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Original Article

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Assessment of Metabolic Syndrome in Patients with Migraine in Central Anatolia

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ABSTRACT

Evidence suggests that migraine is associated with metabolic syndrome (MetS). We aimed to assess the components of MetS in patients with migraine in Yozgat region known as central Anatolia. Forty-two migraine patients and age- and sex-matched 40 control subjects were enrolled in the study. Migraine diagnosis was settled according to the International Classification of Headache Disorders-II diagnostic criteria. The patients' blood pressures and waist circumferences (WC) were measured. Body mass index (BMI) was calculated as well as fasting glucose (FG) and lipid profiles were carried out for each patient. BMI, WC and blood pressure measurements were significantly higher in migraine patients than in controls ($p < 0.05$). FG and Triglycerides were significantly higher in migraineurs as compared to the controls ($p < 0.001$). The diagnosis of MetS was significantly higher in patients with migraine than in controls ($p = 0.001$). Attack frequency was significantly lower in migraineurs with MetS than without MetS ($p < 0.05$). Attack severity and duration were positively correlated with BMI and WC in migraine patients ($p < 0.05$). The present findings may suggest that MetS and its components were associated with migraine.

Key words: *Migraine, metabolic syndrome, body mass index*

İç Anadolu Bölgesindeki Migrenli Hastalarda Metabolik Sendromun Değerlendirilmesi

ÖZET

Migrenin metabolik sendromla (MetS) ilişkili olduğuna dair kanıtlar vardır. Biz, İç Anadolu'da Yozgat Bölgesindeki migrenli hastalarda MetS'un komponentlerini araştırmayı amamçladık. Bu çalışmaya, 42 migren hastası ve yaş ve cinsiyet uyumlu 40 sağlıklı gönüllü alındı. Migren tanısı Uluslararası Başağrısı Hastalıkları Sınflaması-II tanı kriterlerine göre konuldu. Hastaların kan basınçları ve bel çevreleri (BÇ) ölçüldü. Vücut kitle indeksi (VKİ) hesaplandı, açlık glikozu (AG) ve lipid paneli her hasta için çalışıldı. VKİ, BÇ ve kan basıncı ölçümleri, kontrollere göre migren hastalarında anlamlı yüksek saptandı ($p < 0.05$). AG ve trigliseridler, kontrollerle karşılaştırıldığında migrenlilerde anlamlı yüksek bulundu. ($p < 0.001$). MetS tanısı, kontrollere göre migren hastalarında anlamlı yüksek görüldü. ($p = 0.001$). Atak sıklığı, MetS'u olan migrenlilerde olmayanlara göre anlamlı düşük saptandı. ($p < 0.05$). Atak şiddeti ve süresi, migren hastalarında VKİ ve BÇ ile pozitif koreleydi ($p < 0.05$). Bu sonuçlara göre, MetS ve komponentlerinin migren ile ilişkili olduğu düşünülebilir.

Anahtar kelimeler: *Migren, metabolik sendrom, vücut kitle indeksi*

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INTRODUCTION

Migraine is a chronic disorder with complex pathophysiology involving neuronal and vascular mechanisms. An association between migraine, especially with aura, and vascular disorders such as coronary heart disease and stroke has been reported in previous studies (1). Obesity and diabetes are metabolic disorders which also have a complex association with migraine (2,3). Metabolic syndrome (MetS) is a multifaced clinical entity in which genetic, hormonal, and environmental factors are involved. Interactions between components of faulty life style such as consumption of excessive sugar and high calorie diet and inadequate exercise are important in MetS (4). The relationship between migraine and MetS is still obscure. Several studies suggest that obesity and migraine may be directly linked (3-5). Other studies failed to find any association between migraine and obesity (6,7). In the present study, we aimed to assess the components of MetS in patients with migraine in Yozgat region known as central Anatolia.

MATERIALS AND METHODS

Study population

Forty-two newly diagnosed migraine patients and age- and sex-matched 40 control subjects of Caucasian origin ranging 18 to 50 years were enrolled in this cross-sectional prospective study conducted in Yozgat region known as central Anatolia. Migraine diagnosis was settled in Neurology Department, according to the International Classificağtion of Headache Disorders-II diagnostic criteria (8). Twenty-four patients had migraine with aura, while the rest had migraine without aura. The control subjects were enrolled from Gastroenterology Department with dyspeptic complaints and no headache of any kind. The study protocol was approved by the Bozok University Local Research Ethics Committee and written informed consent was obtained from all patients. Patients with malignancy, hepatic, renal or heart failure, diabetes mellitus, hyperlipidemia, hypertension, thyroid disease, anemia, pregnancy, morbid obesity, smoking habit and alcohol use were excluded from the study. The patient's medical history, physical and neurological examinations were performed by the same neurologist. Migraine patients were evaluated according to the headache characteristics including aura, severity, frequency and duration of the migraine attack and the duration of the disease. Based on visual analog scale, the headache was defined as mild (score 1-3), moderate (4-6), severe (score 7-8) or very severe (score 9-10) (9). Migraine headache attack frequency was noted as the number of attacks per month (10). Duration of the headache attack was defined as hours whereas disease duration as the year. All patients were studied during the headache-free period. These subjects were not on any medication. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were obtained from two independent measurements. Waist circumference (WC) were measured for each patient. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (11). MetS was diagnosed according to Adult Treatment Panel III criteria (12). MetS requires at least three of the following five characteristics: trunk obesity as measured by a WC greater than 102 cm for men and 88 cm for women; fasting glucose (FG) greater than or equal to 110 mg/dL; triglycerides (TG) greater than or equal to 150 mg/dL; high-density lipoprotein (HDL) cholesterol less than 40 mg/dL for men and 50 mg/dL for women; and blood pressure greater than or equal to 130/85 mm Hg. Using standard laboratory methods, baseline venous blood samples were obtained from the antecubital vein after an overnight fast for measurements of FG (the averages of repeated measurements), total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, HDL cholesterol, TG, creatinine, transaminases, thyroid stimulating hormone and complete blood count which were rou¬tinely performed for each patient.

Statistical analysis

Histogram and q-q plots were examined and Shapiro-Wilk's test was performed to assess the data normality. Levene test was used for to assess the variance homogeneity. Independent samples t test, Mann-Whitney U test, Kruskal-Wallis H tests were used to compare the differences between continuous variables and Chi-square analysis between categorical variables. Pearson correlation was used to examine the relationship between laboratory data, metabolic components and headache characteristics. Values are expressed as frequencies and percentages, mean and standard deviation or median and interquartile ranges. Analysis was conducted using R 3.0.0 software with considering a $p < 0.05$ statistically significant.

Table 1. Demographic and laboratory data of migraine patients and controls

Variables	Control (n:40)	Migraine (n:42)	p value
Age (years)	32(29-38)	35(28-41) 0.311	
Gender (female/male)	37(92.5)/3(7.5)	39(92.9)/3(7.1)	0.951
BMI (kg/m2) (female/male)	25.4(21.9-26.7)/25.6(21.9-*)	30.9(27-35.5)/25.6(23.4-*)	<0.001
WC (cm) (female/male)	80(72-85)/80(69-*)	90(85-106)/92(90-*)	<0.001
SBP (mmHg)	110(100-120)	120(110-120)	0.008
DBP (mmHg)	70(62-80)	80(70-80)	0.015
FG (mg/dL)	85.5(83.2-88.5)	97(87-102)	<0.001
Creatinine (mg/dL)	0.6(0.6-0.7)	0.6(0.6-0.7)	0.981
WBC (103/mm3)	7.42±1.48	6.78±1.62	0.070
Hemoglobin (mg/dL)	13.9±1.55	13.1±1.49	0.008
Platelet (103/mm3)	264.05±65.79	276.93±68.59	0.389
AST (IU/L)	17(15-19)	17(15-20)	0.560
ALT (IU/L)	15(11-18)	14(12-19)	0.889
TC (mg/dL)	185.3±35.95	194.07±34.81	0.265
TG (mg/dL)	91(76-134.2)	140(102.7-176.2)	<0.001
HDL-C (mg/dL) (female/male)	41(40-48)/50(34-*)	43(41-50)/39(30-*)	0.659
LDL-C (mg/dL)	121.5(92.2-126.7)	126(96.7-137.5)	0.244
TSH (uIU/mL)	1.7(1-2.4)	1.6(0.9-2.3)	0.770
MetS	2(5%)	14(33%)	0.001

*Values are expressed as n(%), mean±SD or median(25th-75th percentiles). *75th percentiles of BMI, WC, and HDL-C are undefined. BMI indicates body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose; WBC, white blood cells; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TSH, thyroid stimulating hormone; MetS, metabolic syndrome.*

RESULTS

The demographic and laboratory data of the migraine and control patients were summarized in Table 1. No significant difference was found between the groups with respect to age or gender (p>0.05). The measurements of BMI, WC, SBP, DBP were significantly higher in migraine patients than in controls (p<0.05). BMI values were 30.9 and 25.6 in females and males in migraineurs; while those were 25.4 and 25.6 in females and males in controls, respectively (p<0.001). WC values were 90 and 92 in females and males in migraineurs, respectively; while those were 80 in both females and males in controls (p<0.001). The laboratory results revealed that FG (p<0.001) was found to increase stastistically while hemoglobin (p<0.05) was to decrease in migraineurs as compared to the controls (p>0.05). Regarding lipid profile, TG was only to be significantly higher in migraine patients than in controls (p<0.001). Also, HDL values were 43 and 39 in females and males in migraineurs; while those were 41 and 50 in females and males in controls, respectively (p>0.05). The presence of MetS was significantly higher in migraineurs as compared to the control group (p=0.001). Clinical features and laboratory parameters did not significantly differ between the migraine patients with and without aura (p>0.05). Regarding headache characteristics, attack frequency was significantly lower in migraineurs with MetS than in those without MetS (p<0.05; Table 2). Based on correlation analysis, attack severity and duration were positively correlated with BMI (r=0.462, p=0.002 and r =0.348 p=0.024; respectively) and WC (r=0.310, p=0.046 and r=0.350, p=0.023; respectively) in migraine patients.

DISCUSSION

The salient findings of our study were as follows: (i) BMI, WC, SBP, DBP were significantly higher in patients with migraine than in controls; (ii) FG and TG were significant-

Table 2. Comparison between headache characteristics and metabolic syndrome (MetS) in migraine patients (n=42)

Variables	Without MetS (n:28)	With MetS (n:14)	p value
Disease duration	8.00(5.00-10.00)	10.50(5.75-20.00)	0.223
Attack severity	8.00(7.00-8.75)	8.00(7.75-9.00)	0.290
Attack frequency	7.00(4.25-8.00)	4.00(3.00-5.75)	0.042
Attack duration	48.00(30.00-72.00)	48.00(48.00-72.00)	0.492

Values are expressed as median(25th-75th percentiles).

ly higher in migraine patients as compared to the controls; (iii) the diagnosis of MetS was significantly higher in migraineurs than in controls; (iv) attack frequency was significantly lower in migraineurs with MetS than without MetS; (v) attack severity and duration were positively correlated with BMI and WC in migraineurs.

The association between migraine and ischemic vascular events has been studied for many years. Migraine, specifically migraine with aura, is an established risk factor for vascular disorders such as coronary heart disease and stroke in epidemiological studies (1). This relation is explained through its effect on small vessel arteriolar intimae thickening because of recurrent vasospasm or other migraine-related mechanisms, suggesting that migraine is related to atherosclerosis overall (1). Accordingly, MetS is also thought to be involved in the migraine pathogenesis. In recent years, association between MetS and migraine has attracted much attention (2,3). The interaction between obesity and migraine is particularly complex and has been the subject of multiple large and conflicting studies. Several studies suggest that obesity and migraine may be directly linked (3-5). Other studies failed to find any association between migraine and obesity (6,7). Bigal et al. reported that obesity was not associated with migraine prevalence (13) but may be a risk factor for the transformation of episodic migraine to chronic migraine (14) in his population-based studies.

In the present study, it is remarkable that 33 % of the migraine patients had MetS however with no difference in whom with aura as compared to without aura. In parallel, we found BMI and WC values higher in patients with migraine. Bigal et al. studied 30,215 subjects, 3,791 of whom reported migraine symptoms. He found that elevated BMI was associated with increasing headache frequency, severity, and disability (13). Winter et al. also confirmed this finding in his cross-sectional study (15). In accordance with previous data, we demonstrated that elevated BMI and WC values were positively correlated with higher attack severity and duration despite the lack of disparity between with and without aura in migraine patients. However, there are some contrary reports revealing no association between increasing weight and migraine-related features in the literature (7,16). It is well known that increase in the WC is one of the indicators of obesity and also one of the diagnostic markers of MetS. In this perspective, weight loss, an important factor for the reduction of the cardiovascular risk in MetS, might be recommended also for the reduction of headache disability in migraineurs (17). The proposed mechanism might be that exercise increases endorphin levels and pain tolerance and in rats decreases opioid usage (18) and increases insulin sensitivity (19). It is yet unclear if migraine, or its treatment, is a cause of obesity, or if obesity causes increased migraine frequency. On the other, Scher et al reported that migraine patients were more likely to have increased blood pressure (SBP > 140 mmHg or DBP > 90 mmHg (OR = 1.76; 1.04–3.0)) and increased Framingham risk scores which was approximately doubled for those with aura when compared to the controls (1). Similarly, we found SBP and DBP measurements higher in patients with migraine but no relation was obtained with headache characteristics. In a published study by Guldiken et al. diabetes was more frequent in patients with migraine than without migraine (3). In agreement with this, we found that migraineurs were more prone to have greater FG value which was an another diagnostic markers of MetS. In addition to these, Scher et al showed that migraineurs, particularly with aura were more likely to have an unfavorable cholesterol profile (1). Low HDL is an important component of MetS and HDL has anti-inflammatory property that may diminish the perception of pain (20). In our study, we found TG levels obviously higher in migraine patients than in controls. However, no significance was observed for HDL and LDL values.

MetS and migraine both were more common in females than males as in our study. Whether it is merely an association or it has a biological basis needs further study (21). Nevertheless, studies investigating the causal relationship between obesity and migraine demonstrated that several inflammatory mediators could induce migraine. Peterlin et al showed that adinopectin, which is nociceptive at low levels, is decreased in obesity and has an impact on the severity of migraine headaches (22). As a matter of fact, both disorders are proinflammatory states (23). Migraine is defined as a 'neurogenic inflammation' and the source of pain in migraine may involve neurogenic plasma extravasation and consequent vascular meningeal inflammation (24). Many inflammatory promoters such as vasoactive intestinal polypeptide, calcitonin gene-related peptide are altered in migraineurs (25). Similarly; in obese subjects adipocytes can secrete a variety of inflammatory cytokines, including interleukin-6 and tumor necrosis factor-alpha, and promotes low-grade inflammation of the vascular system (23). These cytokines interfere in migraine pathogenesis and their levels are found to be elevated at the onset of migraine attacks

in some studies (25). Therefore, migraine and obesity independently give rise to an altered inflammatory and immunemarker milieu which may induce central sensitization leading to the development of chronic migraine. The present study has several limitations. First; sample size is small, and it is cross-sectional, therefore the causal relation is unclear. Second; we lack data on insülin and/or leptin levels in order to elucidate the mechanistic pathways leading to the MetS in migraineurs. Third; the majority of the patients is female and this may limit the applicability of the results to younger men. Fourth; it will be most interesting to see if weight loss is associated with improvements in attack disability in migraineurs.

In conclusions, the literature is conflicting regarding the relation between migraine and MetS components. We investigated this issue in central Anatolia region. The present findings may suggest that MetS and its components were associated with migraine. Further research is required to confirm our results as well as to assess its role in the migraine management.

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