Journal of Neurological Sciences [Turkish] **31:(1)**# 39; 080-089, 2014
http://www.jns.dergisi.org/text.php3?id=743
Research Article

Comorbidities of Migraine Results of Turkish Headache Database Working Group

Sebnem BICAKCI[1], Gulsah SEYDAOGLU[2], Aynur OZGE[3], Turkish Headache Database Working Group[4]

[1]Cukurova University School of the Medicine, Departmant of Neurology, Adana [2]Cukurova University School of the Medicine, Departmant of Bioistatistics, Adana [3]Mersin University School of the Medicine, Departmant of Neurology, Mersin [4]Presented in the appendix in alphabetical order

Summary

Aim: Realizing migraine comorbidities is particularly important for physiopathology, treatment, and progress of the disease. In the present study, we aimed to assess the comorbid conditions in patients with migraine.
Method: This retrospective study was conducted by the Turkish Headache Database Study Group, at 23 headache centers. Diagnosis of migraine was established by a physician based on the International Classification of Headache Disorders-II criteria. Comorbidities of migraine were determined based on the patients' self reports.
Results: A total of 3478 cases, which have been diagnosed with migraine were evaluated. (mean age 43.5±11.2, 81.8% female). Comorbidity was detected in 55.7% (n:1937) of overall cases. Psychiatric diseases have been reported to be the most prevalent comorbidity in these patients (31.5%, p≤0.0001). Cardiovascular diseases (16.5%), and hypertension (16.3%) have been found to be more prevalent in migraine with aura. Prevalence of neurological comorbidity, also, was higher in migraine with aura. Epilepsy (1.5%) and vertigo (4.6%) were detected in migraine with aura cases. Difficulty in falling asleep was found in 35.4% of the cases (p≤0.0001). Prevalence of non-headache pain was found to be 2.9% (p>0.0001).≤0.0001). Patients with comorbidities were more sensitive to migraine triggers and accompanied symptoms were more severe (p≤0.0001).
Conclusion: Comorbidity of migraine is the important component of complex nature of the disease. The present study is important in terms of being the first multicenter study exposing migraine comorbidities and their reflections in clinical practice.

Key words: Migraine, ICHD-II, comorbidity

Migren Komorbiditesi Türk Başğarısı Veritabanı Sonuçları

Özet

Amaç: Migren komorbiditesinin farkında olunması özellikle hastalığın fizyopatolojisi, tedavi seçenekleri ve seyri açısında önem taşımaktadır. Bu çalışmada migren tanısı almış hastalarda komorbid durumların değerlendirilmesi amaçlanmıştır.
Yöntem: Bu çalışma Türk Başağrısı Veritabanı Çalışma Grubu tarafından retrospektif olarak 23 başağrısı merkezinde gerçekleştirilmiştir. Migren tanısı ICD-II tanı ölçütlerine göre konulmuştur. Migren komorbiditesi hasta verilerine dayanılarak belirlenmiştir.
Bulgular: Migren tanısı almış toplam 3478 olgu değerlendirilmiş (ortalama yaş 43.5±11.2, %81.8 kadın hasta), %55.7 (n:1937) oranında komorbid durum saptanmıştır. Bu hastalarda en yüksek oranda komorbid durum olarak psikiyatrik hastalık belirlenmiştir (%31.5, p≤0.0001).

Auralı migrenli olgularda kardiyovasküler hastalık (%16.5) ve hipertansiyon (%16.3) daha yüksek bulunmuştur. Nörolojik hastalık komorbiditesi de auralı migrenlilerde yüksek olup; bu hastaların %4.6'sında vertigo, %1.5 epilepsi saptanmıştır. Uykuya dalma zorluğu olguların %35.4'ünde ($p \leq 0.0001$), başağrısı olmayan ağrı prevalansı %2.9 ($p > 0.000$) belirlenmiştir.
Sonuç: Migren komorbiditesi hastalığın karmaşık doğasının önemli komponentidir. Bu çalışma migren komorbiditesini ve onun klinik pratiğe yansımalarının ortaya konduğu ilk çok merkezli çalışma olma özelliği nedeniyle önem taşımaktadır.

Anahtar Kelimeler: Migren; ICHD-II, komorbidite

INTRODUCTION

Migraine is a prevalent chronic disease that leads to severe disability. It is seen in 18% of females and 6% of males[15]. It involves 16.4% of Turkish population (24.6% of females and 8.5% of males)[6]. Comorbidity refers to the association of various diseases in a patient due to the mechanisms greater than a coincidence and was first defined approximately 40 years ago by Feinsteine[7]. Migraine is comorbid primarily with stroke, subclinical vascular brain lesions, coronary artery disease (CAD), hypertension (HT), patent foramen ovale, psychiatric diseases (depression, anxiety, bipolar disorder, OCD (Obsessive Compulsive Disorder), panic disorder and suicide), restless leg syndrome, epilepsy, allergic diseases and non- headache pain[1,20,21]. This is of great importance in terms of evaluating migraine clinic, understanding its pathogenesis, overcoming difficulties encountered in treatment window (efficacy and adverse event, contraindication), and prognostic prediction[20,21]. Why comorbidity of migraine is higher with some diseases than the others? This question can be answered as the presence of common genetic and environmental factors, causal relationship, underlying common physiopathological processes, and complete coincidental association of common conditions[20,21,23].

The present study aimed to assess comorbid conditions in the patients diagnosed with migraine, distribution of these comorbidities among sub-types of migraine and the reflections in clinical practice (severity, duration, response to therapy, etc.).

MATERIAL AND METHODS

This retrospective study was conducted by the Turkish Headache Database Study Group (THDSG), a subgroup of Turkish Headache Study Group under the roof of Turkish Neurology Association. These tertiary health care centers are served by staff neurologists specialized on headache and algology. The study comprised 23 centres that gave consent for data inclusion. The study population consisted of patients previously diagnosed with migraine.

Data Collection

The consents of centers were obtained first and the study database was created by collecting overall data in a single data pool subsequently. Database was developed by Mersin University department of neurology, headache[3] and statistics teams. All other centers involved in the study acquired patients' data according to this database. The database contains epidemiologic data, history of headache and medication, habits, medical (especially comorbidities) and headache history in patients' first and second degree relatives, physical and neurological examinations. Patients' follow-up visit forms are also included in the database. In this database, known comorbidities before presenting to headache outpatient clinics were recorded based on self-reports of the patients. These comorbidities are neurologic diseases (restless leg syndrome, epilepsy, stroke, subclinical vascular brain lesions),

cardiovascular disease (CVD) (coronary artery disease (CAD), hypertension (HT) patent foramen ovale), psychiatric diseases (depression, anxiety, bipolar disorder, OCD (Obsessive Compulsive Disorder), panic disorder and suicide) and others (non- headache pain, allergic diseases sleep disorders). Diagnosis of migraine and its sub-types (migraine without aura, migraine with aura, childhood periodic syndromes, retinal migraine, complications of migraine, probable migraine) were identified in accordance with International Classification of Headache Disorders-II (ICD-II) criteria[7]. Pediatric patients were excluded. No further investigation was done to verify the reported comorbidity. No control group was included in the study.

Statistical analysis

SD and median (min-max). Statistical analyses were done using SPSS v 19.0 statistical package.±Normality was checked for each continuous variable. Since the data was not distributed normally, appropriate non-parametric test was chosen. Comparisons between groups were done using student t-test for normally distributed data and Mann-Whitney U test was used for the data not distributed normally. Comparison of the categorical variables between the groups was done using Chi square test. Results were presented as mean

*The names of the study centers and participating staff are listed in the appendix.

RESULTS

A total of 3478 cases, which have been diagnosed with migraine according to ICD-II criteria, were evaluated. The mean age of the cases, of whom 81.8% were female and 18.2% were male, was 43.5±12.8 (min:18-max:90) years. Habits as smoking, caffeine, drugs, alcohol, medical history of trauma, periodic vomiting, car sickness, surgery, family history of allergy, atherosclerosis, hyperlipidemia, HT, Diabetes Mellitus (DM), CAD, and basic clinical characteristics (triggers and accompanied symptoms) of the patients according to migraine sub-types are presented in Table 1.

Based on these results, migraine without aura (without aura + probably without aura) in 84.3% of the cases (n:2933) and migraine with aura (with aura+probably with aura) in 14.1% (n:490) were diagnosed. Since pediatric patients were excluded, childhood periodic syndromes that are commonly precursors of migraine do not exist in the study. Complications of migraine were identified in 55 cases. Retinal migraine was not detected in the study group.

Comorbidity was detected in 55.7% (n:1937) of overall cases. With regard to the diagnostic groups, the highest rate of comorbidity was observed in migraine cases with aura (1.1) (67.4% n: 265) and the lowest rate of comorbidity was observed in the group defined as migraine complications (1.5) (27.3% n:15). The most common comorbidity was psychiatric diseases with a rate of 43.6% (n:1516) followed by cardiovascular disease (CVD) (14.8%, n:514), neurological diseases (5.5%, n: 193), and other comorbid conditions (snoring, Obstructive Sleep Apnea Syndrome (OSAS), insomnia, allergy, non-headache pain) (6.5% n: 226) (Table 2). The prevalence of comorbidity with psychiatric and neurological diseases was statistically significantly higher particularly in migraine with aura patients as compared to the other groups ($p \leq 0.0001$). Depression was the most prevalent comorbidity among psychiatric diseases (31.5%, n:1097). Moreover, drug abuse was also found significant under this topic ($p \leq 0.0001$). The title of neurological disease comprises vertigo and epilepsy. Prevalence of vertigo was 13% (n: 51) ($p \leq 0.0001$) and epilepsy was 1.5% (n:6) in the migraine with aura cases. Prevalence of concomitant CVD was not statistically significant. Comorbidity of migraine with

OSAS and insomnia, which are under the title of other diseases, was found significant (p≤0.0001). Prevalence of insomnia was found 47.1% (n: 185) particularly in the migraine with aura cases. Although prevalence of OSAS was found to be statistically significant, making a comment was difficult due to limited patient number. Comorbidity of migraine with allergy, snoring, and non-headache pain was not significant. Distribution of comorbidities among subgroups of migraine is demonstrated in Table 2. No difference was found between the cases with and without comorbidity in terms of duration of migraine (101.9±99.8 month vs. 100.0±101.7 month, p=0.422).

Reflections of comorbidities in migraine clinic have been evaluated. It has been determined that migraine was significantly accompanied by dizziness, sleep disorders and cranial autonomic symptoms in addition to classical initiators (such as emotional stress, intense physical activity, menstrual cycle, and seasonal change) and all concomitant conditions included in diagnostic criteria (excluding photophobia) (p≤0.0001). Frequency, duration and severity of pain are enhanced in the presence of comorbidities (p≤0.0001). Duration of attacks was observed to be longer in the presence of comorbidity despite the use of medications (p≥0.0001). Although duration of remission was not statistically significant at the basis of days, it was found to be shorter in the presence of comorbidity (Table 3).

Table 1. Characteristics of the cases according to the migraine sub-types

	Migraine sub-types n (%)						
	Without Aura (n=2815)	**With Aura (n=393)**	**Probably without Aura (n=118)**	**Probably with Aura (n=97)**	**Complications of migraine (n=55)**	**Total (n=3478)**	**p**
Age Mean±SD	43.6±12.8	42.9±12.7	45.7±13.5	42.1±11.4	42.6±14.6	43.5±12.8	0.159
min-max	18-90	18-77	19-73	18-77	18-75	18-90	
Personal history / habits n(%)							
Periodic vomiting	43(1.5)	8(2.0)	2(1.7)	4(4.1)	1(1.8)	58(1.7)	0.375
Motion sickness	340(12.1)	46(11.7)	13(11.0)	10(10.3)	3(5.5)	412(11.8)	0.627
Accident	140(5.0)	22(5.6)	6(5.1)	2(2.1)	2(3.6)	172(4.9)	0.684
Surgery	376(13.4)	45(11.5)	10(8.5)	13(13.4)	3(5.5)	447(12.9)	0.195
Caffeine abuse	42(1.5)	7(1.8)	0(0.0)	2(2.1)	0(0.0)	51(1.5)	0.542
Oral contraceptive	30(1.1)	5(1.3)	2(1.7)	2(2.1)	2(3.6)	41(1.2)	0.0001
Smoking	783(33.1)	80(27.0)	29(31.5)	39(45.9)	6(28.6)	937(32.7)	0.022
Alcohol	405(17.2)	37(12.6)	16(17.4)	25(30.1)	2(9.5)	485(17.1)	0.005
Substance abuse	3(0.1)	0(0.0)	0(0.0)	2(2.1)	1(1.8)	6(0.2)	0.0001
Family history n(%)							
Epilepsy	7(0.2)	3(0.8)	0(0.0)	1(1.0)	0(0.0)	11(0.3)	0.285
Allergy	161(5.7)	24(6.1)	9(7.6)	6(6.2)	2(3.6)	202(5.8)	0.858
Atherosclerosis	4(0.1)	1(0.3)	0(0.0)	1(1.0)	0(0.0)	6(0.2)	0.313
Hyperlipidemia	114(4.0)	10(2.5)	6(5.1)	1(1.0)	3(5.5)	134(3.9)	0.281
HT	573(20.4)	59(15.0)	28(23.7)	27(27.8)	8(14.5)	695(20.0)	0.017
DM	409(14.5)	41(10.4)	19(16.1)	23(23.7)	3(5.5)	495(14.2)	0.003
CAD	371(13.2)	36(9.2)	15(12.7)	25(25.8)	3(5.5)	450(12.9)	0.0001
Other	836(29.7)	105(26.7)	40(33.9)	27(27.8)	8(14.5)	1016(29.2)	0.994
Trigger n(%)							
Emotional stress	2042(72.5)	264(67.2)	66(55.9)	68(70.1)	25(45.5)	2465(70.9)	0.0001

Physical activity	1383(49.1)	176(44.8)	42(35.6)	53(54.6)	12(21.8)	1666(47.9)	0.0001
Menstrual cycle	885(31.4)	132(33.6)	33(28.0)	41(42.3)	10(18.2)	1101(31.7)	0.025
Seasonal changes	434(15.4)	89(22.6)	11(9.3)	14(14.4)	4(7.3)	552(15.9)	0.0001
Other	564(20.0)	107(27.2)	20(16.9)	18(18.6)	13(23.6)	722(20.8)	0.014
Accompanied symptoms n(%)							
Nausea	2190(77.8)	277(70.5)	75(63.6)	73(75.3)	31(56.4)	2646(76.1)	0.0001
Vomiting	1024(36.4)	130(33.1)	36(30.5)	46(47.4)	17(30.9)	1253(36.0)	0.054
Phonophobia	2117(75.2)	293(74.6)	77(65.3)	79(81.4)	33(60.0)	2599(74.7)	0.006
Photophobia	1908(67.8)	261(66.4)	57(48.3)	73(75.3)	28(50.9)	2327(66.9)	0.0001

Migraine sub-type have been identified according to ICD-II
CAD = Coronary Artery Disease, DM= Diabetes Mellitus, HT= Hypertension,

Table 2. Migraine Sub-types– Comorbidities of migraine

	Migraine without aura (n=2815)	Migraine with aura (n=393)	Probable migraine		Complication of migraine (n=55)	**Total** (n=3478)	**P**
			Probable migraine without aura (n=118)	Probable migraine with aura (n=97)			
Psychiatric disease	1213(43.1)	212(53.9)	48(40.7)	33(34.0)	10(18.2)	1516(43.6)	0.0001
Depression	874(31.0)	158(40.2)	36(30.5)	23(23.7)	6(10.9)	1097(31.5)	0.0001
Anxiety disorder	318(11.3)	55(14)	11.(9.3)	10 (10.3)	4 (7.3)	398(11.4)	0.383
OCD	54(1.9)	9(2.3)	1(0.8)	0 (0.0)	1 (1.8)	65(1.9)	0.568
Psychosis	23 (0.8)	4(1.0)	1(0.8)	0(0.0)	1(1.8)	29(0.8)	0.803
Cardiovascular disease	409(14.5)	65(16.5)	21(17.8)	14(14.4)	5(9.1)	514(14.8)	0.496
Hypertension	403 (14.3)	64(16.3)	21 (17.8)	13(13.4)	11(20)	506(14.5)	0.478
CAD	233 (8.3)	42(10.7)	10(8.5)	12(12.4)	4(7.3)	295(8.5)	0.497
Neurological disease	126(4.5)	55(14.0)	3(2.5)	6(6.2)	3(5.5)	193(5.5)	0.0001
Epilepsy	31(1.1)	6(1.5)	1(0.8)	0(0.0)	0.(0.0)	38(1.1)	0.657
Vertigo	98(3.5)	51(13.0)	2(1.7)	6(6.2)	3(5.5)	160(4.6)	0.0001
Transient ischemic attack	8(0.3)	1(0.3)	0(0.0)	1 (1.0)	0(0.0)	10(0.3)	0.665
Other	168(6.0)	36(9.2)	6(5.1)	9(9.3)	7(12.7)	226(6.5)	0.026
Snoring	7(0.2)	4(1.0)	0(0.0)	1(1.0)	0(0.0)	12(0.3)	0.097
OSAS	1(0.0)	1(0.3)	0(0.0)	1(1.0)	1(1.8)	4(0.1)	0.0001
Insomnia	966(34.3)	185(47.1)	33(28.09)	31(32.0)	17(30.9)	1232(35.4)	0.0001
Allergy	40(1.4)	9(2.3)	0(0.0)	1(1.0)	2(3.6)	52(1.5)	0.245
Non-headache pain	79(2.8)	14(3.6)	3(2.5)	3(3.1)	3(5.5)	102(2.9)	0.735
Total comorbidity	1550(55.1)	265(67.4)	60(50.8)	47(48.5)	15(27.3)	1937(55.7)	0.0001

OCD =Obsessive Compulsive Disorder, OSAS= Obstructive Sleep Apnea Syndrome

Table 3. Impact of comorbidities in migraine clinic

	Comorbidity		
	No	**Yes**	
	n=1541	**n=1937**	**P**
	n(%)	n(%)	
Triggers factors			
Emotional stress	941(61.1)	1524(78.7)	0.0001
Intense physical activity	639(41.5)	1027(53.0)	0.0001
Menstrual cycle	393(25.5)	708(36.6)	0.0001
Seasonal change	164(10.6)	388(20.0)	0.0001
Other	286(18.6)	436(22.5)	0.004
Accompanied symptoms			
Nausea	1109(72.0)	1537(79.3)	0.0001
Vomiting	500(32.4)	753(38.9)	0.0001
Phonophobia	1078(70.0)	1521(78.5)	0.0001
Photophobia	990(64.2)	1337(69.0)	0.003
Dizziness	32(2.1)	179(9.2)	0.0001
Sleep disorder	393(25.5)	839(43.3)	0.0001
Osmophobia	124(8.0)	174(9.0)	0.327
Other	15(1.0)	13(0.7)	0.322
Cranial autonomic symptoms	42 (2.7)	106(5.5)	0.0001
	Mean±SD (Median)	Mean±SD (Median)	
Pain characteristics			
Duration of diagnosis (month)	101.9±99.8(60)	100.0±101.7(60)	0.422
Frequency of pain (day)	10.1±9.6(5)	11.3±10.0(8)	0.0001
Severity of pain (VAS)	7.7±2.1(8)	8.2±1.8(8)	0.0001
Duration of attack with medication (hour)	21.7±22.0(12)	25.8±24.6(24)	0.0001
Duration of remission (day)	13.7±10.9(10)	11.6±11.6(8)	0.035

DISCUSSION

Migraine is a chronic, occasionally progressive, and complex disease that is difficult to treat. Comorbidities are the important components of complex nature of the disease. Realizing comorbidities is particularly important for physiopathology and is a guide for treatment. Results of some studies revealed that migraine and some diseases, notably psychiatric, neurologic and CVD, are seen together beyond coincidence[20,21].

The aim of the present study is to evaluate comorbidities of migraine in Turkey and to obtain data from Turkey. Results are based on the data obtained by face-to-face clinician-patient interview and inquiry. Accordingly, the majority of the patients had migraine without aura cases (migraine without aura + probable migraine without aura). Psychiatric diseases, in particular, have been reported to be the most prevalent comorbidity in these patients ($p \leq 0.0001$). Studies have demonstrated that the prevalence of major depression is 2-3.5 times higher in migraine sufferers as compared to normal population[1,22,10]. An experience that has been considered as depression was determined in 31.5%, i.e.

1/3, of our cases. However, there is limited or no data about other subtitles including psychosis, bipolar disorder, generalized anxiety disorder, and suicidal thought and attempt. This does not indicate the absence of these disorders. Probably, patients do not want to give information about such personal history on the first visit; therefore, these histories are concealed under the topic of depression, or are ignored. In other words, some other diagnoses might have been masked in the patients diagnosed with depression. However, in any way, the prevalence of psychiatric diseases was found to be higher in migraine patients in Turkey even without considering subtitles or performing any scale (Table 2).

Cardiovascular diseases have been found to be more prevalent especially in the cases diagnosed with migraine with aura (16.5%). A large series prospective study conducted by Kurth et al. attracts attention as a corner stone in terms of such comorbidity. According to this study, 40.000 healthy females aged 45 years or over, who had no stroke or transient ischemic attack in the past and had normal neurological examination, were followed for a long time as 9 years. The risk ratio for ischemic stroke was found to be 2.25 for those under the age of 55 years. Subgroup analysis revealed that the risk of ischemic stroke is increased when CVD risks factors such as age, blood pressure, antihypertansive drug use, DM, body mass index, smoking, alcohol consumption, menstrual status, hormone level, oral contraceptive use, and cholesterol level were added in the presence of active migraine with aura and; however, no relation was found with migraine without aura[13]. Kurth found migraine with aura to be associated not only with ischemic stroke but also with overall major cardiovascular diseases (myocardial infarction (MI), angina, coronary revascularization). Comorbidity of active migraine with aura with MI has been demonstrated in the cases having high Framingham risk score, notably in the presence of high cholesterolemia[12]. The present study has been performed based on patients' self-report. As was mentioned before, no investigation was done concerning comorbid condition. Since cholesterol levels of the cases were not known, cardiovascular diseases have not been considered as parameters. Prevalence of atherosclerotic heart disease (10.7%) and HT (16.3%) was found to be higher in the cases having migraine with aura versus other cases. Family history revealed high prevalence of CAD, with coronary artery disease being the leading ($p \leq 0.0001$).

With regard to the neurological disease, prevalence of neurological comorbidity was higher in migraine with aura cases versus the other cases. Prevalence of epilepsy was found to be 5.9% (1-17%) in migraine cases[9]; it was 1.1% in overall cases and 1.5% in migraine with aura cases. It was found to be lower than the literature information but higher than the prevalence of epilepsy in normal subjects (0.5%)[9,3,22]. In migraine cases, prevalence of abnormal vestibular functions was 34-80%, real vertigo was 26%, motion sickness was 30-50%, idiopathic benign paroxysmal positional vertigo was 18.8%, and the rate of coincidental togetherness of two conditions was 1.1%[18,14]. In the present study, vertigo was present in 4.6% of the cases, of whom 13% had been diagnosed with migraine with aura ($p \leq 0.0001$). This ratio attracts attention as being greater than a coincidental association (%1.1). Moreover, presence of periodical vomiting in 1.7%, motion sickness in 11.8% and dizziness in 6.1% of the cases in association with migraine raised suspicion about abnormal vestibular functions. Difficulty in falling asleep was found in 35.4% of the cases. Although prevalence of difficulty in falling asleep showed variations among migraine cases, it reached up to 30-40%[11,5,15]. Some of them (43.3%) had sleep disorder concomitant with attacks ($p \leq 0.0001$). OSAS has been found to be statistically significant, but a definite comment could

not have been done because of patient number. Prevalence of non-headache pain was found to be 2.9%, but was not statistically significant (p>0.0001). It was higher particularly in migraine with aura and migraine with probable aura cases as compared to the other cases. Musculoskeletal pain has been reported to be more prevalent in the patients with headache versus without headache[8]. Migraine-like headache has been defined in the cases with chronic spinal pain (OR:5.2). Likewise, the frequency of fibromyalgia was found to be 22-40% in migraine cases[19]. Association between allergy and migraine was not found to be significant.

An important and interesting data obtained in this present study is the fact that emotional stress, intensive physical activity, menstrual cycle and seasonal attacks have more intensively triggered the attacks in patients with comorbidities. The second data is the fact that comorbidities, notably nausea, vomiting, phonophobia, dizziness, sleep disorder, and cranial autonomic symptoms, were statistically significantly more prevalent in migraine cases versus the other cases ($p\leq0.0001$). Moreover, an interesting result is the fact that frequency of attacks was higher in the cases having comorbidities as compared to the others ($p\leq0.0001$). According to Visual Analog Scale (VAS), intensity of attacks was higher ($p\leq0.0001$), response time to the recovering drug was longer ($p\leq0.0001$) and remission duration between the attacks was shorter ($p\geq0.0001$). It is known that some comorbid conditions have an impact on the prognosis of migraine and certain comorbidities such as psychiatric disease, sleep disorder, snoring and painful syndromes lead to chronicity in migraine[2]. Our findings raise the question whether effect of comorbidities on clinical picture in migraine (severity of migraine, time to the response to the drug, presence of intensive comorbidity, and shortening in remission duration) might be a parameter in progressing to chronicity.

The present study is important in terms of being the first multicenter study exposing migraine comorbidities and their reflections in clinical practice. Self-report of the patients that had not undergone further analysis for definite diagnosis has been evaluated for comorbidity. This can be considered as a limitation. However, obtaining the statement during face-to-face interview with the physician and taking the anamnesis via a physician make this study superior to the questionnaire studies. Well-structured studies are needed to evaluate comorbidities and their impact on migraine progression.

Conflict of Interest: None

Financial support: This work was in part supported with a section grant from the Turkish Headache Study Group

[4] **The Names of the Study Centers and Participating Staff**

Adnan Menderes University School of Medicine, Aydın; **Ali Akyol**, MD, **Emine Yılmaz**, MD.

Bakirkoy Research and Training Hospital for Psychiatric and Neurological Diseases, Istanbul; **Musa Ozturk,** MD.

Baskent University Faculty of Medicine, Adana; **Basak Karakurum Goksel,** MD, **Sibel Karaca,** MD**.**

Celal Bayar University School of Medicine, Manisa; **Deniz Selçuki,** MD.

Cukurova University School of the Medicine, Adana; **Sebnem Bicakci,** MD.

Dokuz Eylul University School of the Medicine, Izmir; **Vesile Ozturk,** MD, **Zumrut Halilova** MD**.**

Dicle University School of the Medicine, Diyarbakir**; Nebahat Tasdemir,** MD.

Ege University School of the Medicine, Izmir; **Hadiye Sirin,** MD

Firat University School of the Medicine**,** Elazig**; Serpil Bulut,** MD

Gazi University School of th Medicine**,** Ankara; **Deniz Eylem Yalcinkaya Tellioglu,** MD **Gamze Aydin,** MD, **Hayrunisa Bolay,** MD.

Hacettepe University School of th Medicine, Ankara; **Tulay Kansu,** MD

Haydarpasa Training and Research Hospital, Istanbul: **Fusun Mayda Domac** MD

Istanbul University Capa School of Medicine, Istanbul; **Zuhal Yapici,** MD**, Betul Baykan,** MD

Istanbul University Cerrahpasa School of Medicine,, Istanbul; **Derya Uluduz,** MD

Kirikkkale University School of th Medicine, Kirikkale ;**Ali Kemal Erdemoglu,** MD

Kocaeli University School of th Medicine, Kocaeli; **Macit Selekler,** MD, **Murat Akbas,** MD**, Nur Altun,** MD, **Rengin Gunay,** MD.

Maltepe University School of th Medicine, Istanbul; **Nilgun Cinar,** MD **Sunay Ayalp,** MD

Mersin University School of th Medicine, Mersin; **Aynur Ozge,** MD**, Emis Eken,** MD, **Erol Unaldi,** MD, **Osman Ozgur Yalin,** MD**, Seda Bayram,** MD**, Selver Burcu Yuksek Yalcın,** MD, **Sema Erol Cakmak,** MD**, Yusuf Dikici,** MD.

Mustafa Kemal University School of th Medicine**,** Antakya**; Taşkın Duman,** MD

Training and Research Hospital, Ankara; **Ozlem Coskun** , MD

Uludag University School of th Medicine**,** Bursa; **Necdet Karli,** MD

Vakıf Gureba Training and Research Hospital, İstanbul; **Azize Esra Gursoy,** MD

Correspondence to:
Sebnem Bicakci
E-mail: sebnembicakci@gmail.com

Received by: 14 December 2013
Revised by: 24 January 2014
Accepted: 25 January 2014

The Online Journal of Neurological Sciences (Turkish) 1984-2014
This e-journal is run by Ege University Faculty of Medicine,
Dept. of Neurological Surgery, Bornova, Izmir-35100TR
as part of the Ege Neurological Surgery World Wide Web service.
Comments and feedback:
E-mail: editor@jns.dergisi.org
URL: http://www.jns.dergisi.org
Journal of Neurological Sciences (Turkish)

Abbr: J. Neurol. Sci.[Turk]
ISSNe 1302-1664

REFERENCES

1. *Bicakci S.Comorbidity of Migraine. Archives of Neuropsychiatry. 2013; 50 Supplement 1: 14-20.*
2. *Bigal ME, Lipton RB. Modifiable Risk Factors for Migraine Progression. Headache. 2006; 46:1334-43*
3. *Bigal ME, Lipton RB, Cohen J, Silberstein SD. Epilepsy and migraine. Epilepsy Behav. 2003; 4 (Suppl 2):13-24.*
4. *Breslau N, Lipton RB, Stewart WF, Schultz LR, Welch KM. Comorbidity of migraine and depression: investigating potential etiology and prognosis. Neurology. 2003; 60: 1308-12.*
5. *Cevoli S, Giannini G, Favoni V, Pierangeli G, Cortelli P. Migraine and sleep disorders Neurol Sci. 2012; 33: (Suppl 1):43–46.*
6. *Ertas M, Baykan B, Kocasoy Orhan E, Zarifoglu M, Karli N, Saip S, Onal AE, Siva A. One-year prevalence and the impact of migraine and tension-type headache in Turkey: a nationwide home-based study in adults. J Headache Pain.2012;13:147–57.*
7. *Feinstein A. The pre-therapeutic classification of co-morbidity in chronic disease. J Chronic Dis. 1970;23: 455-68.*
8. *Hagen K, Einarsen C, Zwart JA, Svebak S, Bovim G. The co-occurrence of headache and musculoskeletal symptoms amongst 51 050 adults in Norway. Eur J Neurol 2002; 9:527-33.*
9. *Hauser WA, Annegers JF, Kurland LT. Prevalence of epilepsy in Rochester, Minnesota: 1940-1980. Epilepsia. 1991;32:429-5.*
10. *Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders, 2nd edn. Cephalalgia. 2004;24 (Suppl. 1):8–160.*
11. *Kelman L, Rains JC. Headache and sleep: examination of sleep patterns and complaints in a large clinical sample of migraineurs. Headache 2005;45:904–10.*
12. *Kurth T, Schürks M, Logroscino G, Gaziano JM, Buring JE. Migraine, vascular risk, and cardiovascular events in women: prospective cohort study. BMJ. 2008; 337: 1-9.*
13. *Kurth T, Slomke MA, Kase CS, Cook NR, Lee IM, Gaziano JM, Diener HC, Buring JE. Migraine, headache, and the risk of stroke in women: a prospective study. Neurology. 2005; 64:1020-26.*
14. *Lempert T, Neuhauser H. Epidemiology of vertigo, migraine and vestibular migraine. J Neurol. 2009; 256:333-8.*
15. *Lipton RB, Bigal ME, Ashina S, Burstein R, Silberstein S, Reed ML et al. . Cutaneous allodynia in the migraine population. Ann Neurol. 2008; 63:148–158.*
16. *Lipton RB, Stewart WF. Prevalence and impact of migraine. Neurol Clin. 1997;15: 1-13.*
17. *Merikangas KR, Angst J, Isler H. Migraine and psychopathology. Results of the Zurich cohort study of young adults. Arch Gen Psychiatry. 1990;47:849-53.*
18. *Neuhauser H, Leopold M, von Brevern M, Arnold G,and Lempert T. The interrelations of migraine,vertigo, and migrainous vertigo. Neurology. 2001;56: 436–4.*
19. *Peres MF, Young WB, Kaup AO, Zukerman E, and Silberstein SD. Fibromyalgia is common in patients with transformed migraine. Neurology. 2001;57:1326–28.*
20. *Sacco S, Olivieri L, Bastianello S, Carolei A. Comorbid neuropathologies in migraine J Headache Pain. 2006; 7:222–230.*
21. *ScherAI, Bigal ME, Lipton RB. Comorbidity of migraine. Curr Opin Neurol. 2005;18:305-10.*
22. *Striano P, Belcastro V, Verrotti A, Parisi P. Epilepsi ‘‘Comorbidity"between epilepsy and headache/migraine: the other side of the same coin. J Headache Pain. 2011;12:577–78.*
23. *Wang SJ, Chen PK, Fuh JL. Comorbidities of migraine. Front Neurol 2010; 23:1-16.*