41 (0.95, 2.07) | 1 (reference) | 0.264 |
| Model 22 | 1.39 (0.91, 2.13) | 1.44 (0.97, 2.15) | 1 (reference) | 0.233 |
| Model 32 | 1.37 (0.88, 2.13) | 1.44 (0.95, 2.18) | 1 (reference) | 0.288 |
| Model 42 | 1.30 (0.83, 2.02) | 1.40 (0.92, 2.12) | 1 (reference) | 0.420 |

1Derived from a Mantel-Haenszel extension chi-square test; 2Model 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](https://www.ncbi.nlm.nih.gov/pubmed/28302406); EPA: Eicosa pentaenoic acid.