Is there a relationship between 24-hour urinary sodium and potassium and mental health in migraine patients?
A cross-sectional study

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Abstract
There is a lack of evidence and consensus in terms of the association between dietary intake of sodium (Na) and potassium (K) with mental health. By using 24-hours urinary samples as the gold standard method, we conducted a study to explore the association between dietary intake of Na and K with parameters of mental health including depression, anxiety, and stress among an Iranian population diagnosed with migraine. In the present study, 262 subjects (20–50 years old), with a confirmed diagnosis of migraine were enrolled. Mental health was investigated by the Depression, Anxiety, and Stress Scales (DASS-21) questionnaire. Dietary intake of Na and K was estimated by means of a 24-hour urine sample. Multinomial logistic regression analysis was implemented and odds ratio (OR) with 95% confidence interval (CI) was stated. After controlling for potential confounders, the 24-hour urinary Na was associated significantly with the risk of depression (OR = 0.55, 95% CI: 0.30, 1.00; P = .053). After adjustment for confounders, those in the highest tertile of the 24-hour urinary Na/K ratio had lower odds for having depression (OR = 0.54, 95% CI: 0.31, 0.93; P = .027), and marginally significantly lower risk of anxiety (OR = 0.58, 95% CI: 0.31, 1.06; P = .079) and stress (OR = 0.56, 95% CI: 0.31, 1.02; P = .061). In conclusion, higher 24-hour urine Na was associated with a significantly lower risk of depression. Moreover, the 24-hour Na/K ratio was significantly associated with lower risk of depression, anxiety, and stress.

Abbreviations: BMI = body mass index, CI = confidence interval, DASS-21 = Depression, Anxiety, and Stress Scales, K = potassium, Na = sodium, OR = odds ratio.

Keywords: 24-hour urine, anxiety, depression, stress

1. Introduction
Migraine is the second leading cause of disability worldwide, with genetic, environmental, dietary, and psychological aspects playing a diverse role in each patient.[1] The societal and individual impact of migraine is both substantial and diverse, and among these effects are a variety of psychiatric disorders.[2] Compared to the general population, mood disorders are nearly two to ten times more prevalent among migraine patients.[3,4] Similarly, post-traumatic stress disorders and stress-related disorders are associated with migraines.[5] The substantial comorbidity observed between mental disorders and migraine may result from common genetic or environmental predictors, estrogen response, and progesterone processing. The latter has an imperative role in mood disorders and migraines pathophysiology.[6,7] Therefore, sufficient attention is desired to address modifiable factors that could lessen mood disorders incidence among individuals diagnosed with migraine.

Sodium (Na) intake has substantially increased in recent years, owing to the consumption of different kinds of highly processed foods[8] and, consequently, most countries have an average salt intake of about 9 to 12 g/d.[9,10] In contrast, previous studies have also shown inadequate potassium (K) intake.[11,12] In addition to strong evidence indicating a link between high Na intake and diseases such as cardiovascular disease and hypertension,[13] kidney disease,[14] gastric

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The research ethics committee of Isfahan University of Medical Sciences approved the protocol of the current study on 26 August 2019 (IR.MUI.REC.1398.352). All participants provided written informed consent. The study was performed in accordance with the ethical standards of the Declaration of Helsinki (1964) and its subsequent amendments.

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cancer,[13] osteoporosis,[14] and obesity,[15] recent documents suggest that there may be an association between Na intake and mental health.[18,19] Moreover, it has been reported that a higher intake of K diminishes the harmful effects of Na; although, this hypothesis has only been shown considering blood pressure.[20] Studies in Iran also reported that the Iranian population consumes a small amount of K and a large amount of Na.[19,21] Also, few reports indicate a positive correlation between low K and high Na dietary intakes with depression.[18,19,22]

A key consideration needs to be mentioned here is that, in conditions such as hypertension, the interaction between low dietary K and high Na is involved in the disease pathogenesis, so the overall effect of low K and high Na diets on blood pressure seems to be more than the effect of each of these factors alone.[23] However, the combined effect of dietary Na and K intake in the pathogenesis of other conditions such as mental health is unknown. No population-based study has estimated the association between Na, K, and Na/K ratio and the risk of mental health disorders among Iranian adults using 24-hour urine collections as the gold standard method. Therefore, we analyzed data from a cross-sectional sample of the Iranian population with migraine to evaluate the link between dietary intake of Na, K, and Na/K ratio with the profile of mental health, including stress, anxiety, and depression.

2. Methods

2.1. Study design and population

A total of 265 migraine patients were enrolled consecutively from August 2019 to June 2020 using a cross-sectional design. Patients were referred to the Imam Musa Sadr clinic and Khorshid clinic, both affiliated with Isfahan University of Medical Sciences (Isfahan, Iran). Participants were selected employing a simple random sampling method. The inclusion criteria were as follows: subjects aged between 20 to 50 years old; with body mass index (BMI) of 18.5 to 30; visiting the neurology clinic for the first time, and with a confirmed diagnosis of migraine based on the International Classification of Headache Disorders 3 criteria by an expert neurologist.[24] Due to possible disease-related changes in diet, individuals with a history of hypertension, cardiovascular disease, diabetes, hepatic and renal conditions, thyroid disease, and malignancies were excluded. Those taking nutritional supplements (i.e., vitamin B2, coenzyme Q10, magnesium, and feverfew) were also ineligible. Isfahan University of Medical Sciences research ethics committee approved the protocol of the current study (IR.MUL.RESEARCH.REC.1398.352). All participants provided written informed consent.

2.2. Mental health assessment

The main investigator (A.A) evaluated mental health by a validated version of the Depression, Anxiety, and Stress Scales (DASS-21) questionnaire.[25] DASS-21 questions consisted of four options ranging from zero (did not apply to me at all) to three (applied to me very much or most of the time) to determine the symptoms of depression, anxiety, and stress. The total scores for each domain should be multiplied to two to evaluate the original options ranging from zero (did not apply to me at all) to three (applied to me very much or most of the time) to determine the symptoms of depression, anxiety, and stress. The total scores for each domain should be multiplied to two to evaluate the original options ranging from zero (did not apply to me at all) to three (applied to me very much or most of the time). The main investigator (A.A) evaluated mental health by a valid

2.3. 24-hour Urine collection

Patients were advised not to make any changes to their eating routines throughout the day of collection. A 24-hour period of urine collection was done at weekend from Friday to Saturday to minimize the chance of missing any of the urine voiding. The researcher distributed the polypropylene containers (2.5 L) for 24-hour urine sampling among participants with guidance on how to proceed. They emptied their bladder on the morning of urine sample collection and discarded that specimen. During the next 24 hours, they placed all urine voided in the urine collection container. Also, the next day, they added the first urine in the morning to the sampling container. Patients were asked to keep the containers in cool and dry places and samples immediately were transferred to the laboratory on Saturday morning following the addition of the last urine. Urine creatinine (Cr) was assessed using the Jaffe reaction method (BT 3000).[26] The laboratory determined urine Na and K through the ion-selective electrode method (ProLyte Electrolyte Analyzer). 24-hour urine volume <500 mL or urinary creatinine <4 mmol/d for women, or <6 mmol/d for men defined suspected inaccurate urine collections, which we excluded.[27] We calculated the 24-hour urinary Na and K excretion value (mmol/d) as the concentration of Na and K (mmol/L) multiplied by the 24-hour urinary volume (L/d). We used coefficients of 39 and 23 to convert from mmol to mg for K and Na, respectively, and the conversion from mg of Na to salt by multiplying by 2.542.[29] All the method of 24-hour sampling and analysis was done on the basis of the WHO suggested protocol.[30]

2.4. Confounder’s assessment

Through a face-to-face interview, additional data (i.e., gender, age, marital status, number of family members, and medication) was obtained by an investigator (A.A). Dietary intake during the past year was gathered via a valid 168-item, semi-quantitative food frequency questionnaire.[31,32] The participants reported their consumption frequency using a given serving size of each food item on the basis of daily, weekly, or monthly. Portion sizes of the consumed foods were transformed into grams using household measures.[33] Food frequency questionnaire data were analyzed by Nutritionist IV software (First Databank, Hearst Corp, San Bruno, CA). Moreover, subjects were also excluded with reported daily energy intakes lower than 800 kcal/d (3347 kJ/d) or higher than 4200 kcal/d (17573 kJ/d).[34] The physical activity status was determined using a reliable and valid version of the International Physical Activity Questionnaire[35] and overall all scores were reported as metabolic equivalent hours per day (METs h/d). Height was obtained via an upstretched tape to the nearest 1 mm and bodyweight was determined to the nearest 100 g using a digital scale (Omron BF511 [Omron Corp, Kyoto, Japan]). BMI was computed using the height (m²) and weight (kg) by the related equation.

2.5. Statistical analyses

Number (percent) and mean ± standard error represented categorical and continuous variables, respectively. We used the chi-square test to assess the distribution of participants’ mental health characteristics (depression, anxiety, and stress) across tertiles of 24-hour urinary Na, K, and Na/K ratio. We performed ordinal logistic regression analysis in different models to explore the association between the 24-hour urinary Na, K, and Na/K ratio with depression, anxiety, and stress. Adjusted odds ratio (OR) s with 95% confidence interval (CI) were presented in 2 different models. First, we adjusted for sex, age, number of family members, marital status, smoking, mean arterial pressure, migraine headache index score, and physical activity. In the next model, we exerted further adjustments for total energy intake and BMI. Data analyses were performed using SPSS version 21 (IBM Corp, Armonk, NY). P < .05 were considered statistically significant. Moreover, a related formula for estimating the mean was used to estimate the sample size. Based on α = 0.05, δ = 0.9,
and $d = 0.1$ based on Na level in patients with migraine, we reached to 260 subjects.\textsuperscript{[17]}

3. Result

A total of 770 patients were evaluated and finally, 265 patients met our inclusion criteria and consented to be enrolled in this study. From 265 participants who completed the 24-hour urine collection, three urine samples were excluded owing to the incompleteness of 24-hour urine sampling. Therefore, 262 participants had complete and valid urinary samples and were included in the final analysis (Fig. 1).

The demographic characteristics of the study population and data on medication and urinary excretion are presented in Table 1. Overall, 38 men and 224 women make up our study population with mean age of 36.10 years old, BMI of 25.55 kg/m$^2$, Cr excretion of 9.15 mmol/L, urine output of 1.14 L/d, urine Na of 3189.38 mg/d, urine K of 1599.08 mg/d, total energy intake of 2651.99 kcal/d, mean arterial pressure of 87.87 mm Hg, and migraine headache index score of 53.83. Participants in the highest tertile of 24-hour urinary Na, compared to the lowest tertile, had higher weight, height, Cr excretion, urine output, and urine K (all $P < .05$). Subjects in the top tertile of 24-hour urinary K were significantly more likely to be male compared to the subjects in the lowest tertile ($P = .037$); as well as, they had higher weight, height, Cr excretion, urine output, and urine Na (all $P < .05$). Moreover, they had greater total energy intake per day ($P < .001$).

Anthropometric measures and dietary intakes of the study population across categories of mental health are indicated in Table 2. As can be seen, no significant differences were detected for any of the studies parameters across categories of mental health (all $P > .05$).

The number and percent of participants across categories of mental health and tertiles of 24-hour urinary Na, K, and Na/K ratio are shown in Table 3. In terms of depression, individuals in the highest tertile of 24-hour urinary Na were more likely to be normal and less likely to have extremely severe depression compared to the lowest tertile ($P = .018$). Furthermore, the greater number of participants in the highest tertile of 24-hour urinary Na/K ratio, compared to the lowest tertile, were normal regarding stress status ($P = .026$).

The results of Pearson’s correlation coefficient test between 24-hour urinary Na, K, and Na/K ratio and mental health including depression, anxiety, and stress are presented in Table 4. 24-hour urinary Na was negatively correlated with depression ($r = -0.014; P = .018$) that implying a moderate correlation. However, no other significant correlation was detected between 24-hour urinary Na, K, and Na/K ratio and mental health.

The findings of logistic regression of 24-hour urinary Na and mental health are shown in Table 5. In the crude model, the 24-hour urinary Na was associated significantly with the risk of depression (OR = 0.52, 95% CI: 0.30, 0.89; $P = .017$). This association remained also marginally significant after further adjustment for sex, age, marital status, smoking, number of family members, migraine headache index score, mean arterial pressure, physical activity, BMI, and total energy intake (OR = 0.53, 95% CI: 0.30, 1.00; $P = .053$). We found no significant association between higher 24-hour urinary Na with the risk of anxiety and stress (all $P > .05$). The results of the association between depression, anxiety, and stress with 24-hour urinary K were shown in Table 6. The 24-hour urinary K was not associated with the risk of depression, anxiety, and stress not only in the crude model but also in the adjusted models (all $P > .05$).

OR and 95% CI for mental health profile according to tertiles of 24-hour urinary Na/K ratio are presented in Table 7. There was a significant association between Na/K ratio and the risk of depression (OR = 0.54, 95% CI: 0.31, 0.93; $P = .027$) in the crude model. After controlling for sex, age, marital status, smoking, number of family members, migraine headache index score, mean arterial pressure, and physical activity, those in the highest tertile of the 24-hour urinary Na/K ratio had lower odds for having depression (OR = 0.54, 95% CI: 0.31, 0.93; $P = .027$). However, further adjustment for total energy intake and BMI attenuated the association (OR = 0.72, 95% CI: 0.40, 1.32; $P = .302$). The 24-hour urinary Na/K ratio was marginally significantly associated with lower risk of anxiety and stress after controlling for potential confounders (OR = 0.59, 95% CI: 0.34, 1.06; $P = .079$). The higher 24-hour urinary Na/K ratio was associated significantly with a lower risk of stress even after controlling for potential confounders (OR = 0.56, 95% CI: 0.31, 1.02; $P = .061$).

Figure 1. Flow chart of the participants’ selection process.
| Characteristics of study population. |
|-------------------------------------|
| **Teriles of 24-h urinary sodium**  |
| **N** | 86 | 87 | 89 | 86 | 87 | 89 | 86 | 87 | 89 |
| **Age (yr)** | 37.11 ± 0.93 | 35.77 ± 0.94 | 35.44 ± 0.89 | 36.04 ± 1.01 | 35.92 ± 0.87 | 36.34 ± 0.89 | 37.68 ± 0.91 | 35.79 ± 0.90 | 34.79 ± 0.93 |
| **Female** | 0.403 | 0.379 | 0.157 | 0.379 | 0.157 | 0.379 | 0.379 | 0.157 | 0.379 |
| **Married** | 297 | 297 | 297 | 297 | 297 | 297 | 297 | 297 | 297 |
| **Current smoker** | 297 | 297 | 297 | 297 | 297 | 297 | 297 | 297 | 297 |
| **Number of family members** | 3.43 ± 0.09 | 3.33 ± 0.10 | 3.34 ± 0.10 | 3.43 ± 0.10 | 3.43 ± 0.10 | 3.36 ± 0.10 | 3.33 ± 0.09 | 3.41 ± 0.10 | 3.49 ± 0.11 |
| **BMI (kg/m²)** | 25.40 ± 0.38 | 25.37 ± 0.36 | 25.87 ± 0.35 | 25.85 ± 0.40 | 25.92 ± 0.33 | 25.86 ± 0.35 | 25.73 ± 0.35 | 26.03 ± 0.36 | 24.89 ± 0.37 |
| **BMI (kg/m²)** | 25.40 ± 0.38 | 25.37 ± 0.36 | 25.87 ± 0.35 | 25.85 ± 0.40 | 25.92 ± 0.33 | 25.86 ± 0.35 | 25.73 ± 0.35 | 26.03 ± 0.36 | 24.89 ± 0.37 |
| **Physical activity (MET/h/d)** | 10.34 ± 3.06 | 6.48 ± 1.18 | 9.81 ± 2.01 | 10.87 ± 2.76 | 6.56 ± 1.42 | 11.20 ± 2.27 | 8.43 ± 1.78 | 9.31 ± 2.05 | 8.88 ± 2.70 |
| **Protein (g/d)** | 69.94 ± 3.48 | 71.65 ± 2.99 | 78.09 ± 3.01 | 76.91 ± 2.87 | 66.44 ± 3.10 | 83.51 ± 3.45 | 73.62 ± 3.54 | 73.08 ± 3.31 | 73.02 ± 2.69 |
| **Carbohydrate (g/d)** | 25.40 ± 0.38 | 25.37 ± 0.36 | 25.87 ± 0.35 | 25.85 ± 0.40 | 25.92 ± 0.33 | 25.86 ± 0.35 | 25.73 ± 0.35 | 26.03 ± 0.36 | 24.89 ± 0.37 |
| **Medication** | 39 (14.9) | 38 (14.5) | 31 (11.8) | 37 (14.1) | 37 (14.1) | 37 (14.1) | 37 (14.1) | 37 (14.1) | 37 (14.1) |
| **Taking beta-blockers** | 5 (1.9) | 2 (0.8) | 6 (2.3) | 7 (3.1) | 6 (3.1) | 7 (3.1) | 5 (1.9) | 5 (1.9) | 5 (1.9) |
| **Taking triptans** | 16 (6.1) | 16 (6.1) | 11 (4.2) | 16 (6.1) | 16 (6.1) | 11 (4.2) | 16 (6.1) | 16 (6.1) | 11 (4.2) |
| **Taking venlafaxine** | 1 (0.4) | 1 (0.4) | 1 (0.4) | 1 (0.4) | 1 (0.4) | 1 (0.4) | 1 (0.4) | 1 (0.4) | 1 (0.4) |
| **Taking gabapentin** | 3 (1.1) | 3 (1.1) | 5 (1.9) | 5 (1.9) | 5 (1.9) | 5 (1.9) | 5 (1.9) | 5 (1.9) | 5 (1.9) |
| **Taking serotonin-norepinephrine reuptake inhibitor** | 25.40 ± 0.38 | 25.37 ± 0.36 | 25.87 ± 0.35 | 25.85 ± 0.40 | 25.92 ± 0.33 | 25.86 ± 0.35 | 25.73 ± 0.35 | 26.03 ± 0.36 | 24.89 ± 0.37 |
| **BMI = body mass index, FFQ = food frequency questionnaire, MAP = mean arterial pressure, MHIS = migraine headache index score, TCA = tricyclic antidepressants, TeCA = tetracyclic antidepressant, SNRI = serotonin-norepinephrine reuptake inhibitor.** |

Data are presented as mean ± standard error or number (percent). P value obtained from chi-square analysis for categorical variables and analysis of variance (ANOVA) for continuous variables.

Note: Table 1 shows the characteristics of the study population, including data on age, gender, marital status, current smoking status, number of family members, weight, height, BMI, physical activity, total energy intake, protein intake, fat intake, carbohydrate intake, and medication use. The table also includes values for sodium and potassium intake, as well as the sodium/potassium ratio. All data are presented as mean ± standard error or number (percent), with statistical significance indicated by p-values.
4. Discussion

The present cross-sectional study is the first to examine the association between mental health and 24-hour urinary Na, K, and Na/K ratio using a sample of Iranian migraineurs. We observed that higher 24-hour urinary Na was an independent predictor of a lower risk of depression. Moreover, the Na/K ratio was significantly associated with a lower risk of anxiety and stress, which similarly was independent of confounders. Furthermore, a higher Na/K ratio was associated with a lower risk of depression independent of total energy intake and BMI. It indicates that the lower risk of depression is not specific to dietary Na alone, and further aspects of diet and body weight might play a significant role in this association. Comprehensive literature exists regarding the contribution of diet to mental health,[38] however, few investigations have done to assess the direct relationship between dietary intake of Na and K with depression, anxiety, and stress using a 24-hour urine sample as the gold standard method.[19,22] Mrug et al.[22] have examined the prospective role of 12-hour urinary Na and K on depressive symptoms among 84 Urban adolescents. This study has suggested that lower K excretion (β = −0.25; \( P = .036 \)) and higher Na excretion (β = 0.41; \( P = .018 \)) predicted more severe depressive symptoms which was in contrast to our findings. This study was used a small sample size and 12-hour urine sample instead of a 24-hour collection and also did not assess the dietary intake of participants and other aspects of mental health. Moreover, the assessment of depressive symptoms was self-reported and no validated tool was implemented. Afshar[10] investigated the relationship between 24-hour urinary Na and depression among 119 patients newly diagnosed with essential hypertension which did not find a relationship between 24-hour urinary Na excretion and depressive behavior. Similarly, this study using small sample size, ignored 24-hour urinary K, and also other aspects of mental health like anxiety and stress. There are some methodological differences between the current study and previous literature which may provide an explanation regarding the controversial findings. Difference in the mental health assessment tools, sample size, study population, and ethnicity may also provide additional explanations for the controversial findings of the current study. Therefore, the present study has been conducted to resolve the previous limitations and also provides new data regarding the Na/K ratio and other aspects of mental health including anxiety and stress.

Na is a ubiquitous ion with vital importance in many physiological functions. Fine adjustment of the Na concentration in the body is crucial for life and growth which is attained by the cooperation of the neural and endocrine control systems. Aldosterone is one of the key players in this regulatory network which can affect nonepithelial tissues like the brain which subsequently promote short-term behavioral and physiological response to a low Na diet.[39] Moreover, it has been proposed that mood status can be affected by aldosterone. Higher serum levels of aldosterone have been described in subjects with depression.[40–42] More recent investigations also report that salivary aldosterone is associated with the duration, severity, and outcome of a depressive episode.[43] Moreover, anxiety-inducing properties of aldosterone was observed in animal models.[44] A previous report suggested that a low Na diet could lead to a negative mood.[44] A sodium-limited diet could stimulate aldosterone secretion through the renin-angiotensin-aldosterone system. A recent Cochrane review revealed that during sodium reduction interventions, aldosterone increased 104 pg/mL.[45] The behavioral effects of aldosterone can be exerted through gene expression changes in the hippocampus which may be related with depression, anxiety, and stress. The proposed alteration in gene expressions can be categorized into synaptic remodeling, increased inflammation, and upregulation of glutamate signaling.[46]
Moreover, a higher serum ratio of Na/K results in the secretion of progesterone, which is proposed as a mood enhancer. In summary, the findings of the current study are of interest; however, further investigations are essential to clarify the exact underlying mechanism regarding the role of dietary Na and K in mental health.

This paper is the first to show the association between Na and K intake and mental health in a sample of the Iranian population. Moreover, we determined dietary intake of Na and K via a 24-hour urine sample as the gold standard method. This study has several limitations that warrant consideration. First, given that our study is cross-sectional, a causal link cannot be drawn. Second, since daily variability can be observed in urinary NaK excretion of individuals, a single collection be drawn. Second, since daily variability can be observed in 24-h urinary Na and K excretion of individuals, a single collection cannot represent the exact underlying mechanism regarding the role of dietary Na and K in mental health.

Table 3
Mental health of participants across tertiles of 24-hour urinary sodium, potassium, and Na/K ratio.

| T1 | T2 | T3 | P value |
|----|----|----|---------|
| Depression | 24-h urinary sodium | 24-h urinary potassium | 24-h urinary Na/K ratio |
| Normal | 28 (10.7%) | 27 (10.3%) | 0.078 |
| Mild | 10 (3.8%) | 12 (4.6%) | 0.64 |
| Moderate | 10 (3.8%) | 12 (4.6%) | 0.64 |
| Severe | 5 (1.9%) | 6 (2.3%) | 0.30 |
| Extremely severe | 17 (6.5%) | 12 (4.6%) | 0.64 |

Data are presented as number (percent). *P* value obtained from chi-square analysis. *P* < .05 was considered statistically significant.

Table 4
Pearson correlation between 24-hour urinary sodium, potassium, and Na/K ratio and parameters of mental health.

| 24-h urinary sodium | 24-h urinary potassium | 24-h urinary Na/K ratio |
|---------------------|------------------------|------------------------|
| Depression score | −0.14 (.018) | 0.05 (.419) | −0.07 (227) |
| Anxiety score | −0.08 (.183) | 0.07 (.258) | −0.05 (411) |
| Stress score | −0.11 (.069) | 0.07 (.262) | −0.05 (.402) |

Data are presented as *r* (*P* value). *P* < .05 was considered statistically significant.

Table 5
Odds ratio and 95% confidence interval for mood status (depression, anxiety, and stress) according to tertiles of 24-hour urinary sodium.

| T1 | T2 | T3 | P trend |
|----|----|----|---------|
| Depression | 24-h urinary sodium | 24-h urinary potassium |
| Crude | Ref | 0.96 (0.65, 1.61) | 0.95 (0.58, 1.62) |
| Model 1 | 1.00 (0.58, 1.62) | 1.15 (0.66, 1.99) |
| Model 2 | 0.90 (0.50, 1.62) | 0.78 (0.42, 1.46) |

Data are presented as odds ratio (95% confidence interval). Crude: Unadjusted. Model: Adjusted for age, sex, marital status, number of family members, smoking status, migraine headache index score, mean arterial pressure and physical activity. Model 2: Model 2 + body mass index and energy intake per day. *P* < .05 was considered statistically significant. P < .1 was considered marginally statistically significant.
of urine samples may underestimate or overestimate the actual Na and K intake. Moreover, measuring 24-hour urinary Na and K at different times to investigate its association with mood swing through a longitudinal study may provide more evidence regarding the association between Na and K and mental health. Third, although we adjusted for several nutritional, clinical, and demographic confounders, we cannot ignore the possible effect of residual confounding on our findings.

5. Conclusion
In conclusion, higher Na intake was associated with a significantly lower risk of depression. Moreover, the Na/K ratio was significantly associated with lower risk of depression, anxiety, and stress. The results of the present study highlight the need to pay attention to the profile of mental health in patients undergoing low-sodium diet. Furthermore, our findings may encourage further studies to examine whether altered Na homeostasis is casual in, or an effect of, mood disorders.

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Table 7
Odds ratio and 95% confidence interval for mood status (depression, anxiety, and stress) according to tertiles of 24-hour urinary Na/K ratio.

| Tertiles of 24-h urinary Na/K ratio | T | P trend |
|-----------------------------------|---|---------|
| **Depression**                     |   |         |
| Crude                             | Ref| 0.61 (0.36, 1.05) | 0.54 (0.31, 0.93) | 0.28 |
| Model 1                           | Ref| 0.61 (0.35, 1.05) | 0.53 (0.30, 0.91) | 0.23 |
| Model 2                           | Ref| 0.70 (0.39, 1.32) | 0.72 (0.40, 1.32) | 0.29 |
| **Anxiety**                       |   |         |
| Crude                             | Ref| 0.56 (0.32, 0.96) | 0.63 (0.37, 1.09) | 0.113 |
| Model 1                           | Ref| 0.52 (0.30, 0.91) | 0.59 (0.34, 1.02) | 0.066 |
| Model 2                           | Ref| 0.58 (0.31, 1.06) | 0.66 (0.36, 1.22) | 0.192 |
| **Stress**                        |   |         |
| Crude                             | Ref| 0.49 (0.28, 0.84) | 0.52 (0.31, 0.89) | 0.021 |
| Model 1                           | Ref| 0.47 (0.27, 0.81) | 0.50 (0.29, 0.86) | 0.016 |
| Model 2                           | Ref| 0.54 (0.30, 0.99) | 0.56 (0.31, 1.02) | 0.062 |

Data are presented as odds ratio (95% confidence interval).
Crude: Unadjusted.
Model 1: Adjusted for age, sex, marital status, number of family members, smoking status, migraine headache index score, mean arterial pressure and physical activity.
Model 2: Model 2 + body mass index and energy intake per day.
P < .05 was considered statistically significant.
P < .1 was considered marginally statistically significant.

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Arab et al. • Medicine (2022) 101:42

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