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Body Mass Index and its Association with Migraine Characteristics in Female Patients

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Abstract

Background: Migraine is a debilitating neurological disorder with a high prevalence. This study was conducted to evaluate the relationship between body mass index (BMI) and disability, severity, frequency and duration of headaches in female migraine patients.

Methods: This cross-sectional study was designed to address the characteristics of migraine attacks (duration of each attack, frequency, and severity) and MIDAS (Migraine Disability Assessment) score in female migraineurs. The diagnosis of migraine was based on ICHD-3 beta criteria. Verbal rating scale (VRS) was used for headache severity. Height and weight were measured to calculate the BMI. Mann-Whitney and Kruskal-Wallis tests were used for comparison of means, and analysis of covariance (ANCOVA) test was used for adjustment of the confounding factors.

Results: In the current study, 170 female migraine patients with a mean (±SD) age of 34.0 ± 8.0 years were enrolled. There were significant differences between the three groups (18.5 ≤ BMI< 25, 25 ≤ BMI < 30 and 30 ≤ BMI) in terms of headache frequency, duration and severity as well as total MIDAS score ($P<0.001$). These differences remained significant after adjustment for age.

Conclusion: This study revealed that migraineurs with higher BMI experienced higher headache frequency, severity and duration as well as higher disability score.

Keywords: Association, Body mass index, Headache, Migraine disorder, Obesity

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Introduction

Migraine is a common and disabling neurovascular headache disorder with a prevalence of about 11% in the general population. It is the seventh most disabling disorder all over the world and is associated with nausea, vomiting, photophobia, phonophobia and exacerbation by physical activity.[1,2] Migraine is more prevalent among female patients (5 to 35% in women and 3 to 20% in men) with the highest rate during their childbearing age.[3,4] Overweight (body mass index [BMI) between 25 and 29.9 kg/m^2] and obesity (BMI ≥ 30 kg/m^2) are becoming increasingly, common, with more than one billion obese adults in the world currently.[5,6] These public health problems affect developing and developed countries alike and are associated with higher risk of different conditions and disorders such as reduced quality of life, diabetes, dyslipidemia, hypertension, cardiovascular diseases, cancer, and pain disorders (chronic pains, fibromyalgia, low back pain, neck pain and, according to some recent studies, headaches).[5-8]

Both migraine and obesity are independently related to poor quality of life. In addition, diverse evidence suggests that overweight or obesity can be associated with greater risk of migraine. Furthermore, higher BMI is reported to be a risk factor for severe and more frequent migraine headache attacks. However, the results are conflicting and not all studies have reported the same relations.[9,10] As obesity increases in prevalence, its association with migraine will become clinically important and BMI control may be a preventive approach for migraine.[6] The association between migraine characteristics and body weight is still unclear and requires more evaluations.[2] This study was conducted to evaluate the relationship between BMI and disability, severity, frequency and duration of headaches in female migraine patients.

Materials and Methods

Patients and Setting

This was a cross-sectional study conducted in a tertiary headache clinic of Tehran University of Medical Sciences

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(TUMS), Tehran, Iran. One hundred and seventy consecutive patients with the following inclusion criteria were enrolled in this study; female gender, aged 18 to 50 years, being visited for the first time in a headache clinic and patients who were newly diagnosed for migraine. The diagnosis of migraine was made according to the International Classification of Headache Disorders, third edition, beta version (ICHD-3 beta)[11] published in 2013. The patients' sociodemographic characteristics including age, marital status, education and job were registered. Patients with any known disorders such as hypertension, diabetes, malignancies and other renal, hepatic, pancreatic, cardiovascular and neurovascular diseases were excluded from the study.

Migraine-Related Disability, Headache Frequency, Duration and Severity

Disability due to headache was assessed using the Migraine Disability Assessment (MIDAS) questionnaire. MIDAS questionnaire has been developed in 2001. In Iran, it was validated and translated into Persian in 2014 by Zandifar et al.[12,13] All patients were evaluated for frequency (number of headache attacks in the last month) and duration (the mean duration of each headache attack in the last month). These data were recorded on the patients' diary form that is designed by the senior investigator.[14] In order to assess severity, verbal rating scale (VRS) was used. VRS is scored from zero to 10, with zero denoting no headache and 10 denoting the most severe attack.

Anthropometric Assessment

For all participants, height and weight were measured to calculate the BMI. Weight was recorded in kilograms using a calibrated digital scale. Height was recorded in meters. BMI was calculated as weight (kg) divided by height squared (m^2). Migraineurs were divided into three groups according to their BMI value: 18.5 ≤ BMI < 25 was defined as normal weight, 25 ≤ BMI < 30 as overweight, and 30 ≤ BMI was classified as obese.[4]

Statistical Analysis

We used descriptive statistics to assess frequencies, means, medians and distributions. Before analysis, data were examined for normality using the Kolmogorov-Smirnov test. As the variables were not normally distributed, non-parametric tests were used for the analysis. For quantitative variables, Mann-Whitney and Kruskal-Wallis tests were used for comparison of the means between two and three different groups, respectively. Effect size was assessed and reported based on Cohen's d.[15] Analysis of covariance (ANCOVA) was used to reduce the effect of confounding factors. Data are given as mean ± standard deviation (SD). In addition, medians and 95% confidence intervals (CIs) are reported. The sample size was calculated using the following formula based on the previous studies.[16, 17]

$$n = \frac{(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2(\sigma_1^2 + \sigma_2^2)}{d^2}$$

In order to calculate the sample size, we considered 80% statistical power and 5% probability of type one error (α). The pain frequency variable was selected to calculate the sample size. The mean values in the two groups were determined at 1.03 and 2.36 days with standard deviations of 1.36 and 1.40, respectively. We calculated 30 patients for each group. *P* value of less than 0.05 was considered statistically significant. Data was analyzed using SPSS software version 16 (SPSS Inc., Chicago, IL., USA).

Results

In the current study, 170 female migraineurs with a mean (± SD) age of 34.0 ± 8.0 years (range: 18 to 50 years) were enrolled. Table 1 reports the characteristics of the study participants. The mean (± SD) height, weight and BMI of the enrolled patients were 1.6 ± 0.0 m, 66.3 ± 11.5 kg, and 25.4 ± 4.3 kg/m^2, respectively and the mean (± SD) total MIDAS score was 12.2 ± 6.9. The migraine characteristics of the study sample including duration, severity and frequency of headache attacks are reported in Table 1.

The minimum BMI of the participants was 18.6 kg/m^2. So, we had no underweight participants in this study. The three groups (18.5 ≤ BMI < 25, 25 ≤ BMI < 30 and 30 ≤ BMI) were significantly different in terms of headache frequency, duration and severity as well as total MIDAS score ($P<0.001$) (Table 2). Patients with 18.5 ≤ BM I < 25 had a significantly lower frequency of headaches, duration of attacks, VRS and total MIDAS scores in comparison to migraineurs with 25 ≤ BMI < 30 ($P<0.001$). Patients with 30 ≤ BMI only had significantly higher VRS than those with 25 ≤ BMI < 30 ($P=0.033$). The comparison for frequency and duration of headaches and total MIDAS score between these two groups revealed no significant differences ($P=0.152$, 0.714 and 0.067, respectively). After adjustment for age, the results remained significant. Furthermore, adjustment for age revealed a statistically significant higher total MIDAS score in subjects with 30 ≤ BMI than those with 25 ≤ BMI < 30. After selecting

Table 1. Basic and Clinical Characteristics of the Study Sample

Characteristic	Mean ± SD or No.(%)
Age (years)	34.0 ± 8.0
Marital status (married/single/divorced)	114 (67.1%)/53 (31.2%)/3 (1.8%)
Education (academic /university student/pre-university level)	92 (54.1%)/16 (9.4%)/62 (36.5%)
Job (employed/non-employed)	53 (31.2%)/117 (68.8%)
Frequency of headaches (attack per month)	9.9 ± 8.3
Headache attack duration (hours)	9.2 ± 11.1
VRS	5.8 ± 2.1

VRS, verbal rating scale; MIDAS, Midas Disability Assessment; SD, standard deviation; n, number.

Table 2. Comparison of the Means of Different Migraine Characteristics between Different BMI Groups

Headache Characteristic	BMI			*P* Value[b]	D1 / D1a	D2/ D2a
	G1 (n = 99)	G2 (n = 43)	G3 (n = 28)			
Frequency [a]	[5] 6.2 ± 5.3 (5.2, 7.3)	[14] 13.7 ± 9.1 (10.9, 16.5) [c]	[16.5] 17.0 ± 8.9 (13.6, 20.5)	<0.001[f]	1.1 (0.7, 1.4)/ 1.0 (0.6, 1.4)	0.3 (-0.1, 0.8)/ 0.4 (0.0, 0.9)
Duration (hours)	[4] 7.5 ± 10.0 (5.5, 9.5)	[7] 13.6 ± 15.1 (9.0, 18.3) [c]	[9] 8.6 ± 4.4 (6.9, 10.4)	<0.001[f]	0.5 (0.1, 0.8)/ 0.5 (0.2, 0.9)	-0.4 (-0.8, 0.0)/ -0.4 (-0.9, 0.0)
VRS	[5] 4.8 ± 1.8 (4.4, 5.1)	[7] 6.8 ± 1.9 (6.2, 7.4) [c]	[8] 7.8 ± 1.0 (7.4, 8.2) [d]	<0.001[f]	1.0 (0.6, 1.4)/ 1.15 (0.7, 1.5)	0.6 (0.1, 1.0)/ 0.5 (0.0, 1.0)
MIDAS total score	[8] 8.5 ± 4.4 (7.6, 9.4)	[18] 16.2 ± 6.5 (14.2, 18.2) [c]	[20] 19.0 ± 6.3 (16.5, 21.4) [e]	<0.001[f]	1.5 (1.0, 1.8)/ 1.4 (1.0, 1.8)	0.4 (0.0, 0.9)/ 0.4 (0.0, 0.9)

G1: 18.5≤ BMI < 25; G2: 25 ≤ BMI < 30; G3: 30 ≤ BMI; VRS, verbal rating scale; MIDAS, Midas Disability Assessment; BMI, body mass index (kg/m^2).
D1: effect size (95% confidence interval) based on Cohen's d between G1 and G2; D1a: D1 after adjustment for age, D2: effect size (95% confidence interval) based on Cohen's d between G2 and G3; D2a: D2 after adjustment for age.
[a] Attack per month; [b] Kruskal-Wallis test; [c] $P < 0.05$ for comparison of G1 and G2 (all remained significant after adjustment for age); [d] $P < 0.05$ for comparison of G2 and G3 (remained significant after adjustment for age); [e] $P < 0.05$ for comparison of G2 and G3 after adjustment for age; [f] Remained significant after adjustment for age using analysis of covariance (ANCOVA) test.
Data are given as [Median] Mean ± SD (95% confidence interval).

BMI = 25 as the cutoff point and grouping the patients into BMI ≥ 25 and <25, the mean frequency, duration and severity of headache attacks as well as MIDAS total score were significantly higher in patients with BMI ≥ 25 than those with BMI < 25 ($P < 0.001$ for all comparisons).

Discussion

The aim of the current study was to evaluate the relationship between BMI and disability, severity, frequency and duration of headaches in female migraine patients. Our results revealed that migraineurs with BMI ≥ 25 (overweight and obese patients) experienced significantly higher headache frequency, severity, duration and disability in comparison to those with BMI < 25 with desirable effect size calculation. No significant differences were observed between overweight (25 ≤ BMI < 30) and obese (BMI ≥ 30) female migraineurs in terms of headache frequency and duration. However, obese patients had significantly higher headache severity and disability than the overweight ones.

Previous studies in our country support our data. Results from a study conducted on 129 migraineurs (aged between 15 and 67 years) in Isfahan, Iran showed that higher waist circumference, waist-hip and waist-height ratios were significantly associated with higher severity and frequency but not the duration of migraine headache attacks. These results remained nearly the same when analyzing the data with men and women as separate groups.[18] Another Iranian study on the effect of BMI on migraine treatment revealed that lower BMI is associated with better response to treatment. They analyzed migraine headache frequency, duration and severity during eight weeks of treatment. After this period, the mean frequency, duration and severity of patients with lower BMI were significantly lower than the individuals with higher BMI.[17] Another study by Jahromi et al reported that the decline in fat-free mass in overweight and obese female individuals is related to higher risk of migraine. The alteration in the fat-free mass and its effect on migraine severity is suggested by the authors for further evaluations.[19] Weight reduction was reported in a non-randomized controlled clinical trial to be effective on mitigation of migraine severity and duration. Moreover, controlling the weight and decreasing it was associated with more migraine-free days in the studied sample (obese female migraineurs).[14]

On the other hand, in a cross-sectional study, Téllez-Zenteno et al concluded that there is no association between BMI and the severity of migraine headache attacks or migraine disability (according to MIDAS questionnaire).[4] Another study on pediatric migraineurs showed that BMI was not associated with duration of headaches, severity of attacks and some other symptoms such as nausea, vomiting, photophobia and phonophobia. The only migraine characteristic associated with body weight in their study was frequency of headaches which is similar to our results.[20] In a study on Chinese adults, Yu et al reported no association between obesity and severity, frequency or disability of migraine headaches.[10] In a population-based telephone interview study on 30 215 individuals from the United States, the results revealed that migraine and obesity are not comorbid. However, according to their findings, an association was found between BMI and frequency and also severity of migraine headaches attacks.[8]

Obesity is associated with a higher prevalence of migraine. Several review articles have addressed the issue of relationship between body weight and migraine disorder; however it appears that further studies are needed to evaluate the association between higher BMI and migraine characteristics such as severity, frequency and duration of headache attacks as well as migraine-related disability. Although the association between BMI and migraine characteristics has been evaluated and reported in some reviews, more studies are required and the results are not confirmed by all reports. Table 3 presents the summary of these studies. Obesity is reported, in a meta-analysis

Table 3. Body Mass Index and its Association with Migraine – Summary of Review Articles

Reference	Findings/Summary
Bigal et al[29] (2007)[a]	- Obesity is linked with increasing various markers such as interleukins and calcitonin gene-related peptide that are important in the pathophysiology of migraine. - These factors can increase the frequency, severity and duration of migraine headache attacks.
Giraud et al[7] (2013)[a]	- Migraine prevalence seems to be higher in obese patients - Weight loss is associated with improvement of migraine (limited data). - Obesity can cause progression of migraine to chronic daily headache or chronic migraine.
Ravid[25] (2014)[a]	- There is an association between migraine and obesity in both children and adults. - Obesity is associated with higher frequency of headaches and higher disability scores among migraineurs. - Weight control should be a part of migraine management.
Oakley et al[26] (2014)[a]	- Children with obesity are at increased risk of migraine. - The risk of migraine will increase by increasing status of obesity. - No specific diet is reported for migraine prevention. - Weight loss and physical activity may reduce the frequency and severity of migraine (limited data available).
Verrotti et al[23] (2014)[a]	- Obesity is associated with higher prevalence, frequency and disability of migraine in children and adults. - Lifestyle modification and weight reduction may be included in migraine management
Chai et al[22] (2014)[b]	- Obesity is increasing the risk of migraine (40 – 80%), especially in those in reproductive age. - Obesity is associated with higher risk of both episodic and chronic migraine. - The direction of migraine-obesity relationship cannot be identified by the available data. - Risk of migraine rises with increasing status of body weight (from normal to overweight to obese).
Recober et al[31] (2014)[a]	- The risk of both episodic and chronic migraine is higher in obese patients. - This relationship should be educated to the migraineurs.
Ornello et al[2] (2015)[c]	- Obesity is associated with increased risk of migraine. PAEE=1.14, 95% CI=1.02-1.27, P=0.017 - Obesity is associated with increased risk of chronic migraine. PAEE=1.75, 95% CI=1.33-2.99, P≤0.001
Wang et al[21] (2016)[c]	- Obesity is associated with increased risk of migraine. OR=1.19, 95% CI=1.02-1.38, P=0.029
Laino et al[32] (2016)[a]	- Obesity is associated with headache and disability in adults and children. - Headache pathophysiology and some mechanisms for food assumption are associated.
Cervoni et al[27] (2016)[a]	- Weight loss can be a useful part of migraine management to reduce frequency and severity of headache attacks.
Pavlovic et al[3] (2017)[a]	- The association between migraine and obesity is seen in female patients in reproductive age more than other groups.
Farello et al[24] (2017)[a]	- Obese children with migraine experience higher severity and frequency of migraine headache attacks. - Body weight management can be a preventive and alternative treatment for chronic migraine.

PAEE, pooled adjusted effect estimate; OR, odds ratio; CI, confidence interval.
[a] Review (narrative); [b]Systematic review; [c]Meta-analysis.

by Wang et al, to be associated with increased risk of migraine. The results of that study showed that obese patients had a higher risk of migraine in comparison to both normal weight and non-obese individuals.[21] Another meta-analysis conducted in 2015 by Ornello et al reported similar results. In addition, they reported that the strongest relationship between obesity and migraine prevalence was seen in female patients in reproductive age. The authors mentioned that more studies are needed, especially for evaluating the association of migraine type, frequency, severity, duration and disability of headache attacks with body weight.[2] Results from a systematic review conducted by Chai et al support these findings.[22] According to some available data, obesity is associated with higher migraine prevalence, frequency and disability. In addition, it is worth mentioning that the associations are not supported by all studies and evidences.[23] A review of pediatric migraineurs indicated increased frequency and severity of headache attacks in obese children in comparison with control groups. They reported that these associations were seen in both girls and boys.[24] Similarly, in a review, Ravid mentioned that obesity and migraine are associated (in both children and adults) and obese patients will show more frequency of headache attacks and higher disability scores. As psychiatric problems such as anxiety and depression are more prevalent among sufferers of both disorders (obesity and migraine), these mental conditions can be a reason for the higher frequency of headaches and disability.[25] Further studies have reported that an increase in status of obesity is associated with rising migraine risk in pediatric populations and obesity can cause the progression of migraine to chronic daily headache or chronic migraine.[7,26] According to the current data, weight reduction might be a useful intervention to decrease the frequency and severity of migraine headache attacks. This effect is more remarkable in obese migraineurs.[27] Inflammatory state is mentioned to be related with the pathophysiology of migraine disorder. Although inflammation can be a linking factor between obesity and migraine, this association seems to be more complex than an increase in body fat and rising inflammation. Changes in distribution of fat and also interactions between sexual hormones, peptides and neurotransmitters must be considered.[3,19,28] Several mechanisms appear to be involved

in the association between body weight and migraine. Obesity is linked with increasing various markers such as interleukins and calcitonin gene-related peptide that are important in the pathophysiology of migraine. These factors can increase the frequency, severity and duration of migraine headache attacks.[29,30]

There are several limitations in the current study that should be taken into consideration. First of all, the sample consisted of female migraineurs in reproductive age. In this study, we selected female patients with migraine because they are more prone to this disorder than males. Accordingly, the study lacks further evaluations and comparison between genders. Therefore, further studies including both genders are recommended to increase the generalizability of the findings. Second, other disorders such as anxiety, depression, hypertension and sleep disorders, which are among comorbidities of migraine disorder, seem to have an impact on the results and are recommended for consideration in future studies. Third, this study is not able to define the true direction of causality due to the nature of its design; therefore, reverse causality or even simultaneity are probable. For example, migraineurs with the more severe form of the disease are probable to have a more sedentary lifestyle and accordingly have a higher BMI. Fourth, in addition to the influence of age, this study may have been influenced by uncontrolled confounding factors which highlights the importance of further studies in the future. Finally, considering the study design and the fact remembering previous events may be difficult for the patients, this study might suffer from recall bias and further evaluations are highly recommended.

In conclusion, this study revealed that migraineurs with higher BMI experienced higher headache frequency, severity and duration as well as higher disability score. Although the comparisons of migraine characteristics showed that obese migraineurs were approximately similar to overweight ones, the differences between normal weight and overweight patients were considerable. These findings warrant more studies to evaluate the effect of weight reduction, as a possible intervention, in better management of migraine disorder.

Authors' Contribution

MT and SRJ jointly conceived and designed the study and contributed to the draft. FH, FK, and ZGh involved in data gathering and performed the research. FH drafted the manuscript. All authors critically revised the manuscript for important intellectual contents. MT gave final approval of the version to be published.

Conflict of Interest Disclosures

None.

Ethical Statement

The study protocol was approved by the Iranian Center of Neurological Research, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran (Ethical code: IR.TUMS.NI.REC.1398.010 and Research number: 97-03-54-39314). Before inclusion and interview, the study was described to the patients and informed consent was obtained.

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