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Original Article

The association between obesity and migraine in a population of Iranian adults: a case-control study

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ABSTRACT

Aim: To assess the association between obesity and risk of migraine with aura and features of migraine attacks among a population of Iranian adults.
Methods: In this case-control study, 102 confirmed cases of migraine with aura were matched based on age and gender with 102 healthy subjects. Data on demographic characteristics and anthropometric measurements were collected from all cases and controls by the same methods. Overweight and obesity were considered as body mass index $\geq$25–30 kg/m^2 and $\geq$ 30 kg/m^2, respectively. Features of migraine attacks including frequency, duration and headache daily result were determined for patients based on international headache society criteria.
Results: Mean age of subjects was 34.5 $\pm$ 7.4 years and 77.9% of them were female. Compared with subjects with normal body mass index, those with obesity had greater odds for having migraine with aura (OR: 3.06, 95% CI: 1.11–8.43). Such finding was also seen even after adjusting for confounding variables; in a way that subjects with obesity were 2.92 times more likely for having migraine with aura compared with those with normal weight (OR: 2.92, 95% CI: 1.03-8.33). Among migraine with aura patients, we found that those with obesity had higher headache daily result compared with subjects with normal weight. However, obesity was not associated with frequency and duration of migraine attacks.
Conclusions: We found that obesity was positively associated with risk of migraine with aura. In addition, subjects with obesity had higher headache daily result compared with those with normal weight.

1. Introduction

Migraine is a chronic neurovascular disorder which is mostly prevalent in middle-aged individuals [1,2]. In Islamic Republic of Iran as a developing country, a review of studies between 1998 and 2014 has shown that 7.14%–18.11% of adults experienced migraine headache [3]. A quarter of migraine patients perceive migraine with aura (MA), a transient disturbance in visual, sensory, language, or motor function before attack occurrence [4,5].

It seems that genetic and environmental factors are involved in etiology of migraine. Investigations have indicated that genetic polymorphisms [6], alcohol and coffee consumption [7], low physical activity [8], nutritional deficiencies [9,10], and psychological difficulties[11] affect adversely migraine risk and symptoms. Recently it has been shown that obesity might contribute to risk of migraine [12–15], but findings in this regard are conflicting and some studies have failed to reach any significant associations or have shown an inverse association [16–18]. So, it seems that further studies from different parts of the world are required to shed light on this issue.

Most studies on the association between obesity and risk of migraine carried out in Western countries, whereas the pattern of obesity is markedly different from Middle East countries. In Middle East, a pattern of obesity, named Middle Eastern pattern, is prevalent particularly among women and it is characterized by abdominal fat accumulation and enlarged waist circumference

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(WC) [19]. In addition, there is a dearth of knowledge about the association between obesity and MA, and most previous studies have assessed migraine without aura (MOA) or undermined kinds of migraine [13,17,20]. Given to limited and conflicting evidences, and high prevalence of migraine and obesity in Iranian, current study aimed to assess the association between obesity and risk of MA as well as features of migraine attacks among a population of Iranian adults. We hypothesized that obesity might increase the risk of MA and features of migraine attacks.

2. Material and methods

This case-control study was done, based on SROBE statement, in Isfahan, Islamic Republic of Iran, between January 2014 and July 2016. Patients with MA were selected from Khorshidand and Emam Mosa Sadr clinics of Isfahan University of Medical Sciences, Isfahan, Iran.

The study was ethically approved by Isfahan University of Medical Sciences, Isfahan, Iran, and AJA University of Medical Sciences, Tehran, Iran, and all procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki declaration. Prior to study enrolment, a written informed consent was obtained from all subjects. Patients were included if had: 1) 18–50 years old, 2) history of migraine for ≥5 years, 3) 1-year history of severe, recurrent, and long-lasting migraine attacks (at least one attack per month lasting 4 h), and 4) a current diagnosis of MA approved by an experienced neurologist according to International Headache Society (IHS) (third revision) beta diagnostic criteria [5]. Patients with tension-type headache and MOA were excluded. Healthy subjects living in the same area compared with MA patients were selected as control group. They were between 18–50 years old and with no history of migraine headache. Both cases and controls were selected by the convenience non-random sampling method. Totally, 102 MA patients and 102 healthy subjects participated in this study. Cases and controls were matched in terms of age and gender. We gathered complete data about demographic characteristics and anthropometric measurements for all cases and controls using the same methods.

Features of migraine attacks including attacks frequency, duration and headache daily result (HDR) were determined by an experienced neurologist. Attacks frequency was considered as the number of migraine attacks during a month. Attacks duration was defined as mean of hours that attacks last. We also determined the mean duration of migraine attacks per day, named HDR, using the following formula: frequency of attacks × duration of headache [21,22].

A questionnaire was used to collect data on age (year), gender, weight (Kg) and height (cm). Weight was measured by a digital scale with minimum clothing and without shoes with a precision of 100 g. In addition, height was measured in a standing position without shoes by a tape measure with the nearest 0.5 cm. To calculate body mass index (BMI) in both case and control groups, we used following formula: weight (Kg)/height (meter square). We classified total subjects into three categories based on their BMI as follows: normal (BMI < 25), overweight (BMI ≥ 25–30), and obese (BMI ≥ 30).

All statistical analyses were done using SPSS software version 19.0 (SPSS Inc, Chicago IL). Independent sample *t*-test was used to examine significant differences in continuous variables between cases and controls. To examine significant differences in continuous variables across categories of BMI, we applied one-way analysis of variance (ANOVA). In addition, to examine the distribution of categorical variables across categories of BMI or between cases and controls, we used Chi-square test. The association between obesity and risk of migraine was assessed using binary logistic regression in crude and two adjusted models. Gender was adjusted as continuous variable in the first model. Age was additionally adjusted in the second model. In these analyses, normal category based on BMI (< 25) was considered as the reference category. The overall trend of OR across increasing categories of BMI was examined by considering these categories as a continuous variable. P values were considered significant at < 0.05.

3. Results

Mean age of subjects was 34.5 ± 7.4 years and 77.9% of them were female. Overall, the prevalence of overweight and obesity among study population were 43.6% and 11.8%, respectively.

General characteristics of subjects based on case and control groups are shown in Table 1. Patients with MA had lower height, and were more likely to be obese compared with healthy subjects. No significant difference was found in terms of age, gender and BMI between MA patients and healthy subjects. The mean frequency and duration of migraine attacks among MA patients was 10.2 ± 9.2 and 20 ± 17.3, respectively.

General characteristics of subjects across categories of BMI are presented in Table 2. Compared with subjects with normal BMI, those with obesity were older with greater weight and lower height. In MA patients, HDR was significantly different across categories of BMI. However, no significant difference was found in terms of attacks frequency and duration.

Adjusted odds ratios and 95% confidence intervals for MA across categories of BMI are indicated in Table 3. Compared with subjects with normal BMI, those with obesity had greater odds for having MA (OR: 3.06, 95% CI: 1.11-8.43). Such finding was also seen even after adjusting for confounding variables; in a way that subjects with obesity were 2.92 times more likely for having MA compared with those with normal weight (OR: 2.92, 95% CI: 1.03-8.33). However, such findings were not observed for subjects with overweight (OR: 0.76, 95% CI: 0.42-1.40).

4. Discussion

Migraine is known as the 19 th cause of disability around the world [23]. It has been shown that patients with migraine, especially MA, have increased odds of cardiovascular diseases (CVDs) and stroke [24,25]. Given that obesity is a main risk factor for incidence of CVDs and stroke [26,27], it might be a reason for the association between migraine and mentioned diseases. However, data on the association between obesity and migraine are conflicting.

Table 1
General characteristics of subjects in case and control groups.

Variables	Case group (n = 102)	Control group (n = 102)	P-value*
Age (year)	34.9 ± 8.4	34.1 ± 6.3	0.43
Gender (female) (%)	78.4	77.5	0.86
Weight (Kg)	68.1 ± 12.2	69.3 ± 10.6	0.46
Height (cm)	162.2 ± 9.2	165.6 ± 8.6	0.007
BMI (Kg/m^2)	25.9 ± 4.6	25.2 ± 3.1	0.18
Obesity (%)	17.6	5.9	0.02
Attacks frequency (per month)	10.2 ± 9.2	–	
Attacks duration (hour)	20 ± 17.3	–	
HDR[a]	163.3 ± 175.4	–	

Data are presented as mean ± standard deviation or percent.
Abbreviation: BMIbody mass index, HDR headache daily result.
[a] Determined as attacks frequency × attacks duration.
* Obtained from independent sample t-test or Chi-square test, where appropriate.

Table 2
General characteristics of subjects based on categories of BMI.

Variables	Normal (BMI < 25)	Overweight (BMI ≥ 25–30)	Obesity (BMI ≥ 30)	P-value*
Total (Case and control)				
Number	91	89	24	
Age (year)	32.4 ± 6.9	35.7 ± 7	37.7 ± 8.8	0.001
Gender (female) (%)	75.8	75.3	95.8	0.07
Weight (Kg)	60.9 ± 8.2	72.9 ± 9.2	82.4 ± 8	<0.001
Height (cm)	165.2 ± 8.8	164 ± 9.2	158.5 ± 8.3	0.006
BMI (Kg/m^2)	22.2 ± 2	27 ± 1.3	32.8 ± 2.9	<0.001
MA patients (Case)				
Number	43	38	15	
Attacks frequency (per month)	8.1 ± 6.9	11.6 ± 10.1	12.6 ± 11.5	0.1
Attacks duration (hour)	18.7 ± 17.4	19.8 ± 16.7	24.2 ± 19.2	0.5
HDR[a]	114.9 ± 104.3	208.5 ± 214	187.4 ± 204.6	0.04

Data are presented as mean ± standard deviation or percent.
Abbreviation: MA: migraine with aura, BMI: body mass index, HDR: headache daily result.
[a] Determined as attacks frequency × attacks duration.
* Obtained from one-way ANOVA or Chi-square test, where appropriate.

Table 3
Odds ratios and 95% confidence intervals for MA across categories of BMI.

Variables	Normal (BMI < 25)	Overweight (BMI ≥ 25–30)	Obesity (BMI ≥ 30)	P-trend
Total number	91	89	24	
Number of cases	43	38	15	
Crude	1	0.79 (0.44-1.43)	3.06 (1.11-8.43)	0.17
Model 1	1	0.79 (0.44-1.43)	3.12 (1.12-8.65)	0.18
Model 2	1	0.76 (0.42-1.40)	2.92 (1.03-8.33)	0.25

Data are presented as OR and 95% CI.
Abbreviation: MA: migraine with aura, BMI: body mass index.
Model 1: adjusted for gender.
Model 2: further adjustment for age.

In the current study, obesity was positively associated with risk of MA. Such finding was also seen even after adjustment for age and gender; in a way that subjects with obesity were 2.92 times more likely for having MA compared with those with normal weight. To the best of our knowledge, present study is the first case-control study in the Middle East to examine the association between obesity and risk of MA. In line with our findings, Yu et al., in general population of Chinese cohort reported that incidence of migraine in people with general obesity (BMI ≥ 30) was higher than those with normal weight [12]. In a national sample of US adults, Ford et al., indicated that BMI was associated with the prevalence of severe headaches or migraines in a non-linear manner [15]. In another general population survey, Peterlin et al., reported a significant positive association between general obesity and migraine among people less than 55 years but no in those over 55 years [17]. In contrast, Mattsson et al., showed that the prevalence of general obesity was not different between women with and without migraine [18]. Although it seems that results of mentioned study were in opposite to our findings, but it was done on females and we assessed the association between obesity and migraine in both genders. In addition, conflicting results in previous studies could be attributed to different methods used for diagnosis of migraine. In some studies, migraine was assessed by a self-reported questionnaire, while in this study it was diagnosed by an experienced neurologist based on IHS criteria. Furthermore, MOA or non-determined kind of migraine was assessed in relation to obesity in earlier studies, while we considered just MA.

In the current study, HDR was significantly higher in MA patients with overweight or obesity than those with normal weight. However, we did not find such association for frequency and duration of migraine attacks. To the best of our knowledge, no study was found to assess the association between obesity and HDR. However, in previous studies on the current MA patients [28,29], results of linear regression for the association of BMI and WC with mentioned features showed a significant positive association of BMI and WC with frequency and duration of migraine attacks. When potential confounding variables were taken into account, such findings were also seen. However, no significant association was found between BMI, WC and duration of migraine attacks.

The mechanisms that might be responsible for the relationship between obesity and migraine are still unknown. This relationship might be explained by the effects of obesity-related inflammation [30,31]. Earlier studies have shown that individuals with obesity have increased level of inflammatory cytokines [31]. Also, it has been shown that inflammation is involved in development and progression of migraine [32,33]. In addition, hypertension contributes to incidence of migraine, and obesity is considered as one of the most important risk factor for hypertension [34,35]. Furthermore, obesity is known as a pro-thrombotic state that associated with increased risk of migraine [14,36].

Some limitations should be taken into account when interpreting present findings. Based on case-control design of the study, we cannot confer a causal link between obesity and migraine. Therefore, prospective studies are required to confirm these findings. In addition, studies with case-control design are highly susceptible to several biases including selection. Total number of subjects in current study was relatively low, which might decrease statistical power. Finally, despite adjustment of age and gender, further control for other residual confounders including physical activity, health status and psychological factors are required for obtaining independent association between obesity and MA.

5. Conclusions

We found that obesity was positively associated with risk of migraine with aura. In addition, subjects with obesity had higher headache daily result compared with those with normal weight.

Authorship

OS contributed in design, concept, data collection, analysis, and interpretation and draft extration. AM and MN analysed and interpreted data and drafted the manuscript. GA and ADM assisted

in design, concept, interpretation of data and critical review of the draft. SZ, FY and MA analysed and interpreted data and edited the final draft. All authors were approved the final version submitted for publication.

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Conflicts of interest

Authors declared no personal or financial conflicts of interest.

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