



Dietary Intake Assessment and Its Impact on Migraine with Aura and Migraine without Aura

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Abstract: Background: There are strong evidences indicating that oxidative stress is decisively involved in the pathophysiology of migraine with aura, which indicates the possible role of food in its occurrence. **Aim of work:** Evaluate of the consumption rate of nutrients between migraine patients and study the difference between nutritional statuses of participants with migraine with aura (MA) versus migraine without aura (MO). **Methods:** Across-Sectional Analytical study was conducted through face to face interview with the researcher; 124 adult subjects with migraine were recruited from headache clinics in Cairo and Alexandria university hospitals, Reliable Socioeconomic Status Scale in Arabic was used to assess socioeconomic status, Branching Logic Questionnaire in Arabic was used to check aura symptoms according to international headache society criteria, and 24- Hour Recall Questionnaire was used to evaluate the actual daily intake of nutrients. **Results:** Females were 81.5% of participants with mean age 31 years, 62% of participants had (MA) who were associated with mean daily intake of 1742.9 ml of Water and 32.1 mg of Vitamin-C, represented about 77% and 42% of the reference values of Water and Vitamin-C respectively, which were significantly differ compared by participants with (MO) at (P-values = 0.04 and 0.03 respectively), while, there were no significant differences between (MA) and (MO) in their daily intake of calories, protein, fat, carbohydrate, fiber, sodium, potassium, calcium, magnesium, phosphorous, zinc, copper, iron, vitamin-A, thiamin, riboflavin. **Conclusion:** Low daily intake of Water and Vitamin-C were associated with (MA) more than (MO), so this must be taken into account during diet planning.

[Alyaa N. Abdel-Fattah, Thanaa A. Elkholy, Ensaf M. Yassen, Nirmeen A. Kishk, and Reham M. Shamloul. **Dietary Intake Assessment and Its Impact on Migraine with Aura and Migraine without Aura.** *Nat Sci* 2020;18(8):6-13]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). <http://www.sciencepub.net/nature>. 2. doi:[10.7537/marsnsj180820.02](https://doi.org/10.7537/marsnsj180820.02).

Key words: Migraine with aura - Nutrients - Water - Oxidative stress - Vitamin-C.

1. Introduction

There are a strong evidences indicating that oxidative stress is decisively involved in the pathophysiology of migraine with aura^[1], metabolism of fat and proteins causes a great oxidative burden on body cells^[2], the resulting superoxide molecules cause cerebral vasoconstriction and cerebral vasospasm^[3], which will lead to activating the trigeminal sensory nerve by innervating the dural blood vessels^[4], this's wave of slowly propagating of neuronal and glial depolarization and hyperpolarization is what happens during "the migraine aura"^[5]. Aura often occurs as collection of disabling symptoms such as bright or dark points, zigzag lines and blurry vision that patient suffers from it^[6]. Because low daily intake of antioxidants lead to decreasing their levels in plasma^[7]; we have investigated in the hypothesis that low daily intake of some nutrients that are considered as antioxidants may be associate with the occurrence of the migraine aura which results by oxidative stress.

2. Methods:

Aim of study:

Assessing daily intake of macronutrients and micronutrients in patients with migraine and identifying nutrients whose consumption rate is associated with the occurrence of aura symptoms after neutralizing all other factors.

Study design and participants:

Across-Sectional Analytical study carried out among 124 subjects with migraines included in the study according to "Steven k. Thompson" equation for the calculating of sample size^[8]. Inclusion criteria were subjects with migraine fulfilling the International Headache Society (IHS) criteria^[9], both sex, and age above 18 years. While, we excluded patients with memory problems or poor reporting, patients with other headaches, patients with other neurological disease and clinically relevant disorders as head injuries and epilepsy, and pregnant women. Subjects were recruited from headache clinics in Cairo university hospital and Alexandria university hospital, Patients are diagnosed as having migraines by neurologist then they were individually interviewed by

the nutritionist to filling the detailed questionnaires; each interview took about 45 minutes.

Demographic and socioeconomic data assessment of participants was assessed by valid and reliable socioeconomic status scale for health research in Egypt, with permission of the original author; it was translated into Arabic by translation and back-translation. This scale has seven domains with a total score 84 ^[10].

Migraine assessment: with permission of the original author; the branching logic questionnaire for the automated classification of migraine was translated into Arabic by translation and back- translation, and it was used to classify subjects into migraine with aura (MA) and migraine without aura (MO) in order to standardize the diagnostic criteria of neurologists on the International Headache Society criteria. This's tool has been designed to be used in researches, with a good specificity ^[11].

Dietary intake assessment: the 24- hour recall questionnaire is one of the most reliable and widely used tools in nutritional assessment ^[12]. According to Food and Agriculture Organization criteria; the 24 hours dietary recall consists of record all foods patient eats, drink, appetite, use of vitamins & minerals, number of meals & snacks, drinking coffee or any caffeine beverages and exercise for a 24-hour period for 3 consecutive days included weekend day to account the food fluctuations that occur during the week. It was reported that coefficient of alpha reliability 0.92. Trained investigator asked each

subject to inform about all foods and drinks that it had been consumed during the past 24 hours with it quantities and cooking method. Pictures of different sizes of food, standard cups and spoons have been used to help each respondent to estimate how much food he ate ^[13].

Data of the 24-hour food intake were coded; average of the three days was taken and it entered into a computer program of food analysis. The analysis by this program based on food composition tables of Egyptian National Nutrition Research Institute ^[14]. Then, percentage (%) of the mean daily intake of nutrients was calculated from the next formula:

Factors such as age and gender were taken into account when assigning Dietary Reference Intakes (DRI) values for each respondent ^[15].

Statistically analysis: Results were analyzed by the statistical package for social science (SPSS) ^[16]. Descriptive statistics such as; arithmetic mean, standard deviation and range were used for quantitative variables, qualitative variables were expressed as percentages and association measures available within cross tabs are used as tests of independence between the categorical variables, (chi-square) test was used for comparison among proportions, Independent T-test was used to compare between the two sample means with the assumption that variables are normally distributed, $P < 0.05$ was adopted as the level of significance.

3. Results:

Table (1): Demographic and Socioeconomic characteristics of participants

Migraine without aura (n = 47)	Migraine with aura (n = 77)	P. value
Age		
Mean = 36 years SD = 12	Mean = 31 years SD = 10	0.043*
Gender		
Female	68.1%	89.6%
Male	31.9%	10.4%
Educational level		
Pre-university education	38.3%	39.0%
University education	51.1%	51.9%
Postgraduate	10.6%	9.1%
Socioeconomic status		
Low	12.8%	27.3%
Moderate	57.5 %	53.3%
High	29.8%	19.5%
Occupation		
Housewives	31.9%	58.4%
Students	25.5%	10.4%
Employees	27.7%	16.9%
Hard workers	14.9%	14.3%
Marital status		
Married	74.5%	89.6%
Not married	25.5%	10.4%

* Statistically significant

There were a significant higher of females, with younger age, married, and housewives between migraine with aura (MA), at P- values = 0.003, 0.04, 0.02, and 0.01 respectively, while; both (MA) and (MO) didn't have significant differences in terms of education level and socioeconomic status.

As regarding type of migraine headache using the branching logic questionnaire and the diagnosis of

neurologist; 62% of participants were (MA) and 38% of them were (MO). Clinical features which have been reported by subjects with (MA) were visual or physical symptoms, or both, which included blurring vision, seeing dark spot, zigzag lines, or blind light flashes, localized numbness around the mouth and in upper limbs, and disability in one side of the body or paraplegia.

Table (2): The mean daily intake of macronutrients by subjects with (MO) and subjects with (MA)

Macronutrients	Migraine without aura (n = 47)			Migraine with aura (n = 77)			P. value
	Mean	±	SD	Mean	±	SD	
Water (milliliters)	2084.6	±	873.6	1742.9	±	745.1	0.041*
Energy (calories)	2525.8	±	788.7	2640.7	±	954.1	0.538
Protein (gram)	111.0	±	34.4	110.5	±	38.0	0.945
Fat (gram)	80.9	±	27.4	75.4	±	29.3	0.355
Fibers (gram)	9.2	±	3.8	10.4	±	4.4	0.205
Carbohydrate (gram)	338.4	±	128.9	380.1	±	163.6	0.187

* Statistically significant

Table (3): The mean daily intake of minerals by subjects with (MO) and subjects with (MA)

Minerals	Migraine without aura (n = 47)			Migraine with aura (n = 77)			P. value
	Mean	±	SD	Mean	±	SD	
Sodium (mg)	4157.1	±	1627.1	4276.8	±	1801.0	0.740
Potassium (mg)	2959.1	±	1008.7	2903.7	±	1001.4	0.790
Calcium (mg)	783.5	±	339.2	782.2	±	367.2	0.986
Phosphorous (mg)	1400.1	±	493.6	1484.0	±	528.3	0.435
Magnesium (mg)	106.0	±	44.8	95.9	±	48.9	0.307
Iron (mg)	21.7	±	7.8	23.3	±	9.4	0.392
Zinc (mg)	15.4	±	5.6	16.1	±	5.9	0.601
Copper (mg)	1.0	±	0.4	1.1	±	0.5	0.511

Table (4): Daily intake of vitamins by subjects with (MO) and subjects with (MA)

Vitamins	Migraine without aura (n = 47)	Migraine with aura (n = 77)	P. value
Vitamin-A (mg)			
Interquartile range	164.4 – 331.5	109.0 – 348.7	0.083
Vitamin-C (mg)			
Interquartile range	3.2 – 46.2	6.9 – 43.8	0.743
Thiamin (mg)			
Interquartile range	0.9 – 1.6	1.0 – 2.0	0.222
Riboflavin (mg)			
Interquartile range	0.9 – 1.6	0.8 – 1.4	0.600

Table (5): Consumption ranges of macronutrients by subjects with (MO) and subjects with (MA) "results of chi-square test"

Macronutrients	Migraine without aura (n = 47)			Migraine with aura (n = 77)			P. value
	Low. C	Normal. C	Over. C	Low. C	Normal. C	Over. C	
Water (milliliters)	27 (57.4%)	8 (17%)	12 (25.5%)	52 (68.4%)	7 (9.2%)	17 (22.4%)	0.346
Energy (calories)	3 (6.4%)	7 (14.9%)	37 (78.7%)	6 (7.9%)	9 (11.8%)	61 (80.3%)	0.858
Protein (gram)	7 (14.9%)	11 (23.4%)	29 (61.7%)	12 (15.8%)	12 (15.8%)	52 (68.4%)	0.573
Fat (gram)	3 (6.4%)	3 (6.4%)	41 (87.2%)	9 (11.8%)	3 (3.9%)	64 (84.2%)	0.530
Fibers (gram)	47 (100%)	0 (0%)	0 (0%)	75 (98.7%)	1 (1.3%)	0 (0%)	0.430
Carbs (gram)	6 (12.8%)	7 (14.9%)	34 (72.3%)	6 (7.9%)	14 (18.4%)	56 (73.7%)	0.630

For the purpose of statistical analysis and examining the association between variables; participants were classified into 3 categories: Participants who consumed less than 90% of their DRI were classified as low consumption; participants who consumed from 90% to 110% of their DRI have been

classified as normal consumption, while those who consumed more than 110% of their DRI have been classified as over consumption. Data is represented in the table on this basis "number of subjects (their percentage)".

Table (6): Consumption ranges of micronutrients by subjects with (MO) and subjects with (MA) "results of chi-square test"

Micronutrients	Migraine without aura (n = 47)			Migraine with aura (n =77)			P. value
	Low. C	Normal. C	Over. C	Low. C	Normal. C	Over. C	
Sodium (mg)	0 (0%)	0 (0%)	47 (100%)	0 (0%)	0 (0%)	76 (100%)	----
Potassium (mg)	2 (4.3%)	7 (14.9%)	38 (80.9%)	11 (14.5%)	6 (7.9%)	59 (77.6 %)	0.119
Calcium (mg)	34 (72.3%)	3 (6.4%)	10 (21.3%)	51 (67.1%)	11 (14.5%)	14 (18.4%)	0.385
Phosphorous (mg)	0 (0%)	1 (2.1%)	46 (97.9%)	1 (1.3%)	3 (3.9%)	72 (94.7%)	0.624
Magnesium (mg)	47 (100%)	0 (0%)	0 (0%)	76 (100%)	0 (0%)	0 (0%)	----
Iron (mg)	8 (17%)	5 (10.6%)	34 (72.3 %)	18 (23.7%)	7 (9.2%)	51 (67.1%)	0.675
Zinc (mg)	1 (2.1%)	4 (8.5%)	42 (89.4%)	6 (7.9%)	4 (5.3%)	66 (86.8%)	0.335
Copper (mg)	47 (100%)	0 (0%)	0 (0%)	76 (100%)	0 (0%)	0 (0%)	----
Vitamin-A (mg)	43 (91.5%)	0 (0%)	4 (8.5%)	65 (85.5%)	3 (3.9%)	8 (10.5%)	0.351
Vitamin- C (mg)	34 (72.3%)	7 (14.9%)	6 (12.8%)	66 (86.8%)	2 (2.6%)	8 (10.5%)	0.033*
Thiamin (mg)	17 (36.2%)	3 (6.4%)	27 (57.4%)	19 (25%)	12 (15.8%)	45 (59.2%)	0.186
Riboflavin (mg)	23 (48.9%)	8 (17%)	16 (34%)	39 (51.3%)	9 (11.8%)	28 (36.8%)	0.719

*Statistically significant

For the purpose of statistical analysis and examining the association between variables; participants were classified into 3 categories: Participants who consumed less than 90% of their DRI were classified as low consumption; participants who consumed from 90% to 110% of their DRI have been classified as normal consumption, while those who consumed more than 110% of their DRI have been classified as over consumption. Data is represented in

the table on this basis "number of subjects (their percentage)".

Table (6) pointing to significant differences between subjects with (MA) and subjects with (MO) in their daily consumption of "vitamin- C", as, most subjects in both groups had a low consumption of "vitamin- C" but the dietary deficiency of vitamin- C was significantly associated with (MA) more than (MO) at (P = 0.03).

Table (7): Results of multivariate analysis logistic regression for type of migraine

Variables	Unstandardized Coefficients	Standard Error	*: Statistically significant at p < 0.05	Odds ratio	Confidence interval 95%	Lower limit	Upper Limit
Age	-0.034	0.023	0.139	0.967	0.924	1.011	
Gender	1.344	0.683	0.049*	3.834	1.006	14.614	
Occupation	-1.916	1.321	0.147	0.147	0.011	1.961	
Marital status	-0.102	0.707	0.886	0.903	0.226	3.609	
Water intake	0.008	0.002	0.001*	1.009	1.003	1.015	
Vitamin C intake	-0.001	0.004	0.812	0.999	0.991	1.007	

Variables with significant results in univariate analysis were included in the regression model. An intake of about 1743 milliliters of water / day and gender in favor of females has three times chance to develop migraine with aura (MA) compared by water intake of about 2085 milliliters / day and males at (P=0.001 & 0.049, respectively).

4. Discussion:

Contrary to the common that ratio of migraine with aura (MA) to migraine without aura (MO) ratio is about 33% to 66% [17], our results showed that the ratio of (MA) to (MO) ratio was about 62% to 38%. Which is nearly agreeing with other study indicated

that the actual ratio of (MA) to (MO) ratio was about 51% to 43% when diagnosis is made with more accurate and restricted criteria^[18].

The occurrence of aura symptoms were significantly associated with married females in the rate of 89.6%, especially at average of 31 years "reproductive age", which is consistent with the results of Sacco and his colleagues who indicated that fluctuations of estrogen levels which are occur in reproductive age of women increase migraine with aura through their effect on cellular excitability or cerebral vasculature and it may further increase the risk for ischemic, strokes, and cardiovascular diseases in women with (MA)^[19].

Majority of subjects with (MA) were housewives in the rate of 58.4%, this may be due to the severe disability which is resulting of aura symptoms, where, only about 18% of employers give some support to workers who suffer from migraine^[20].

Results of dietary assessment showed a significant association at (P= 0.03) between (MA) and the daily intake of about 42% of the reference value of vitamin-C in 86.8% of subjects with (MA) which is agree with other study indicated that supplement of vitamin-C can be reckoned as a preventive medication for migraine because of its role as a scavenger of reactive oxygen species (ROS), so it can be used for treating neurogenic inflammation in migraine^[21]. In addition to its role as electron donor, this characteristic is responsible for all of its functions as antioxidant^[2].

Food antioxidants prevent oxidative stress by inhibiting the initiation and spread of the oxidation chain, vitamin-C one of the most vital no enzymatic antioxidants^[22], it affects (MA) more than (MO) because oxidative stress is more intense in (MA) than (MO), where, the levels of oxidative molecules such as malondialdehyde (MDA) and nitric oxide (NO) increase in (MA) more than (MO)^[1]. In addition to, the activity of superoxide dismutase (SOD) decreases in (MA) more than (MO), this enzyme is a radical-scavenging enzyme, it scavenges superoxide radicals which are causing a vasospasm, vasoconstriction, and damage cellular functions^[3]. Therefore, according to the foregoing, it becomes clear that oxidative stress is involved in the occurrence of the migraine aura and the reason for the significant association between (MA) and the lack of daily intake of vitamin-C.

Our results showed a significant association between (MA) and low daily intake of water, which is agree with two studies indicated that increased daily intake of water led to reduce the duration and severity of migraine attacks^[23, 24], and another study indicated that cortical spreading depression (CSD) which is the mechanism of (MA)^[25], led to reducing water consumption in rats^[26].

The significant association between (MA) and

low daily intake of water maybe due to the water's containment of many minerals such as zinc and copper, which act as antioxidants, where, water contributes to an amount that may reach to 20% of the daily requirements of calcium and magnesium, so increased water intake can reduce the oxidative stress which will lead to (MA)^[27]. Some assumed that increased drinking of water reduce headache by increased removal of headache-causing substances which resulting from increased renal perfusion^[24], or because of impaired concentration and irritability that occur when dehydration extends from the meninges to the brain^[28], or because dehydration affects the brainstem nuclei that in turn affects the cranial vessels in a decisive process of the pathophysiology of migraine with aura^[29, 30].

Participants with both (MA) and (MO) had an over daily intake of carbohydrates with no significant differences between them, which agrees with another study found a significant increase in carbohydrate intake in women with migraines compared to normal women^[31]. It may because carbohydrate contribute significantly to the process of inflammation associated with diseases, where, during adopting a high carbohydrate diet; the serum cytokine levels increase and significant depletion of antioxidant enzymes occur^[32].

Although fat play a significant role in promoting oxidative stress and local inflammation in hypothalamus through microglial proliferation^[33], our results did not show significant differences between (MA) and (MO) in the daily intake of fat.

There were no significant differences between (MA) and (MO) in their daily intake of iron, which confirms that both iron deficiency and iron overload can affect redox state, where, it is well established that iron metabolism underlies the dynamic reaction between oxidative stress and antioxidants in many pathophysiological processes^[34]. Studies showed that iron deficiency anemia more prevalent in (MA) than (MO)^[35, 36], but our results don't support that increased the daily intake of iron is associated with (MO) although the essential role of cellular iron metabolism as a part of metabolic requirements under conditions of increased oxidative stress^[37].

Although the significant role of fiber in reducing the elevated level of serum C- reactive protein and the elevated oxidative and systemic inflammatory status^[38], there were no significant association between (MA) and the low daily intake of fiber. Our results disagreed with another study indicated that eating foods rich in fiber such as vegetables and fruits were associated with the occurrence of migraines in women^[39].

Although the effects of calcium, potassium, and sodium on (CSD)^[25], their daily intake wasn't

associated with (MA).

Although zinc, copper, and vitamin-A are antioxidants ^[40], but there were no significant differences between (MA) and (MO) in the daily intake of them.

Although increased energy metabolism leads to increased (CSD) ^[41], the high daily intake of calories wasn't associated with (MA).

Conclusion:

Low daily intake of water and vitamin-C were associated with (MA) more than (MO), while, there were no significant differences between (MA) and (MO) in their daily intake of calories, protein, fat, carbohydrate, fiber, ASH, sodium, potassium, calcium, magnesium, phosphorous, zinc, copper, iron, vitamin-A, thiamin, riboflavin. So this must be taken into account during diet planning.

Recommendations:

Drinking at least 2085 milliliters of water / day, and increased meals content of fruits and vegetables representing all the colors of the rainbow to obtainment of the reference values of vitamin-C may relieve the burden of migraine with aura.

Strength and Limitations:

To our knowledge, this study is the first of its kind that assesses this problem among our population, results of this study will lead to take adequate measures to manage migraine with aura nutritionally which may relieve its burden and its economic cost.

This was a cross-sectional Analytical study, which limits the establishment of causality, despite our attempts to eliminate all defects in 24 hour recall method, we still with some of the same defects such as the tendency to overestimate low intakes and underestimate high intakes.

Ethical considerations:

Before participating in this study, protocol was fully explained to patients and their informed consent was obtained, approval from the Scientific Research Ethics Committee, faculty of medicine, Alexandria University was obtained.

Abbreviations:

(IHS): International Headache Society, (MA): Migraine with Aura, (MO): Migraine without Aura, (DRI): Dietary Reference Intakes, (SPSS): Statistically Package for Social Science, (SOD): Superoxide Dismutase, (ROS): Reactive Oxygen Species, (MDA): Malondialdehyde, (NO): Nitric Oxide, (CSD): cortical spreading depression.

Acknowledgement:

We would like to thank both of Dr: Mohammed Hamdi, and Dr: Eman Hamdi from Department of Neurology, Alexandria University Hospitals for their great contribution to the implementation of the practical part of the study. And patients who participated in the study.

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