Current Journal of Neurology

Original Paper

The prevalence of metabolic syndrome parameters and their association with headache characteristics among migraineurs

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Abstract

Background: Migraine is associated with metabolic syndrome (MetS). There are evidences that components of MetS are more prevalent among migraine patients than non-migraineurs. Since both migraine and MetS are associated with a high risk of cardiovascular events, it is likely that the parameters of MetS increase the occurrence of cardiovascular disease (CVD) in migraineurs. The present research project was conducted for the purpose of investigating the relationship between MetS parameters and different items of migraine headaches.

Methods: This descriptive-analytical, cross-sectional study was performed on 240 migraineurs [according to International Headache Society (HIS) II criteria] within the 17+ age range. The participants were selected via consecutive and convenience sampling method. The evaluated parameters for each subject included 2 arms: migraine characteristics (intensity, frequency of attacks, subtype, duration, and treatment regimen) and indices of MetS according to the National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP-III) report criteria [high-density lipoprotein-cholesterol (HDL-C), triglyceride (TG), fasting plasma glucose (FPG), height, waist circumference (WC), systolic and diastolic blood pressure (BP), and body mass index (BMI)]. All data were analyzed in SPSS software.

Results: Total prevalence of MetS was 16.25% (39 patients). There was a statistically meaningful relationship between hypertriglyceridemia and gender (P = 0.021), hypertriglyceridemia and prophylactic antimigraine regimen (P = 0.022), hyperglycemia and age group (P = 0.010), hyperglycemia and the intensity of headache (P = 0.048), hyperglycemia and prophylactic treatment (P = 0.001), systolic

How to cite this article: Maghbooli M, Jameshorani M, Afshar S, Kamali K. The prevalence of metabolic syndrome parameters and their association with headache characteristics among migraineurs. Curr J Neurol 2021; 20(4): 190-201.

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hypertension and migraine subtype (P = 0.004), systolic hypertension and the duration of migraine disease (P = 0.005), diastolic hypertension and migraine subtype (P = 0.002), WC and gender (P = 0.001), WC and the intensity of headache (P = 0.028), WC and prophylactic medication (P = 0.017), HDL and gender (P = 0.001), HDL and the prophylactic regimen (P = 0.023), and MetS and gender (P = 0.005). The prevalence of MetS was increased with increase in the severity of migraine headache.

Conclusion: Due to the relative increase in the prevalence of MetS in patients with more severe migraine, an evaluation of the mechanisms of MetS is recommended in this population.

Introduction

As a headache, migraine has a complex pathophysiology in which vascular and neural mechanisms are involved.[1] Migraine requires greater attention because it can cause personal and occupational disability and dysfunction, thereby reducing the quality of life (QOL) and undermining personal health.[2] The overall prevalence of migraine worldwide is assessed to be 8-19%.[3] However, it has been reported to be 12-22.1% in some countries.[4]

The prevalence of this severe headache among men, women, and children and adolescents is 3%-7%, 6%-22%, and 8%-28%, respectively.[5,6] Furthermore, its prevalence is 8.4%-12.7% among the general population in Asia,[7] 11.0% among adults in Western countries, and 6.1%-12.3% among Iranian children.[8] Migraine and obesity are 2 major public-health issues among children and adults.[9] According to a classification by the World Health Organization (WHO), migraine is considered to be among the 20 primary disabling conditions in the world.[10] Annual healthcare costs of migraine are estimated at $11 billion.[11]

Metabolic syndrome (MetS) is a combination of metabolic disorders, which are regarded as multiple metabolic risk factors for cardiovascular disease (CVD) or diabetes mellitus (DM) type 2.[2] MetS is also a serious health issue.[12] The overall prevalence of MetS in Iran has been reported as 25% based on the Adult Treatment Panel III (ATP-III) criteria, and 30% according to the International Diabetes Federation (IDF); in addition, the prevalence of MetS sections including high triglyceride (TG), low high-density lipoprotein-cholesterol (HDL-C), high blood pressure (BP), and high fasting blood sugar (FBS) has been reported as 43%, 54%, 38%, and 22%, respectively, among the adult Iranian population.[13] The prevalence of

MetS has been reported to be 12.8%-41.1% in different parts of the world, 21.9%-31.1% in Iran,[14] and 23.7% in the urban population of Zanjan (23.1% among men and 24.4% among women).[15]

Migraine is associated with MetS.[1] This association is stronger in young people.[16] Some studies have only shown an association between migraine and MetS in women with a past history of migraine.[17] It is likely that components of MetS are more prevalent among migraine patients than non-migraine patients.[18] Moreover, the prevalence of migraine is higher among patients with MetS than the general population.[11] It has been shown that common risk factors in the classification of MetS could be the primary mechanism for the association between migraine and cardiovascular events; however, this statement is cautiously made with regard to the elderly.

The high prevalence of migraine among women with morbid obesity and the effect of obesity on the progression of an episodic headache to a chronic headache indicate that the same factors could affect the pathogenesis of migraine and metabolic disorders.[19] The intensity and frequency of headache episodes are higher among migraineurs with a high body mass index (BMI); in addition, there is a relationship between daily migraine and obesity.[20]

The prevalence of migraine among men and women suffering from MetS is 11.9% and 22.5%, respectively.[3] On the one hand, migraine, obesity, and CVD are prevalent in the general population; on the other hand, MetS is also very prevalent.[21,22] MetS is accompanied by a high risk of a stroke, CVD, and DM type 2.[12,23] Moreover, migraine and obesity are risk factors for CVD.[24] Incidentally, migraine with aura is very prevalent, entails a high risk of a stroke and CVD, and doubles the risk of having an ischemic stroke, which is more common among women under 45 years of age.[10,25] In fact, migraine is accompanied by countless central and peripheral disorders such as ischemic stroke, obesity, and MetS.[21]

According to previous research studies, the concurrence of migraine and hypertension is noteworthy and the medical history of patients suffering from this concurrence shows more cerebrovascular accidents, as compared with the history of patients with only hypertension.[26] Hypertension is associated with chronic migraine and may trigger it.[27] In contrast to patients with a tension-type headache or without a headache, the prevalence of hypertriglyceridemia in migraineurs is higher.[12] A low prevalence of DM is observed

among elderly migraineurs while a high or similar to elderly prevalence of DM is observed among young migraine patients. The effect of age on abdominal obesity is also noted so that the prevalence of abdominal obesity is higher among young migraineurs than elderly migraineurs. Hence, migraine has a relationship with the prevalence of MetS among young people at lower risk of CVD.[16] Common risk factors of CVD could be one of the mechanisms involved in the association between migraine with aura and CVD.[10] Since the prevalence of MetS is higher among patients suffering from migraine with and without aura and among patients with non-migraine headaches compared to the general population, common risk factors in classifying MetS could possibly be the primary mechanisms for the relationship between migraine and cardiovascular events.[16]

The present research project was carried out with the aim of exploring the relationship between MetS parameters and different signs of migraine headaches so as to be an introduction to future studies on the role of MetS and each of its parameters in managing migraine treatment and preventing its vascular complications.

Materials and Methods

The present cross-sectional study was conducted on 240 migraineurs who were within the 17+ age range and had received the Vali-e-Asr Hospital neurology outpatient services in Zanjan, Iran. The participants were selected using consecutive and convenience sampling procedures. They were diagnosed with migraine by an expert neurologist based on the International Classification of Headache Disorders (ICHD-3 beta-2013) criteria. Any underlying diagnoses that caused headache-related disease and the comorbidity of migraine and musculoskeletal disorders (MSDs) were excluded from the study. To measure headache characteristics, the severity of headaches were determined on a scale of 0-10, and the mean number of attacks per month (within the last year) and mean attack duration (in minutes) were noted.

Enrollment was conducted between October 2016 and May 2017. The sample size was calculated using OpenEpi software considering type one statistical error of 0.05, prevalence of MetS of 0.32, and confidence limit for prevalence of 0.06. The final sample size was 240 patients.

The study applicants completed a headache questionnaire and were interviewed by an expert neurologist. The participants' age, history of smoking, and alcohol use were recorded based on their own reports. The intensity of migraine headache attacks was assessed according to the visual analog scale (VAS); the 3-grade VAS was chosen to categorize pain intensity (1-3: mild pain, 4-6: moderate pain, and > 6: severe pain). The frequency of attacks was determined according to the incidence rate of headaches per month. Headache features, attendance of aura, severity of headache, location, time, and migraine history of the family were also noted. Medication treatment (anti-hypertensive drugs, anti-diabetic drugs, and oral contraceptives) was documented. Furthermore, the subjects' BP values were measured using a standard sphygmomanometer. The patients' height, BMI (kg/m^2), and waist circumference (WC) were measured using a tape measure and recorded.

MetS was diagnosed based on the National Cholesterol Education Program (NCEP ATP III) by the expert internist at Vali-e-Asr Hospital in Zanjan. The MetS criteria included WC ≥ 94 cm in men, and ≥ 80 cm in women plus any 2 of the following 4 factors: fasting plasma glucose (FPG) ≥ 100 mg/dl or undergoing treatment for type 2 DM, elevated BP (systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg).

MetS parameters were measured using an auto-analyzer (automatic analyzer) in the laboratory of Vali-e-Asr Hospital. The parameters included HDL-C, TG, low-density lipoprotein (LDL), levels of FPG), and glycated hemoglobin (HbA1c).

Exclusion and inclusion criteria: Patients between the ages of 18 and 65 years were entered into the study. Patients who suffered from drug-induced MetS, used immunosuppressive drugs, antiepileptic drugs, suffered from possible medication overuse headache, or used antipsychotic medications or oral contraceptives were excluded. In addition, patients who had undergone cardiac, bariatric, or any other surgery to the abdominal area were excluded.

The SPSS software (version 16, SPSS Inc., Chicago, IL, USA) was used to analyze the collected data. Descriptive results are reported as number, percent, mean and standard deviation. The frequency of MetS and its parameters (BMI, WC, systolic and diastolic BP, TG, HDL-C, and FPG) was determined in connection with migraine characteristics including gender, age, migraine subtype, migraine duration, treatment technique, frequency of attacks, and intensity of attacks. Chi-square and Fischer's exact tests were used to

compare the results. P-values of less than 0.05 were considered as statistically significant.

The researchers of the current study adhered to all ethical considerations in the Helsinki Declaration and necessary principles of research ethics, and all of the participants signed informed consent forms. This study was approved by the Committee of Research Ethics at Zanjan University of Medical Sciences (IR.ZUMS.REC.1395.90). No patient suffered any harm in this study. The collected data remained nameless and confidential. All the participants had submitted written informed consent forms.

Results

In the present study, 70 men (2.29%) and 170 women (8.70%) suffering from migraine participated. The number of those who had MetS was 39 (16.25%)-4 men (7.50%) and 35 women (6.20%). This difference was statistically significant (P = 0.005). Of the subjects suffering from MetS, 9.76% were over 30 years of age and 1.23% of them were under 30 years of age; this difference was not statistically significant (P = 0.078). The frequency of the syndrome was 6.10% in the subjects under 30 years of age and was 35.19% in those over 30 years of age (P = 0.330). Moreover, in the subgroup of MetS, 2.69% had migraine without aura and 8.30% suffered from migraine with aura, which showed no statistically significant difference (P = 0.402). On the contrary, among the patients suffering from migraine with aura, 12 (67.19%) had MetS, while 27 patients (15.80%) of those with migraine without aura suffered from MetS (P = 0.220). Of the patients with MetS, 8.53% had been suffering from migraine for 5 years and 2.46% had been suffering for 1-5 years, which demonstrated no statistically significant difference (P = 0.143). Those who had been suffering from migraine for less than 1 year did not have MetS, but the prevalence of the syndrome was 8.19% in those suffering from migraine for 1-5 years and 7.15% in those who had been suffering for more than 5 years (P = 0.143). Among the patients with MetS, 1.50% experienced headache attacks more than 16 times per month, 3.10% between 11-15 times, 8.30% between 7-10 times, and 8.53% between 3-6 times a month, indicating no statistically significant difference (P = 0.596). Of the patients suffering from MetS, 7.89% received palliative treatment and 3.10% received a prophylactic medication, showing no statistically significant difference (P = 0.876). In the current study, 4.17% of the subjects who had taken the prophylactic medication had MetS and 1.16% of the group who had not undergone the prophylactic treatment suffered from MetS. This difference was not statistically significant (P = 0.876). Moreover, 8.53% and 2.46% of the subjects with MetS experienced severe and moderate migraine headache attacks, respectively. However, no mild headache was reported in this population. This difference was not statistically significant (P = 0.217). The frequency of the syndrome in those with severe and moderate headaches was 9.18% and 5.15%, respectively, indicating that no significant difference existed (P = 0.217). Older age (P = 0.150) and the high intensity of migraine (P = 0.047) were associated with MetS; however, the frequency and duration of migraine were not associated with the syndrome. High systolic and diastolic BP (P = 0.001), a low HDL level (P = 0.028), and a high TG level (P = 0.001) were related to MetS. Nevertheless, FBS was not related to the syndrome. A high BMI in the patients was associated with MetS (P = 0.001) (Tables 1 and 2).

In the study population with migraine, there was a statistically significant relationship between hypertriglyceridemia, gender (P = 0.021), and the administration of prophylactic medication (P = 0.022). Furthermore, hyperglycemia was significantly associated with age grouping (P = 0.010), the intensity of headache attacks (P = 0.048), and prophylactic treatment (P = 0.001). There was a significant relationship between systolic hypertension, the migraine subtype (P = 0.004), and the duration of suffering from migraine (P = 0.005). Moreover, there was a significant association between diastolic hypertension and the migraine subtype (P = 0.002). There was a significant relationship between a WC of above normal, gender (P = 0.001), the intensity of headache attacks (P = 0.028), and the administration of prophylactic medication (P = 0.017). In addition, there was a significant relationship between an HDL of below normal, gender (P = 0.001), and the prophylactic diet (P = 0.023) (Table 3). Moreover, 4.30% of the study population (73 patients) had increased WC and this component depicted statistically significant differences according to gender (P < 0.001) and prophylactic treatment (P = 0.017) (Figure 1).

Discussion

In the current study, out of 240 participants suffering from migraine, 39 (16.25%) had MetS.

Table 1. The frequency distribution of hypertriglyceridemia [triglyceride (TG) > 150] and hyperglycemia [fasting blood sugar (FBS) > 100] by the study variables

Variables		Hypertriglyceridemia [n (%)]		P	Hyperglycemia [n (%)]		P
		No	Yes		No	Yes	
Age (year)	< 30	64 (75.3)	21 (7.24)	0.473	85 (100)	0 (0)	0.010*
	> 30	110 (71.0)	45 (29.0)		143 (92.3)	12 (7.7)	
Gender	Female	116 (68.2)	54 (31.8)	0.021	162 (95.3)	8 (4.7)	0.745
	Male	58 (82.9)	12 (17.1)		66 (94.3)	4 (5.7)	
Migraine type	With aura	46 (75.4)	15 (24.6)	0.556	60 (98.4)	1 (1.6)	0.163
	Without aura	128 (71.5)	51 (28.5)		168 (93.9)	11 (6.1)	
Disease duration (year)	< 1	12 (80.0)	3 (20.0)	0.717	15 (100)	0 (0)	0.413*
	1-5	64 (70.3)	27 (29.7)		88 (96.7)	3 (3.3)	
	> 5	98 (73.1)	36 (26.9)		125 (93.3)	9 (6.7)	
Attack duration (times per month)	< 2	2 (100)	0 (0)	0.256*	2 (100)	0 (0)	0.231*
	3-6	73 (70.2)	31 (29.8)		95 (91.3)	9 (8.7)	
	7-10	56 (68.3)	26 (31.7)		80 (97.6)	2 (2.4)	
	11-15	31 (79.5)	8 (20.5)		38 (97.4)	1 (2.6)	
	> 16	12 (92.3)	1 (7.7)		13 (100)	0 (0)	
Attack intensity	Light	12 (92.3)	1 (7.7)	0.137	13 (100)	0 (0)	0.048*
	Moderate	79 (68.1)	37 (31.9)		106 (91.4)	10 (8.6)	
	Severe	83 (74.8)	28 (25.2)		109 (98.2)	2 (1.8)	
Prophylactic treatment	Yes	12 (52.2)	11 (47.8)	0.022	18 (78.3)	5 (21.7)	< 0.001
	No	162 (74.7)	55 (25.3)		210 (96.8)	7 (3.2)	

P-values are calculated by chi-square and *Fischer's exact tests.

The frequency of the syndrome among the women and men was 20.6% and 5.7%, respectively, showing a significant difference (P = 0.005). Furthermore, the frequency of the syndrome in the general female and male populations is approximately 20.5%-41.2% and 17.5%-31.0%, respectively.[28]

Ansarimoghaddam et al. conducted a systematic review of the prevalence of MetS in Middle-Eastern countries, they reported a range of 2.2%-44% in Turkey, 16%-41% in Saudi-Arabia, 14-63 in Pakistan, 26-33 in Qatar, 9-36 in Kuwait, 22-50 in Emirate, 6-42 in Iran, and up to 23 in Yemen.[29] They also reported an attributable risk of 15.87, 11.7, and 16.23 for CVD, coronary heart disease (CHD), and stroke, respectively.[29] In a meta-analysis, Kalan et al. have reported a 30.4% overall prevalence for MetS in Iran and a higher frequency in women compared with men.[30]

Table 2. The frequency distribution of systolic hypertension and diastolic hypertension by study variables

Variables		Systolic BP > 130 mmHg [n (%)]		P	Diastolic BP > 85 mmHg [n (%)]		P
		No	Yes		No	Yes	
Age (year)	< 30	75 (88.2)	10 (11.8)	0.299	81 (95.3)	4 (4.7)	0.057
	> 30	129 (83.2)	26 (16.8)		136 (87.7)	19 (12.3)	
Gender	Female	146 (85.9)	24 (14.1)	0.551	154 (90.6)	16 (9.4)	0.888
	Male	58 (82.9)	12 (17.1)		63 (90.0)	7 (10.0)	
Migraine type	With aura	45 (73.8)	16 (26.2)	0.004	49 (80.3)	12 (19.7)	0.002
	Without aura	159 (88.8)	20 (11.2)		168 (93.9)	11 (6.1)	
Disease duration (year)	< 1	15 (100)	0 (0)	0.005*	15 (100)	0 (0)	0.558*
	1-5	69 (75.8)	22 (24.2)		82 (89.1)	9 (9.9)	
	> 5	120 (89.6)	14 (10.4)		120 (89.6)	14 (10.4)	
Attack duration (times per month)	< 2	2 (100)	0 (0)	0.773*	2 (100)	0 (0)	0.656*
	3-6	85 (81.7)	19 (18.3)		91 (87.5)	13 (12.5)	
	7-10	72 (87.8)	10 (12.2)		75 (91.5)	7 (8.5)	
	11-15	34 (87.2)	5 (12.8)		36 (92.3)	3 (7.7)	
	>16	11 (84.6)	2 (15.4)		13 (100)	0 (0)	
Attack intensity	Light	13 (100)	0 (0)	0.312*	13 (100)	0 (0)	0.066*
	Moderate	99 (85.3)	17 (14.7)		109 (94.0)	7 (6.0)	
	Severe	92 (82.9)	19 (17.1)		95 (85.6)	16 (14.4)	
Prophylactic treatment	Yes	23 (100)	0 (0)	0.030*	23 (100)	0 (0)	0.141*
	No	181 (83.4)	36 (16.6)		194 (89.4)	23 (10.6)	

P-values are calculated by chi-square and *Fischer's exact tests.
BP: Blood pressure

Table 3. The frequency distribution of high-density lipoprotein and metabolic syndrome by study variables

Variables		Hyper HDL [n (%)]		P	MetS [n (%)]		P
		No	Yes		No	Yes	
Age (year)	< 30	46 (54.1)	39 (45.9)	0.692	76 (89.4)	9 (10.6)	0.078
	> 30	88 (56.8)	67 (43.2)		125 (80.6)	30 (19.4)	
Gender#	Female	75 (44.1)	95 (55.9)	<0.001	135 (79.4)	35 (20.6)	0.005
	Male	59 (84.3)	11 (15.7)		66 (94.3)	4 (5.7)	
Migraine type	With aura	34 (55.7)	27 (44.3)	0.986	49 (80.3)	12 (19.7)	0.402
	Without aura	100 (55.9)	79 (44.1)		152 (84.9)	27 (15.1)	
Disease duration (year)	< 1	11 (73.3)	4 (26.7)	0.363	15 (100)	0 (0)	0.135*
	1-5	49 (53.8)	42 (46.2)		73 (80.2)	18 (19.8)	
	> 5	74 (55.2)	60 (44.8)		113 (84.3)	21 (15.7)	
Attack duration (times per month)	< 2	0 (0)	2 (100)	0.672*	2 (100)	0 (0)	0.663*
	3-6	57 (54.8)	47 (45.2)		83 (79.8)	21 (20.2)	
	7-10	46 (56.1)	36 (43.9)		70 (85.4)	12 (14.6)	
	11-15	23 (59.0)	16 (41.0)		35 (89.7)	4 (10.3)	
	>16	8 (61.5)	5 (38.5)		11 (84.6)	2 (15.4)	
Attack intensity	Light	9 (69.2)	4 (30.8)	0.580	13 (100)	0 (0)	0.224*
	Moderate	65 (56.0)	51 (44.0)		98 (84.5)	18 (15.5)	
	Severe	60 (54.1)	51 (45.9)		90 (81.1)	21 (18.9)	
Prophylactic treatment	Yes	18 (78.3)	5 (21.7)	0.023	19 (82.6)	4 (17.4)	0.876
	No	116 (53.5)	101 (46.5)		182 (83.9)	35 (16.1)	

P-values are calculated by chi-square and *Fischer's exact tests.

MetS: Metabolic syndrome

#HDL in women < 50 and in men < 40

Although the prevalence of the syndrome in the present study among the women was in line with that of the general population, the prevalence of the illness among the male migraineurs in the present study was estimated to be lower. Another rationale for the lower prevalence of MetS among the men was the selection of the cut-off point for WC (102 cm) in men; however, in a study by Delavari et al. in Iran, the cut-off points for WC in men and women were 89 cm and 91 cm, respectively.[28] Due to this, the prevalence of MetS among the men in the current study was much lower. The cut-off point for WC in the present study was based on the NCEP ATP III, which is approximately consistent with the cut-off point recommended for Iran; therefore, the prevalence of the syndrome in the women in the current study was the same as that in other studies.

In a systematic review, Andreeva et al. revealed significant gaps in data and weaknesses in research that must provide an impetus for future epidemiological investigations using more rigorous methodology, larger general-population prospective cohorts, and substantial data on association between MetS and migraine.[31] The assessment of the 1-year prevalence of migraine in MetS by Guldiken et al. in Turkey in 2009 revealed that the prevalence of migraine among those who suffered from the syndrome was greater than that in the general population.[11]
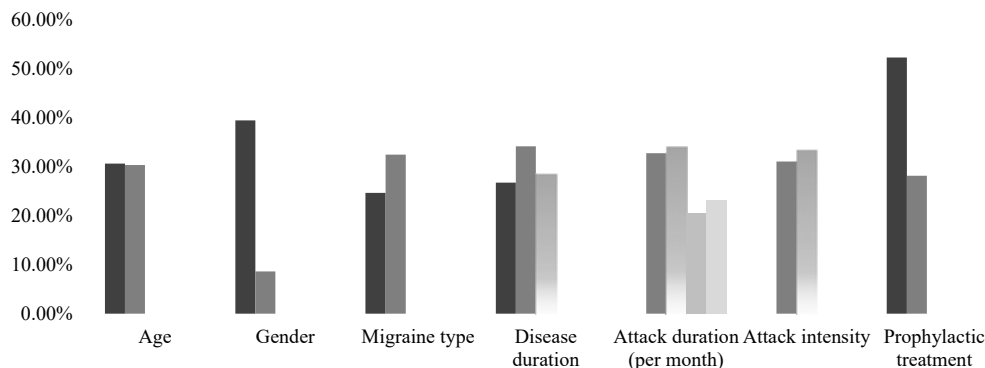

Figure 1. The frequency distribution of waist circumference (WC) of higher than normal (WC in women > 88 cm and WC in men > 102 cm)

In the United States of America, Voss and Scher explored the association between headache and the prevalence of MetS.[16] Their 11-year follow-up showed that there was an association not only between migraine and MetS, but also between the syndrome and all types of headaches.[16] Salmasi et al. conducted a study in Iran and compared the prevalence of MetS between patients with and without migraine headaches. Their study demonstrated that there was no major link between the syndrome and migraine; however, a high BMI and WC as components of MetS were related to migraine.[18] In this research, the prevalence of the syndrome in migraineurs was estimated at around 17%, which was consistent with the results of this review. He et al. found an association between chronic migraine and MetS, especially when it is comorbid with analgesic overuse.[32] Medication overuse headache (MOH) may be the risk factor for MetS in female migraine patients and is associated with abdominal obesity and hypertension.[32] The prevalence of MetS has been reported to be 12.8%-41.1% in different parts of the world and 21.9%-31.1% in Iran.[1] Moreover, in a study by Sharifi et al., the prevalence of MetS in the general population of Zanjan was explored and found to be 23.7%.[15] Hence, although the prevalence of MetS in migraineurs was slightly lower than that in the general population, this difference was not significant. The difference in the prevalence of the syndrome between migraineurs in the current study and the general population in other studies could have been partly due to the difference in the age composition between the current study and other studies. No subject was over 50 years old in the present study; however, in the study by Sharifi et al.,[15] 45.6% of the population over 50 years of age had MetS.

According to the examination of MetS and migraine by Sachdev and Marmura in the United States of America, they are 2 complex biochemical processes which coexist and interact; however, it is unclear how they do so.[21] Weight loss, increased physical activity, good sleep hygiene, and the management of life stressors are the cornerstones of preventive healthcare in the adult population. It must be noted that the exact efficacy of current medications in patients who suffer from the MetS and migraine are unclear. The consumption of nutraceuticals and pharmaceuticals and the avoidance of triggers are commonly accepted migraine therapies. The choice of pharmaceuticals may have implications for the management of MetS. It is necessary to consult the patient about the possible pharmacologic side effects.[21] The frequency of MetS in the present study in the patients under 30 years of age was 10.6% and in those over 30 years of age was 19.3%. In the study by Sharifi et al., the frequency in patients under 30 years of age was 7.5% (this prevalence increased as age increased) and was 45.6% in those above 50 years of age.[15] This difference could have been partly due to the study population. Most cases of MetS in the study by Sharifi et al. were patients over 50 years of age with a prevalence of 45.6%; however, no patient over 50 years of age had been included in the current study.[15] In a recent study, Ozcan and Ozmen found no association between insulin resistance (IR) and MetS, and migraine in women.[17] They showed an inverse relationship between central obesity and migraine.

In the current study, 17% of the patients suffering from migraine without aura had MetS, which showed no significant difference. A study carried out by Winsvold et al. in Norway explored the incidence of MetS and its relationship to migraine with and without aura and to non-migraine headache using the Poisson regression model and demonstrated that migraine with aura increased the risk of developing MetS.[10] However, a moderate risk increase was seen in cases of non-migraine headache and migraine without aura.[10] Migraine with aura is associated with a high risk of cardiovascular events and a higher prevalence of family history of CVDs is observed in these sufferers. The study also indicated that MetS criteria could be one of the major factors and mechanisms through which migraine with aura is linked to a high risk of cardiovascular events. Harandi et al. compared the prevalence of cardiovascular risk factors between migraineurs and non-migraineurs and concluded that there was no difference between them except for higher risk of hypertension in cases of migraine without aura.[33]

The higher prevalence of MetS in migraine with aura may be linked to the relationship between non-alcoholic fatty liver disease (NAFLD) and migraine with aura.[1] It should be noted that the association between MetS and fatty liver is so strong that NAFLD is regarded as a manifestation of MetS.[34]

In a cross-sectional study by Celikbilek et al. in Italy, the relationship between migraine and NAFLD in migraineurs was explored. The study indicated that, in migraineurs, NAFLD was associated with a higher frequency of aura, longer

disease duration, and longer attack duration.[1] In the present study, the migraine duration had no effect on the frequency of MetS. The higher prevalence of the syndrome in patients with a history of migraine for less than 5 years could have been partly due to the higher prevalence of obesity in this group. Data of the present study confirmed this minor difference. The lower prevalence of obesity in individuals with longer disease duration could have been due to long-term effects of the disease and the patients' nutrition.

Verrotti et al. evaluated the relationship between the prevalence, frequency, and severity of migraine and obesity among children and adults in Italy.[35] They found that an increased BMI and obesity were linked with the prevalence, frequency, and severity of migraine. Nevertheless, this result is not verified by some other previous studies. Evidently, obesity is one of the criteria for MetS. Hence, the result of their study is consistent with that of the present study. Santos et al. conducted a study in 2014 and evaluated the association between obesity and migraine in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil).[20] In their sample of individuals aged 35+ years of age, obesity, but not abdominal obesity, was related to daily migraine; moreover, abdominal obesity influenced the relationship between BMI and daily migraine in migraineurs in the 35-49 year age range.[20] In Italy, Verrotti et al. carried out a study which demonstrated that the effects of obesity and weight change on headache outcomes might have important implications for clinical care.[9] Results of a study by Winter et al. in 2012 did not show a consistent association between migraine and overweight or obesity.[22]

In the present study, 39.4% and 8.6% of the female and male migraineurs, respectively, had above-normal WC; moreover, approximately 30.4% of the subjects of the study had above-normal WC, which was 42% without sex segregation in the study by Salmasi et al.[18] The low prevalence of high WC in the men is justifiable on the grounds of the cut-off point. In their study among the MetS components, a high BMI and WC were very frequent in migraineurs. There was a statistically significant difference between women and men in terms of WC (P < 0.001), which could have resulted from the difference in obesity types among men and women and effects of hormones. Moreover, in the current study, there was no frequency of above-normal WC in the subjects with mild migraine attacks, but 31.0% and 33.3% of the subjects had moderate and severe attacks, respectively, which indicates a statistically significant difference (P = 0.028) and shows the effectiveness of obesity in increasing the intensity of migraine attacks. The study by Verrotti et al. also showed that obesity (and increased WC as one of its criteria) was associated with the increased intensity of headaches.[35] Moreover, there was a statistically significant difference in the frequency of above-normal WC according to the consumption or non-consumption of prophylactic medication (P = 0.017), which caused migraineurs to put on weight.

In the United States of America, Bond et al. conducted a study to describe the symptoms, epidemiology, and pathophysiology of migraine.[36] They also reviewed studies that had examined the epidemiological association between migraine and obesity followed by a discussion of possible mechanisms which could link the two disorders. They finally explored the potential role of weight loss in treating migraine and potential mechanisms through which weight loss could alleviate headache attacks.[36] According to their study, a possible link exists between migraine and obesity. In fact, obesity either exacerbates migraine or increases the risk of having migraine. A large number of psychological, physiological, and behavioral mechanisms may contribute to their co-occurrence; however, the majority of them can be effectively targeted with weight loss. Thus, it is necessary to perform randomized controlled trials to evaluate the effects of weight loss on migraine. Behavioral weight loss interventions, in particular, could provide a useful treatment model for showing whether a modest weight loss reduces headache severity and frequency in obese migraineurs. The interventions can also enhance understanding of different mechanisms through which weight loss might affect migraine.[4] In the USA, Peterlin et al. explored the prevalence of migraine and severe headaches among the non-obese and obese (individuals with both general obesity and abdominal obesity) and effects of age and gender on the migraine-obesity association.[24] Their study showed that the migraine-obesity association varied depending on age, gender, and adipose tissue distribution. The prevalence of migraine in 55-year-old men and women with general obesity was higher, but was not associated with abdominal obesity and this relationship among women did not rely on general obesity. There was no association between

migraine and general or abdominal obesity in men of over 55 years of age. The prevalence of migraine in women of over 55 years of age with abdominal obesity was lower, but was not associated with general obesity.[24] In this study, the frequency of MetS had no significant relationship with the intensity of migraine headaches. Nevertheless, the reason why MetS was higher, even slightly higher, in the subjects with severe headaches was that some of the criteria for MetS such as BP were higher in them. The present study confirmed this relationship. The higher intensity of migraine is associated with higher BP; moreover, hypertension transforms episodic migraine into chronic migraine. According to Gardener et al., hypertension, particularly uncontrolled and of long duration, is associated with migraine, both with and without aura.[37] The data available from a mean follow-up of 12.2 years by Rist et al. revealed that woman with migraine exhibit a higher relative risk of developing hypertension compared to women without migraine.[38] In addition, hypertension amplifies the effects of migraine on the vascular wall. Among the effects of migraine on the vascular wall are hypercoagulation and vascular endothelial dysfunction, according to a study by Barbanti et al.[27] This study was conducted in Italy in 2010 to investigate the effects of hypertension on inducing the progression of episodic migraine to chronic migraine. It indicated that hypertension might stimulate this progression and maximize the effects of migraine on the vascular wall; therefore, the study recommended monitoring BP values in migraineurs, showing an increase in attack frequency.[27]

In Italy, Mancia et al. estimated the prevalence of hypertension-migraine comorbidity, determined their demographic and clinical characteristics versus patients with hypertension or migraine alone, and explored whether a history of cerebrovascular events was more common in the comorbidity group.[26] They found that the prevalence of hypertension-migraine comorbidity was considerably high and that the patients with comorbidity, compared to hypertensive patients, were more likely to have a history of cerebrovascular events.[26] Of the migraineurs of the present study, 15.0% had systolic hypertension, 9.6% had diastolic hypertension of above normal, and 16.6% had hypertension. In the study by Salmasi et al., 13.0% of migraineurs had hypertension,[18] which is consistent with the results of the current study. Moreover, the prevalence of

hypertension in the general population is approximately 20%; therefore, according to the present study and previous studies, the prevalence of hypertension among migraineurs will not be higher than that in the general population. Furthermore, in the present study, the frequency of systolic BP of above normal in the sufferers from migraine with aura was higher than that in the sufferers from migraine without aura (P = 0.004). This result was the same for the frequency of diastolic BP of above normal (P = 0.002). The reason for these results could have been the difference in the mechanisms and pathophysiology of migraine with and without aura. In a study conducted by Tana et al., the prevalence of hypertension in sufferers from migraine with aura was higher than that in sufferers from migraine without aura, which could be one of the justifiable reasons for the incidence of most cardiovascular events in patients suffering from migraine with aura.[39] Hence, monitoring BP in these patients is recommended. The current study revealed that the frequency of systolic BP of above normal in patients with short disease duration was higher than in those with long disease duration (Fisher's exact test, P = 0.005).

In a study conducted by Fava et al. in Italy in 2013, the researchers assessed serum glucose, insulin levels, and insulin resistance in a sample of chronic migraineurs, episodic migraineurs, and non-pain healthy controls.[19] They drew the conclusion that chronic migraine was associated with the insulin-resistance status, particularly when it was in partnership with obesity.[19] Gozke et al. performed a study in Turkey in 2013 on the relationship between migraine and tension-type headaches in patients with MetS.[12] They came to the conclusion that, the association of headaches with MetS should be taken into account; moreover, they should be especially observed with respect to their response to analgesics and the presence of hyperlipidemia and hypertension.[12] Streel et al. showed that low HDL-cholesterol, hyperglycemia, and abdominal obesity had a positive association with migraine with aura (MA) and higher risk of MetS, while there was not such a relation in non-migraineurs and migraine without aura (MO) patients.[3]

In a study in Italy, disclosed that MetS components, such as increased WC, impaired glucose metabolism, and obesity, were more frequent among migraineurs. It was also suggested that insulin resistance might underlie a common

pathogenesis of both diseases, which might be responsible for the higher migraine prevalence among patients with MetS.[25] In India, Bhoi et al. compared the clinical characteristics of migraine in patients with and without MetS and insulin resistance. Their study indicated that the syndrome existed in 31.9% of the migraineurs, who were mainly elderly individuals who had longer duration of headaches and multiple triggers.[40] In the present study, the frequency of migraine attacks had no effect on the frequency of MetS and no particular association was observed between the frequency of attacks and the prevalence of MetS. Additionally, the consumption or non-consumption of prophylactic medication had no effect on the frequency of MetS. The results of the current study demonstrated that 27.5% and 5.0% of the migraineurs had hypertriglyceridemia and above-normal glucose, respectively. In the study by Salmasi et al., 14% and 11% of migraineurs had hypertriglyceridemia and above-normal glucose, respectively.[18] This difference could be due to a difference in climate conditions and different diets the study populations had. In the general population in Iran, hypertriglyceridemia was approximately 46.0% and impaired FPG was 17.5%. This substantial difference in hypertriglyceridemia and glucose between our study population and the general population could have resulted from a difference between the age compositions of the studies.

In the present study, the prevalence of below-normal HDL was 55.9% in the women and 14.3% in the men. Moreover, in all the subjects, it was 43.8%. In the study by Salmasi et al., it was reported to be 40.5% in all the subjects, which is in line with the results of the present study.[18] In the general population in Iran, the prevalence of below-normal HDL was 40-50%. By comparing the results of the present study, it was revealed that below-normal HDL in the migraineurs was not different from that in the general population. Findings of Saberi et al. suggested that the prevalence of hypertriglyceridemia and hypercholesterolemia was higher in migraineurs compared with non-migraineurs. This frequency comparison was contrariwise for low HDL-C.[41] An investigation into MetS components, migraine characteristics, and gender and age groups demonstrated that the relative frequency of TG of over 150 was 31.7% in the women and 17.2% in the men and was significantly different (P = 0.021), which could be relevant to the higher frequency of

obesity in the women of the present study. Furthermore, the prevalence of hypertriglyceridemia was 47.8% among the migraineurs consuming prophylactic medication and was 25.4% among those not undergoing prophylactic drug treatment, which shows a statistically significant difference (P = 0.022). Hence, TG plasma levels in patients consuming prophylactic medication were higher than those in patients who did not receive prophylactic medication. This result could have been due to the effects of the medication. The study by Tana et al. demonstrated that the LDL plasma levels of subjects decreased after they received prophylaxis.[39] Therefore, assuming that HDL and cholesterol levels were constant, increased TG levels in the present study could have been related to decreased LDL levels; however, the current study did not examine LDL levels. Moreover, in the present study, the frequency of FBS of over 100 was 12. All of patients in MetS group considering the age groups, all of them were over 30 years old. This difference was statistically significant (P = 0.010). The justifiable reason for it could be the greater possibility of impaired FBS in older age groups, as compared to the younger population.

The frequency of above-normal FBS was 21.7% in the subjects who received prophylactic medication and was 3.2% in those without a prophylactic diet, showing a statistically significant difference (P = 0.001). This difference might have been due to the effect of the medication. The current study revealed that FBS was normal in migraineurs group with mild migraine attacks, but it was 8.6% and 1.8% in patients with moderate and severe attacks, respectively. This was a statistically significant difference (Fisher's exact test, P = 0.048). Therefore, the prevalence of hyperglycemia in moderate migraine was higher than that in severe migraine. Nevertheless, with an increase or decrease in the intensity of migraine attacks, the frequency of above-normal FBS did not alter.

One of the other findings of the current study was the presence of a statistically significant difference in the frequency of below-normal HDL between women and men (P < 0.001), which could have resulted from hormonal and genetic differences in the two genders and the effects on the lipid profile. In addition, this result was in line with the results of the study by Sharifi et al.[15] Another result of the current study was that the frequency of below-normal HDL in the patients

who consumed prophylactic medication was lower than that in those without this diet (P = 0.023). This difference could have been due to the effects of analgesics administered to these patients. Moreover, it is likely that those who do not consume any prophylactic medication may suffer from more migraine attacks, thereby having less activity and resting more. Furthermore, the overconsumption of analgesics may lead to an impaired lipid profile.

Conclusion

In the present study, the occurrence of MetS in migraineurs was not higher than that in the general population. However, the severity of migraine can somewhat increase the prevalence of MetS. Furthermore, those who benefit from the prophylactic drug treatment have high plasma FBS and TG levels; moreover, migraine with aura is associated with higher BP. Hence, in patients with severe migraine headaches, it is recommended that physicians consider the MetS criteria, the BP of patients affected by migraine with aura be controlled (especially because this kind of migraine is associated with a greater risk of CVD and strokes), and people taking prophylactic medication be examined for dyslipidemia and blood glucose disorders.

Limitations: The current study faced some limitations, such as the absence of a control group and, therefore, the impossibility of exploring the causal relationship between MetS and migraine. Moreover, considering the multiplicity of MetS parameters, the research was carried out in stages, which caused some patients to discontinue their cooperation with the research. Therefore, the researchers of the current study tried to facilitate the inclusion process of the patients and carried out assessments on time and in the most convenient way so that, on the same day that a patient underwent a blood test, the questionnaire was filled out for him or her and his or her height, weight, and WC were measured. This enhanced the patients' cooperation.

Conflict of Interests

The authors declare no conflict of interest in this study.

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