Breakfast consumption is inversely associated with primary headaches in university students: The MEPHASOUS study

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Abstract

Background

The prevalence of primary headaches has been increasing at an alarming rate, particularly in university students. Previous studies have shown that diet-related behaviors can affect neurological disorders. Therefore, this study was conducted to examine the association between breakfast consumption patterns and primary headaches in a large population of university students.

Methods

In total, 83,677 university students, aged ≥18 years, from 28 provinces of Iran were included in the current cross-sectional study. Dietary intakes and breakfast consumption patterns were assessed using a validated self-administered dietary habits questionnaire. Primary headaches were determined according to the International Classification of Headache Disorders-3 (ICHD-3) criteria.

Results

The mean age of participants was 21.50 ± 4.01. Primary headaches were prevalent among 9% of university students. A significant inverse association was seen between breakfast consumption and odds of primary headaches (OR: 0.57, 95% CI: 0.51-0.62). This association remained significant even after taking potential confounders into account; such that students who consumed breakfast frequently had 26% lower odds of primary headaches compared with those who consumed it rarely (OR: 0.74, 95% CI: 0.65-0.85). Moreover, such a significant inverse association was observed in female students (OR: 0.54, 95% CI: 0.49-0.61) as well as those with normal weight (OR: 0.68, 95% CI: 0.58-0.79). However, it became non-significant in male students and those with overweight or obesity.
Conclusions

We found that frequent breakfast consumption was inversely associated with the odds of primary headaches. Further prospective studies are needed to confirm our findings.

INTRODUCTION

Primary headaches are the chronic and disabling neurological disorders that are associated with recurrent and persistent head pain (1). Based on the most recent iteration of the International Classification of Headache Disorders, Third Edition (ICHD-3), Beta Version, primary headaches consist of migraine, tension-type headache and also non-classifiable headaches (2). The prevalence of primary headaches has been increasing at an alarming rate, particularly in early ages (3). For migraine, it is estimated an incidence of 18.2 per 1000 women aged 20 to 24 years and 6.2 per 1000 men aged 15 to 19 years (4, 5). Primary headaches impose a high burden to individuals and the health care system (1, 6). Therefore, finding effective factors to prevent these headaches is necessary.

The etiology of primary headaches has not been completely elucidated; however, it has been shown that a combination of genetic and environmental factors are involved (7, 8). Among environmental factors, diet has an important role. There is evidence indicating that intakes of dairy products, fruits, vegetables, and B-vitamins are associated with a lower incidence of primary headaches, while intakes of red and processed meat, refined grains, and coffee contribute to increased risk of these headaches (9–16). Previous studies have mainly focused on dietary intakes and little attention has been paid on dietary behaviors such as breakfast consumption. Breakfast consumption might inhibit the activity of the hypothalamic-
pituitary-adrenal axis and subsequently reduce the secretion of stress hormones such as cortisol, which contribute to the onset of primary headaches (17, 18). Therefore, breakfast consumption may be involved in the onset and management of primary headaches. However, we are aware of no study that examined the association between breakfast consumption and primary headaches in adults. Few studies have investigated the link between breakfast consumption and other chronic neurological disorders such as depression and psychological distress (19–21). In a population-based study, Milajerdi et al. reported that breakfast consumption reduced the odds of depression and psychological distress (21). The association between breakfast consumption and primary headaches is of great importance in university students who had different dietary behaviors than others (22). They usually skip breakfast and are willing to have an unhealthy dietary pattern rich in fast foods, snacks, sugar-sweetened beverages and poor in fruits and vegetables (23, 24). Besides, the prevalence of primary headaches is estimated to be high among university students (25). Considering the aforesaid points, the current study was conducted to examine the association between breakfast consumption patterns and primary headaches among a large population of university students in the Middle East.

MATERIAL AND METHODS
Participants
This cross-sectional study was performed in the framework of the MEPHASOUS (Mental and Physical Health Assessment of University Student) study which was designed by the Counseling and Health Organization of the Ministry of Science and Technology (CHOMST), Tehran, Iran, in 2012–2013. The purpose of this project was
to evaluate the health status of Iranian university students. Detailed information about the study design, participants and data collection methods has been published elsewhere (26, 27). Briefly, all students who were admitted to 74 governmental eligible universities (from 28 provinces of Iran), affiliated to the Ministry of Science and Technology (MST), were invited to participate in this project. Students were included if newly admitted at university and were at the age range of ≥ 18 years. To gather the required data, students were invited to the health center of universities. Data on demographic characteristics, anthropometric measures, medical history, and dietary habits were collected from each student. Overall, 84,332 university students participated in the MEPHASOUS project. After excluding those students with missing information, 83,677 students remained for the final analysis. All participants provided a signed written consent form. The whole project was ethically approved by the Ministry of Science and Technology, Tehran, Iran.

Dietary assessment
We used a self-administered dietary habits questionnaire to collect dietary data (26). The questionnaire was specifically designed and validated for the MEPHASOUS project. Participants were asked to report the consumption frequency of fresh and dried fruits, vegetables, whole grains, dairy products, fast foods, sugar-sweetened beverages (SSBs), and sweets during the last year. In the questionnaire, the response categories were different for each food according to its usual intake among the Iranian population. For example, the response categories for fruits which are frequently consumed by Iranian were in daily format (< 1 serv/day, 1 serv/day, 2–3 serv/day, ≥ 4 serv/day), while these categories for sweets which are infrequently consumed were in weekly format (< 1 serv/wk, 1 serv/wk, 2–3 serv/wk, ≥ 4 serv/wk).

Assessment of breakfast consumption
Breakfast consumption pattern was assessed using a self-administrated question, as an item in the dietary habits questionnaire. Participants were asked to report how many days in a week they consumed breakfast. They were able to select one of these choices: <1 day/wk (rarely), 1–2 days/wk, 3–4 days/wk, and ≥ 5 days/wk. Breakfast consumption was defined as the consumption of any food, beverage, or both of them between 5:00 and 10:00 AM. In the present study, breakfast skippers were defined as those who consumed breakfast less than 5 days/wk. The reliability and validity of the dietary habits questionnaire were examined in a separate study which was done on a subgroup of 70 students in the University of Tarbiat Modares (26). Based on the validation study, this questionnaire presented reliable and valid data on the dietary habits of university students. The reliability and validity of the questionnaire were also confirmed by previous studies that used it for dietary habits assessment (27–29).

Assessment of primary headaches
Primary headaches were determined using a self-reported question in which students were asked whether they had experienced primary headaches (including migraine, tension-type headache, and non-classifiable headache) during the last 12 months. They were asked to not report the headaches related to cold, fever or any other type of illness. Students could select two options (yes/no). If yes, they were referred to a general practitioner, who was experienced in terms of neurovascular diseases, for further examination. Primary headaches were defined based on the criteria introduced by the International Classification of Headache Disorders-3 (ICHD-3) with the exceptions that the number of attacks and the duration of headaches were not included (30).

Assessment of other variables
Data on age, gender (male/female), education [advanced diploma/bachelor of
science (BSc)/master of science (MSc)/medical science (MD)/philosophy of doctor (Ph.D.)), marital status (single/married), occupation (having/not-having), health insurance (having/not-having), smoking (non-smoker/ex-smoker/current smoker), sleep pattern (regular/irregular), and current use of nutritional supplements (including Fe, Ca, vitamins and other nutritional supplements) (yes/no) were collected using a self-reported questionnaire. We considered students in the advanced diploma, BSc and MD courses as under-graduate and those in the MSc and Ph.D. courses as post-graduate students. Since health insurance in Iran can cost a lot for people, it was considered as an index for evaluation of economic status. Therefore, we considered students who had health insurance as economically “good” and those who did not have any type of health insurance as economically “weak”. To assess physical activity, we asked a question as follows: “how often do you exercise lasting 30 min?” The response categories of this question were “rarely”, “1–2 times/wk”, “3–4 times/wk”, “≥5 times/wk”. Students who did exercise 3 times/wk or more were considered physically active. We also assessed the time that each student spend in a day for the use of electronic devices including computer, cell phone, and notebook. They were able to choose one of these choices: “rarely”, “<2 hours/day”, “2–4 hours/day”, and “>4 hours/day”. In terms of anthropometric measures, weight was measured with minimal clothing and without shoes by an analog scale with a precision of 100 g and height was determined in a standing position without shoes by a tape measure with the nearest 0.5 cm. Body mass index (BMI) was calculated as weight in kilograms divided by height in square meters. Overweight and obesity were defined as BMI between 25–30 and ≥ 30 kg/m², respectively (6, 31). Blood pressure was measured two times in a seated position after a 5-min rest with a 20-minute interval. The average of two
measurements was considered as the final systolic and diastolic blood pressure. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg and diastolic blood pressure (DBP) ≥ 90 mmHg (32).

Statistical analysis
We classified participants into four categories according to their frequencies of breakfast consumption as follows: rarely, 1–2 days/wk, 3–4 days/wk, and ≥ 5 days/wk. One-way analysis of variance (ANOVA) was used to assess differences in quantitative variables across the categories of breakfast consumption. To assess the distribution of qualitative variables across patterns of breakfast consumption, the Chi-square test was used. By using the binary logistic regression, we obtained multivariable odds ratios (ORs) and 95% confidence intervals (CIs) for the association between breakfast consumption pattern and primary headaches among the whole population and separately by gender (male/female) and BMI status (< 25/≥ 25 kg/m²). We controlled for the confounding effects of age and gender in the first model. Further adjustment was made for marital status, education, occupation, physical activity, economic status, smoking, electronic devices use, sleep pattern, hypertension and supplement use in the second model. We additional adjusted for dietary intakes of fruits, vegetables, fast foods, SSBs, whole grains, and sweets in the third model. In the final model, BMI was additionally controlled to obtain an obesity-independent association between breakfast consumption patterns and odds of primary headaches. In these analyses, students in the first category of breakfast consumption were considered as the reference group. To obtain the overall trend of odds ratios across increasing categories of breakfast consumption, we considered these categories as an ordinal variable in the logistic regression models. All statistical analyses were done using SPSS software (version 19.0; SPSS Inc, Chicago
P values were considered significant at < 0.05.

RESULTS

The mean age of university student participated in the current study was 21.50 ± 4.01. Also, 54.7% of study participants were female. Primary headaches were prevalent among 9% of participants. In addition, 45.6% of students consumed breakfast less than 5 days/wk, defined as breakfast skippers. Demographic characteristics and dietary intakes of participants across the categories of breakfast consumption are shown in Table 1. Participants with frequent breakfast consumption were more likely to be female, married, post-graduate, physically active, hypertensive, have a job, regular sleep pattern, good economic status, and were less likely to be current smoker, frequently use electronic devices, have overweight or obesity, and primary headaches compared with those who consumed breakfast infrequently. In the case of dietary intakes, frequent breakfast consumption was associated with greater intakes of dairy products, fruits, vegetables, and lower intakes of fast foods, SSBs, and sweets.
Table 1
Demographic characteristics and dietary habits of participants across categories of breakfast consumption pattern

| Variables                        | Rarely† | 1–2 day/wk | 3–4 day/wk | ≥ 5 day/wk | P-value* |
|----------------------------------|---------|------------|------------|------------|----------|
| n                                | 4066    | 12492      | 21597      | 45522      |          |
| Age (year)                       | 20.96 ± 3.51 | 21.07 ± 3.65 | 21.45 ± 3.86 | 21.69 ± 4.20 | < 0.001  |
| Weight (kg)                      | 65.58 ± 14.44 | 64.58 ± 14.52 | 64.27 ± 14.16 | 64.14 ± 13.86 | < 0.001  |
| BMI (kg/m²)                      | 22.68 ± 4.13 | 22.61 ± 4.13 | 22.45 ± 4.16 | 22.52 ± 3.93 | 0.001    |
| Gender (female) (%)              | 48.1    | 54.4       | 52.7       | 56.4       | < 0.001  |
| Marital status (married) (%)     | 6.8     | 8.7        | 9.5        | 11.0       | < 0.001  |
| Education (graduated) (%)        | 32.4    | 34.2       | 39.0       | 40.3       | < 0.001  |
| Current smoker (%)               | 16.9    | 10.0       | 9.0        | 7.9        | < 0.001  |
| Physical activity (active) †† (%)| 33.4    | 34.8       | 37.9       | 42.8       | < 0.001  |
| Sleep pattern (regular) (%)      | 32.6    | 41.9       | 53.4       | 69.4       | < 0.001  |
| Overweight and obesity (%)       | 23.5    | 23.6       | 22.2       | 22.4       | < 0.001  |
| Recurrent headache (%)           | 13.1    | 11.2       | 9.3        | 7.9        | < 0.001  |
| Economic status (good) (%)       | 77.7    | 82.8       | 83.3       | 83.1       | < 0.001  |
| Electronic devices use (> 4 hour/day) (%) | 29.5 | 25.9 | 22.6 | 20.0 | < 0.001 |
| Occupation (%)                   | 8.0     | 9.3        | 9.7        | 10.6       | < 0.001  |
| Supplement use (%)               | 9.9     | 10.3       | 10.4       | 9.8        | 0.10     |
| Hypertension (%)                 | 4.0     | 4.2        | 5.9        | 8.4        | < 0.001  |
| Overweight and obesity (%)       | 23.5    | 23.6       | 22.2       | 22.4       | 0.006    |
| Primary headaches (%)            | 13.1    | 11.2       | 9.3        | 7.9        | < 0.001  |
| Dietary intakes                  |         |            |            |            |          |
| Fruits (more 500 g) (%)          | 8.7     | 8.3        | 8.8        | 11.5       | < 0.001  |
| Vegetables (daily) (%)           | 12.8    | 8.3        | 10.2       | 17.0       | < 0.001  |
| Dairy (daily) (%)                | 15.8    | 17.6       | 18.9       | 29.0       | < 0.001  |
| Fast foods (daily) (%)           | 6.6     | 1.7        | 0.8        | 0.7        | < 0.001  |
| SSBs (daily) (%)                 | 15.4    | 8.9        | 6.4        | 4.7        | < 0.001  |
| Sweets (daily) (%)               | 16.9    | 13.9       | 11.8       | 12.3       | < 0.001  |

Data are presented as mean (SD) or percent
Abbreviation: BMI: body mass index, SSBs: sugar-sweetened beverages
†Rarely: < 1 day/wk
††Those who exercised 3 time/wk or more lasting 30 minutes in each time
*Obtained from ANOVA or Chi-square, where appropriate

Multivariable ORs and 95% CIs for primary headaches across categories of breakfast consumption are illustrated in Table 2. A significant inverse association was seen between breakfast consumption and odds of primary headaches (OR: 0.57, 95% CI: 0.51–0.62). This association remained significant even after controlling for socio-demographic variables, hypertension and physical activity (OR: 0.66, 95% CI: 0.58–0.75). Further adjustments for dietary intakes and BMI did not alter the significant inverse association; such that students who consumed breakfast ≥ 5 days/wk had
26% lower odds of primary headaches compared with those who consumed breakfast rarely (OR: 0.74, 95% CI: 0.65–0.85).

| Table 2 | Multivariable-adjusted ORs and 95% CIs for primary headaches across categories of breakfast consumption pattern |
|---------|----------------------------------------------------------------------------------------------------------------|
|         | Rarely† | 1–2 day/wk | 3–4 day/wk | ≥ 5 day/wk | p-trend* |
| Crude   | 1.00    | 0.84 (0.75–0.93) | 0.68 (0.62–0.76) | 0.57 (0.52–0.63) | < 0.001 |
| Model 1 | 1.00    | 0.81 (0.73–0.90) | 0.66 (0.60–0.73) | 0.53 (0.49–0.59) | < 0.001 |
| Model 2 | 1.00    | 0.84 (0.73–0.97) | 0.74 (0.64–0.84) | 0.67 (0.58–0.76) | < 0.001 |
| Model 3 | 1.00    | 0.90 (0.78–1.03) | 0.81 (0.70–0.93) | 0.75 (0.65–0.86) | < 0.001 |
| Model 4 | 1.00    | 0.89 (0.77–1.03) | 0.81 (0.70–0.93) | 0.75 (0.65–0.86) | < 0.001 |

Data are presented as OR (95% CI)
Abbreviation: OR: odds ratio, CI: confidence interval, wk: week, SSBs: sugar-sweetened beverages, BMI: body mass index
†Rarely: <1 day/wk
*Obtained from binary logistic regression
Model 1: adjusted for age and gender
Model 2: additionally adjusted for marital status, education, occupation, physical activity, economic status, smoking, electronic devices use, sleep pattern, hypertension and supplement use
Model 3: further adjustment for dietary intake of fruits, vegetables, fast foods, SSBs, whole grains, and sweets
Model 4: more adjustment for BMI

Gender and BMI status-stratified ORs and 95% CIs for primary headaches across patterns of breakfast consumption are presented in Table 3. We found a significant inverse association between breakfast consumption and odds of primary headaches in both genders (males; OR: 0.56, 95% CI: 0.48–0.66, females; OR: 0.53, 95% CI: 0.46–0.60). However, after taking potential confounders into account, the inverse association became non-significant in male students, but remained significant in female ones; such that women with frequent breakfast consumption were 32% less likely to have primary headaches compared with those women who consumed breakfast rarely (OR: 0.54, 95% CI: 0.49–0.61). Regards to stratified analyses based on BMI status, a significant inverse association was found between breakfast consumption and odds of primary headaches either in normal-weight participants (OR: 0.68, 95% CI: 0.57–0.81) or those with overweight or obesity (OR: 0.62, 95% CI: 0.50–0.76). However, in the fully adjusted model, this association remained
significant in normal-weight students (OR: 0.68, 95% CI: 0.58-0.79), whereas it became non-significant in those with overweight or obesity.

Table 3
Multivariable-adjusted ORs and 95% CIs for primary headaches across categories of breakfast consumption pattern stratified based on gender and BMI status

| Gender          | Rarely†  | 1-2 day/wk | 3-4 day/wk | ≥ 5 day/wk | P-trend* |
|-----------------|----------|------------|------------|------------|----------|
| **Gender**      |          |            |            |            |          |
| Males           |          |            |            |            |          |
| Crude           | 1.00     | 0.82 (0.69-0.97) | 0.67 (0.57-0.78) | 0.57 (0.49-0.66) | < 0.001  |
| Model 1         | 1.00     | 0.82 (0.69-0.97) | 0.67 (0.57-0.79) | 0.57 (0.49-0.67) | < 0.001  |
| Model 2         | 1.00     | 0.88 (0.69-1.11) | 0.85 (0.67-1.06) | 0.86 (0.68-1.07) | 0.01     |
| Model 3         | 1.00     | 0.88 (0.70-1.12) | 0.85 (0.67-1.07) | 0.86 (0.68-1.08) | 0.335    |
| Model 4         | 1.00     | 0.88 (0.69-1.12) | 0.85 (0.67-1.07) | 0.86 (0.68-1.08) | 0.332    |
| **Females**     |          |            |            |            |          |
| Crude           | 1.00     | 0.81 (0.70-0.93) | 0.66 (0.58-0.76) | 0.53 (0.47-0.60) | < 0.001  |
| Model 1         | 1.00     | 0.81 (0.70-0.93) | 0.65 (0.57-0.75) | 0.52 (0.46-0.59) | < 0.001  |
| Model 2         | 1.00     | 0.89 (0.74-1.07) | 0.78 (0.65-0.93) | 0.68 (0.57-0.81) | < 0.001  |
| Model 3         | 1.00     | 0.88 (0.73-1.06) | 0.77 (0.64-0.92) | 0.68 (0.57-0.81) | < 0.001  |
| Model 4         | 1.00     | 0.88 (0.73-1.06) | 0.77 (0.64-0.92) | 0.68 (0.57-0.81) | < 0.001  |
| **BMI status**  |          |            |            |            |          |
| Normal-weight (BMI < 25 kg/m²) |          |            |            |            |          |
| Crude           | 1.00     | 0.81 (0.71-0.92) | 0.67 (0.60-0.75) | 0.55 (0.49-0.62) | < 0.001  |
| Model 1         | 1.00     | 0.78 (0.69-0.88) | 0.65 (0.57-0.73) | 0.52 (0.46-0.58) | < 0.001  |
| Model 2         | 1.00     | 0.80 (0.68-0.93) | 0.69 (0.59-0.81) | 0.62 (0.54-0.73) | < 0.001  |
| Model 3         | 1.00     | 0.83 (0.71-0.98) | 0.74 (0.63-0.87) | 0.68 (0.59-0.80) | < 0.001  |
| Overweight/obese (BMI ≥ 25 kg/m²) |          |            |            |            |          |
| Crude           | 1.00     | 0.93 (0.74-1.16) | 0.71 (0.57-0.88) | 0.62 (0.51-0.76) | < 0.001  |
| Model 1         | 1.00     | 0.09 (0.72-1.13) | 0.68 (0.55-0.85) | 0.58 (0.48-0.72) | < 0.001  |
| Model 2         | 1.00     | 1.03 (0.75-1.40) | 0.91 (0.68-1.24) | 0.84 (0.63-1.13) | 0.028    |
| Model 3         | 1.00     | 1.13 (0.82-1.56) | 1.06 (0.77-1.44) | 1.01 (0.74-1.37) | 0.442    |

Data are presented as OR (95% CI)
Abbreviation: OR: odds ratio, CI: confidence interval, wk: week, SSBS: sugar-sweetened beverages, BMI: body mass index
†Rarely: <1 day/wk
*Obtained from binary logistic regression

Model 1: adjusted for age and gender (for BMI status-stratified analysis)
Model 2: additionally adjusted for marital status, education, occupation, physical activity, economic status, smoking, electronic devices use, sleep pattern, hypertension and supplement use
Model 3: further adjustment for dietary intake of fruits, vegetables, fast foods, SSBS, whole grains, and sweets
Model 4: more adjustment for BMI (for gender-stratified analysis)

DISCUSSION
In the current study, we found that breakfast consumption was inversely associated with the odds of primary headaches. Such a significant association was seen even after taking potential confounders into account. Moreover, a significant inverse association was observed between breakfast consumption and primary headaches in female students as well as normal-weight ones. To the best of our knowledge, this study was the first to examine the association between breakfast consumption patterns and primary headaches in adults.

Breakfast can provide some essential micronutrients after overnight fasting. Some of these nutrients affect the neurological system (33). Previous studies have examined the relationship between breakfast consumption and some neurological disorders such as depression, anxiety, and stress (21, 34). However, the association between breakfast consumption and incidence of headache has long been a question for researchers. Based on our findings, we found that frequent breakfast consumption was inversely associated with the odds of primary headaches. In line with our findings, in a cross-sectional observational study in U.S. high schools, Gelfand et al. reported that adolescents with migraine usually missed breakfast compared with healthy ones (35). In another cross-sectional study, it had been shown that headache was more prevalent among adolescents who consumed breakfast rarely (36). In a cross-sectional study on 13,570 U.S. adolescents, Walter et al. reported a significant positive association between breakfast skipping and odds of recurrent headaches (37). Also, Moschiano et al. indicated that individuals with headache had irregular meals (especially irregular breakfast) and sleep disturbance compared to those without headache (38). Most studies mentioned above evaluated the different types of headaches, not just the primary headaches, and were performed on adolescents. As seen in our study, breakfast consumption
may have a protective effect against primary headaches in adults, particularly adult students.

The inverse association between breakfast consumption and primary headaches might be explained through some proposed mechanisms. Breakfast is the first meal in a day that is consumed after overnight fasting. Therefore, if this important meal is skipped, the neurological system will be deprived of some essential macronutrients and micronutrients (33). As reported in previous studies, hunger has a key role in the incidence of primary headaches (39). In addition, breakfast preparation is an active behavior that involves individuals in social activity (40); through which it might further help in preventing primary headaches. Moreover, consuming breakfast might decrease the activity of the hypothalamic-pituitary-adrenal axis (17). This axis contributes to the secretion of stress hormones such as cortisol and epinephrine, which can induce the incidence of primary headaches (17, 18, 41).

Surprisingly, we observed a gender disparity in the association between breakfast consumption and primary headaches. This disparity might be due to the different influence of sex hormones on the neurological system and primary headaches (42, 43). In addition, the accuracy of dietary data might be different between males and females (44, 45). Earlier studies demonstrated that actual dietary behaviors, self-reported preferences for foods and accuracy of reported dietary intakes are different between men and women (46, 47). Besides, unlike normal-weight students, we found no significant association between breakfast consumption and primary headaches in students with overweight or obesity. Obesity is associated with increased concentrations of inflammatory cytokines (48, 49). Given the inflammation is a potential risk factor for primary headaches (50, 51), it may
interfere with the beneficial effects of breakfast consumption on headache in obese individuals.

Several strengths of the current study need to be highlighted. This study was the first that recruited a large sample size of university students in the Middle East to investigate the relation between breakfast consumption patterns and primary headaches. Furthermore, a wide range of potential confounders was taken into account to obtain an independent association between breakfast consumption and primary headaches. In addition to the whole population, we performed stratified analyses based on gender and BMI status. Employing university students might increase the accuracy of the collected data. Given these strengths, some limitations must be considered when interpreting our findings. Because of the cross-sectional design of our study, establishing a cause-and-effect relationship between breakfast consumption and primary headaches is impossible. Further studies, in particular of prospective design, are required to confirm our findings. In the current study, we focused on primary headaches generally, whereas the association of breakfast consumption with specific types of primary headaches might be different. Also, we considered only health insurance (having/not-having) as an index for the assessment of economic status. The lack of information on house possession or having a car made us unable to evaluate economic status more accurately. Although several confounders were taken into account to reach an independent association between breakfast consumption and primary headaches, further control for other variables such as psychological disorders and residual lifestyle factors might be needed. In addition, the study was conducted on a population of university students, and extrapolating our findings to the general population must be done cautiously. Although we applied validated questionnaires, the misclassification of
study participants in terms of breakfast consumption cannot be excluded.

In conclusion, we found a significant inverse association between breakfast consumption and odds of primary headaches in university students. This association was more relevant in female students and those with normal weight. Further studies are needed to confirm our findings. Furthermore, considering different types of primary headaches including migraine, tension-type headache and non-classifiable headache in relation to breakfast consumption in future research can provide further information in this regard.

DECLARATIONS

**Ethics approval and consent to participate**: All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All participants provided a signed written consent form.

**Consent for publication**: Not applicable

**Availability of data and materials**: The dataset that was analyzed in the current study is available from the corresponding author on reasonable request.

**Competing interests**: The authors declare that they have no competing interests.

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**Authors' contributions**: MM, FS, MV, YMT, and HY designed research and conducted research; OS analyzed data; OS and AS wrote the paper; OS and MM had primary responsibility for final content. All authors read and approved the final
Conflict of interest: The authors have no conflicts of interest to declare.

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REFERENCES

1. Mier RW, Dhadwal S. Primary Headaches. Dent Clin North Am 2018;62:611-28.
2. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018;38:1-211.
3. Sadeghi O, Nasiri M, Saiedi SG. The prevalence of migraine in different parts of Iran: review of the current evidence. Jundishapur Journal of Chronic Disease Care 2015;4.
4. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology 2007;68:343-9.
5. Stewart WF, Wood C, Reed ML, et al. Cumulative lifetime migraine incidence in women and men. Cephalalgia 2008;28:1170-8.
6. Miri A, Nasiri M, Zonoori S, et al. The association between obesity and migraine in a population of Iranian adults: a case-control study. Diabetes Metab Syndr 2018;12:733-6.
7. Nasiri M, Arsanjani Shirazi A, Sadeghi O, et al. The Relationship between Homocysteine Levels and Spontaneous Abortion in Iranian Women with Migraine. Iran J Public Health 2017;46:1149-51.
8. Charles A. The pathophysiology of migraine: implications for clinical
management. *Lancet Neurol* 2018;17:174-82.

9. Nazari F, Eghbali M. Migraine and its relationship with dietary habits in women. *Iran J Nurs Midwifery Res* 2012;17:S65-71.

10. Askari G, Nasiri M, Mozaffari-Khosravi H, et al. The effects of folic acid and pyridoxine supplementation on characteristics of migraine attacks in migraine patients with aura: A double-blind, randomized placebo-controlled, clinical trial. *Nutrition* 2017;38:74-9.

11. Millichap JG, Yee MM. The diet factor in pediatric and adolescent migraine. *Pediatr Neurol* 2003;28:9-15.

12. Jafarpour M, Yousefi G, Hamedi A, et al. Effect of a traditional syrup from Citrus medica L. fruit juice on migraine headache: A randomized double blind placebo controlled clinical trial. *J Ethnopharmacol* 2016;179:170-6.

13. Sadeghi O, Askari G, Maghsoudi Z, et al. The association between abdominal obesity and characteristics of migraine attacks in Iranian adults. *Iran J Nurs Midwifery Res* 2016;21:271-7.

14. Sadeghi O, Maghsoudi Z, Khorvash F, et al. The relationship between different fatty acids intake and frequency of migraine attacks. *Iran J Nurs Midwifery Res* 2015;20:334-9.

15. Sadeghi O, Maghsoudi Z, Khorvash F, et al. Assessment of pyridoxine and folate intake in migraine patients. *Adv Biomed Res* 2016;5:47.

16. Sadeghi O, Nasiri M, Maghsoudi Z, et al. Effects of pyridoxine supplementation on severity, frequency and duration of migraine attacks in migraine patients with aura: A double-blind randomized clinical trial study in Iran. *Iran J Neurol* 2015;14:74-80.

17. Smith AP. Stress, breakfast cereal consumption and cortisol. *Nutr Neurosci*
2002;5:141-4.

18. Noseda R, Borsook D, Burstein R. Neuropeptides and Neurotransmitters That Modulate Thalamo-Cortical Pathways Relevant to Migraine Headache. *Headache* 2017;57 Suppl 2:97-111.

19. Lee SA, Park EC, Ju YJ, et al. Breakfast consumption and depressive mood: A focus on socioeconomic status. *Appetite* 2017;114:313-9.

20. Widaman AM, Witbracht MG, Forester SM, et al. Chronic Stress Is Associated with Indicators of Diet Quality in Habitual Breakfast Skippers. *J Acad Nutr Diet* 2016;116:1776-84.

21. Milajerdi A, Keshteli AH, Esmailzadeh A, et al. Breakfast consumption in relation to lowered risk of psychological disorders among Iranian adults. *Public Health* 2019;167:152-8.

22. Vilaro MJ, Colby SE, Riggsbee K, et al. Food Choice Priorities Change Over Time and Predict Dietary Intake at the End of the First Year of College Among Students in the U.S. *Nutrients* 2018;10.

23. Hilger J, Loerbroks A, Diehl K. Eating behaviour of university students in Germany: Dietary intake, barriers to healthy eating and changes in eating behaviour since the time of matriculation. *Appetite* 2017;109:100-7.

24. Betancourt-Nunez A, Marquez-Sandoval F, Gonzalez-Zapata LI, et al. Unhealthy dietary patterns among healthcare professionals and students in Mexico. *BMC Public Health* 2018;18:1246.

25. Wang X, Zhou HB, Sun JM, et al. The prevalence of migraine in university students: a systematic review and meta-analysis. *Eur J Neurol* 2016;23:464-75.

26. Mansouri M, Sharifi F, Varmaghani M, et al. Iranian university students lifestyle and health status survey: study profile. *J Diabetes Metab Disord* 2017;16:48.
27. Mansouri M, Hasani-Ranjbar S, Yaghubi H, et al. Breakfast consumption pattern and its association with overweight and obesity among university students: a population-based study. *Eat Weight Disord* 2018.

28. Mansouri M, Miri A, Varmaghani M, et al. Vitamin D deficiency in relation to general and abdominal obesity among high educated adults. *Eat Weight Disord* 2019;24:83-90.

29. Mansouri M, Sharifi F, Yaghubi H, et al. Sugar-sweetened beverages consumption in relation to hypertension among Iranian university students: the MEPHASOUS study. *Eat Weight Disord* 2019.

30. McAbee GN, Morse AM, Assadi M. Pediatric Aspects of Headache Classification in the International Classification of Headache Disorders-3 (ICHD-3 beta version). *Curr Pain Headache Rep* 2016;20:7.

31. Dabbagh-Moghadam A, Mozaffari-Khosravi H, Nasiri M, et al. Association of white and red meat consumption with general and abdominal obesity: a cross-sectional study among a population of Iranian military families in 2016. *Eat Weight Disord* 2017;22:717-24.

32. Vaduganathan M, Pareek M, Qamar A, et al. Baseline Blood Pressure, the 2017 ACC/AHA High Blood Pressure Guidelines, and Long-Term Cardiovascular Risk in SPRINT. *Am J Med* 2018;131:956-60.

33. Hoyland A, Dye L, Lawton CL. A systematic review of the effect of breakfast on the cognitive performance of children and adolescents. *Nutr Res Rev* 2009;22:220-43.

34. Ferrer-Cascales R, Sanchez-SanSegundo M, Ruiz-Robledillo N, et al. Eat or Skip Breakfast? The Important Role of Breakfast Quality for Health-Related Quality of Life, Stress and Depression in Spanish Adolescents. *Int J Environ Res Public*
35. Gelfand AA, Pavitt S, Greene K, et al. High School Start Time and Migraine Frequency in High School Students. *Headache* 2019;59:1024-31.

36. Torres-Ferrus M, Vila-Sala C, Quintana M, et al. Headache, comorbidities and lifestyle in an adolescent population (The TEENs Study). *Cephalalgia* 2019;39:91-9.

37. Walter S. Lifestyle behaviors and illness-related factors as predictors of recurrent headache in U.S. adolescents. *J Neurosci Nurs* 2014;46:337-50.

38. Moschiano F, Messina P, D’Amico D, et al. Headache, eating and sleeping behaviors and lifestyle factors in preadolescents and adolescents: preliminary results from an Italian population study. *Neurol Sci* 2012;33 Suppl 1:S87-90.

39. Gazerani P, Cairns BE. Dysautonomia in the pathogenesis of migraine. *Expert Rev Neurother* 2018;18:153-65.

40. Graham PL, Russo R, Defeyter MA. The Advantages and Disadvantages of Breakfast Clubs According to Parents, Children, and School Staff in the North East of England, UK. *Front Public Health* 2015;3:156.

41. Feuerecker M, van Oosterhout WP, Feuerecker B, et al. Headache under simulated microgravity is related to endocrine, fluid distribution, and tight junction changes. *Pain* 2016;157:1072-8.

42. Merki-Feld GS, Imthurn B, Gantenbein AR, et al. Effect of desogestrel 75 microg on headache frequency and intensity in women with migraine: a prospective controlled trial. *Eur J Contracept Reprod Health Care* 2019;24:175-81.

43. Roque C, Mendes-Oliveira J, Duarte-Chendo C, et al. The role of G protein-coupled estrogen receptor 1 on neurological disorders. *Front Neuroendocrinol* 2019;55:100786.
44. Sadeghi O, Hassanzadeh-Keshteli A, Afshar H, et al. The association of whole and refined grains consumption with psychological disorders among Iranian adults. *Eur J Nutr* 2019;58:211-25.

45. Anjom-Shoae J, Sadeghi O, Hassanzadeh Keshteli A, et al. The association between dietary intake of magnesium and psychiatric disorders among Iranian adults: a cross-sectional study. *Br J Nutr* 2018;120:693-702.

46. Anjom-Shoae J, Keshteli AH, Sadeghi O, et al. Association between dietary insulin index and load with obesity in adults. *Eur J Nutr* 2019.

47. Sadeghi O, Keshteli AH, Afshar H, et al. Adherence to Mediterranean dietary pattern is inversely associated with depression, anxiety and psychological distress. *Nutr Neurosci* 2019:1-12.

48. Sadeghi O, Saneei P, Nasiri M, et al. Abdominal Obesity and Risk of Hip Fracture: A Systematic Review and Meta-Analysis of Prospective Studies. *Adv Nutr* 2017;8:728-38.

49. Sadeghi O, Sadeghian M, Rahmani S, et al. Whole-Grain Consumption Does Not Affect Obesity Measures: An Updated Systematic Review and Meta-analysis of Randomized Clinical Trials. *Adv Nutr* 2019.

50. Rahmani S, Sadeghi O, Sadeghian M, et al. The Effect of Whole-Grain Intake on Biomarkers of Subclinical Inflammation: A Comprehensive Meta-analysis of Randomized Controlled Trials. *Adv Nutr* 2019.

51. Cavestro C, Ferrero M, Mandrino S, et al. Novelty in Inflammation and Immunomodulation in Migraine. *Curr Pharm Des* 2019;25:2919-36.