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Demographic, clinical and comorbidity data in a large sample of 1147 patients with migraine in Mexico City

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Abstract The objective was to identify the sociodemographic and clinical characteristics of a large sample of patients with migraine in Mexico City. This cross-sectional study was performed in two tertiary centers in Mexico City and affiliated hospitals. We evaluated the presence of migraine through a standardised interview according to the criteria of the International Headache Society. We studied 1147 patients. The mean age was 37.1±13.6 (6–77) years. Nine hundred and twenty one patients were female (80%). The age of onset of migraine was 19.4±10.3 (1–69) years. Six hundred and four patients had migraine with aura (53%) and 543 without aura (47%). The female/male ratio was 4:1. One hundred and forty-seven patients had cardiovascular problems (13%), 72 had neurological problems (6%), 233 had gastrointestinal problems (20%) and 323 had psychiatric problems (28%). In this study we described the clinical characteristics of a large sample of patients with migraine in Mexico City. Our sample has similar characteristics to other countries.

Key words Migraine • Migraine with aura • Headache • Triggers • Associated conditions • Tertiary centre • Developing countries • Migraine clinic

Introduction

Epidemiology has several important implications for the diagnosis and treatment of migraine. Migraine's prevalence and distribution in different countries and its impact on individuals and on societies needs to be addressed. Examination of sociodemographic, familial and environmental risk factors helps to identify the groups at highest risk for headache and may ultimately provide clues to preventive strategies or mechanisms of the disease [1]. At the present time clinical studies of migraine are more reliable because they use the criteria of the International Headache Society (IHS), which are more complete, explicit and rigorous than the criteria that were used in previous studies [2–4].

Migraine prevalence varies by age and gender. Before puberty, migraine prevalence is higher in boys than in girls; then the prevalence increases more rapidly in girls than in boys as adolescence approaches [5, 6]. Prevalence increases until approximately age 40, when it declines [7, 8]. The gender ratio also changes with age. Cyclical hormonal changes associated with menses may account for some aspects of the migraine prevalence ratio. However, hormonal factors cannot account for all of the gender differences; prevalence remains substantially higher in women than men, even at 70 years of age, well beyond the time that cyclical hormonal changes may be considered a predisposing factor [9].

Migraine is comorbid with a number of neurological and psychiatric disorders. Understanding the comorbidity of migraine is potentially important from a number of different perspectives. First the occurrence of comorbidity has implications for the diagnosis of headache because migraine has a substantially symptomatic overlap with several of the comorbid conditions, for example migraine and epilepsy can cause transient alterations of consciousness as well as headache. Second, comorbidity has important implications for treatment. Comorbid conditions may impose therapeutic limitations, but may also create therapeutic opportunities. For example, when migraine and depression occur together, an antidepressant may successfully treat both conditions. Finally the study of comorbidity may provide epidemiological clues to the fundamental mechanism of migraine [10].

The American Migraine Study [9] found that approximately 23 million Americans suffered severe migraine; more than 85% of women and 82% of men with severe migraine had a headache-related disability. This is a chronic disorder that usually accompanies the patient from his diagnosis through the rest of his life. Epidemiological information in developing countries is scant and is necessary because risk factors and social attitudes toward migraine can be identified, which may influence health care. In this study we described the characteristics of a large population of patients with migraine that were prospectively included in a genetic study exploring clinical characteristics and comorbidity.

Materials and methods

This cross-sectional study was performed at the Neurology Department of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ) and the Migraine Clinic of the National Institute of Neurology. These hospitals are national reference centres for different neurological diseases in Mexico. The study was approved by the local Institutional Review Board of the two institutions. The data collection was performed between March 2003 and July 2004. Patients with known secondary causes of headache and patients who declined the interview and the clinical examination were not included. Patients were approached for consent to participate in our study in a consecutive manner. Through a standardised interview according to the criteria of the IHS and a physical examination performed by a physician, we evaluated the presence of migraine. The headache test uses 49 questions and classifies headache into migraine with aura (MA), migraine without aura and tension headache; it also assesses the type and frequency of pain medications used for the treatment of headache. For this study we only used the migraine section. It has been previously tested in a healthy Mexican population [11–13]. This questionnaire measures some sociodemographic data and disability. All previous or present disease manifestations were recorded from patient's clinical files and with a clinical interview. A blood sample was taken from all patients to perform a genetic analysis (these results will be available at the end of 2005). We used the MIDAS questionnaire to evaluate headache-related disability [14]. The presence of migraine in the last year was ascertained according to the validated questionnaire [11]. The percentage of patients who refused to participate was 5%.

Statistical analysis

A descriptive analysis was used in accordance with the level of measurement of the variables. Patients were grouped according to the presence or absence of aura, to compare several sociodemographic, clinical and morbidity characteristics. Mann-Whitney or *t*-test and Chi-square tests were performed to evaluate associations with quantitative and categorical variables respectively; the significance was adjusted at $p<0.05$. To compare the frequency of migraine in the different age groups we calculated the risk ratio (RR) and its 95% CI. Statistical analysis was performed with SPSS v10 for Windows.

Results

General description

We studied 1147 patients. Mean age was 37.1±13.6 years (6–77). Nine hundred and twenty-one patients were female (80%) and 226 male (20%). The age onset of migraine was 19.4±10.3 years (1–69). The majority of patients had nausea during the episodes of headache (88%), phonophobia (80%) and photophobia (92%). In the analysis by gender, males had an early onset of migraine, higher height and weight and higher frequency of alcoholism and smoking habit. Six hundred and four patients had MA (53%). The rest of the characteristics are shown in Table 1.

Disability and comorbidity

The migraine disability scale showed 341 patients in grade I and II (30%), 399 in grade III (35%) and 407 in grade IV (36%). One hundred and forty-seven patients had cardiovascular problems (13%); the most frequent were hypertension in 120 patients (11%). Seventy-two had neurological problems (6%); the most frequent was benign paroxysmal positional vertigo (BPPV) in 28 (2%). Two hundred and thirty-three had gastrointestinal problems (20%), functional bowel disorders being the most frequent, in 180 (16%). Three hundred and twenty-three patients had psychiatric problems, with depression as the most frequent in 212 (18%). Cardiovascular, neurological and psychiatric medical conditions were more frequent in females with migraine ($p<0.05$) (Tables 2 and 4).

Risk ratio female/male

Table 3 shows the risk ratio (RR) female/male according to different groups of age and types of migraine. The

Table 1 General description of the cohort

	Females (*n*=921)	Males (*n*=226)	*p**	Total (*n*=1147)
General characteristics				
Age, mean±SD	39.3±13.1	31.3±13.8	0.39	37.1±13.6
Age of onset of migraine, mean±SD	20.1±10.3	16.6±10.9	0.001	19.4±10.3
Height, mean±SD	157.1±168.6	168.6±12.4	0.001	159.4±10.3
Weight, mean±SD	63.1±12.0	71.8±14.7	0.001	64.8±13.7
Body mass index, mean±SD	25.4±4.6	24.8±4.4	0.82	25.3±4.5
Migraine with aura, *n* (%)	494 (54)	110 (49)	0.20	604 (53)
Smoking, *n* (%)	184 (20)	73 (32)	0.001	257 (22)
Alcoholism, *n* (%)	43 (5)	26 (12)	0.001	69 (6)
Accompanying symptoms, *n* (%)				
Nausea	816 (89)	187 (83)	0.01	1012 (88)
Vomiting	572 (62)	130 (58)	0.20	741 (66)
Phonophobia	543 (59)	123 (54)	0.21	921 (80)
Photophobia	480 (52)	110 (49)	0.34	1050 (92)

*Comparison between males and females

Table 2 Disability, comorbidity and triggers

	Females, *n* (%) (*n*=921)	Males, *n* (%) (*n*=226)	*p**	Total, *n* (%) (*n*=1147)
Migraine disability				
Grade I and II	264 (29)	77 (34)	0.11	341 (30)
Grade III	326 (35)	73 (32)	0.38	399 (35)
Grade IV	331 (36)	76 (33)	0.51	407 (36)
Comorbidity				
Cardiovascular problems	139 (15)	8 (4)	0.001	147 (13)
Neurological problems	62 (7)	10 (4)	0.20	72 (6)
Gastrointestinal problems	214 (23)	19 (8)	0.001	233 (20)
Psychiatric problems	283 (31)	40 (18)	0.001	323 (28)
Triggers				
Stress	339 (37)	82 (36)	0.88	421 (36)
Menstruation	108 (12)	0 (0)	NC	108 (9)
Food	88 (10)	14 (6)	0.11	102 (9)
Alcohol	60 (7)	16 (7)	0.39	76 (7)
Smoking	49 (5)	12 (5)	0.64	61 (5)
Food	88 (10)	14 (6)	0.28	102 (9)
Stress	339 (37)	82 (36)	0.13	421 (37)
Exercise	25 (3)	17 (8)	0.001	42 (4)
Others	11 (1)	1 (0.4)	0.06	12 (1)

*Comparison between males and females. *NC*, not calculated

female/male RR in the whole population was 4.8 (95% CI 3.8–4.3), in patients with migraine without aura was 3.3 (95% CI 3.0–3.7) and in patients with aura was 4.4 (95 CI 4.1–4.9).

Triggers

The main triggers were stress in 421 patients (36%), menstruation in 108 (9%), food in 102 (9%) and alcohol in 76 (7%). Exercise as a trigger was most frequent in males ($p<0.05$). The other triggers are shown in Table 4.

Comparison between patients with and without aura

We did a comparison between patients with and without aura. We found differences in the clinical symptoms; patients with aura had a higher frequency of nausea, vomiting, phonophobia and photophobia ($p<0.05$). The other characteristics are shown in Table 5.

Discussion

The public health significance of migraine is often overlooked; probably because of its episodic nature and the lack of mortality due to the disorder. Migraine is, however, a frequently incapacitating disorder with considerable impact on social activities and work in the people who suffer it, and may lead to significant consumption of drugs.

The female preponderance in migraine is consistent across the different studies; the majority of the studies show that migraine is more common in females than in males with a ratio of about 1:2 to 3. Both migraine with and without aura show female preponderance [4] and the over-representation of women seems more clear-cut in migraine without aura [3]. In our study all the groups showed a preponderance of females, including the general population and the two groups of migraine analysed in our study. Interestingly the female/male RR in patients of less than 15 years is slightly favourable to the males in the general population of migraineurs and in migraineurs without aura. Only the patients with aura showed a female preponderance in this age group (Table 3). This observation agrees with the previous observations of Bile [15]. They showed that the prevalence of migraine rises from 1% at 6 years of age to 5% at 15 years of age. No sex difference was apparent until age 11; above that age a female preponderance appeared.

The most common age of onset of migraine is in the second and third decade and onset is infrequent after middle age [16]. The mean age of onset of migraine in our cohort is in the second decade, in accordance with the observations in previous studies. Interestingly, the

Table 3 Female/male risk ratio in different groups of age and type of migraine

	Females, *n* (%)	Males, *n* (%)	RR (95% CI)
General population			
Less than 15 years	22 (2)	29 (13)	0.7 (0.4–1.1)
15–29 years	202 (22)	74 (33)	2.7 (2.3–3.1)
30–45 years	367 (40)	86 (38)	4.2 (3.4–4.7)
45–59 years	272 (30)	31 (14)	8.7 (7.7–9.8)
Over 60 years	58 (6)	6 (3)	9.6 (7.3–12.5)
Overall	921 (100)	226 (100)	4.8 (3.8–4.3)
Migraine without aura			
Less than 15 years	9 (2)	21 (17)	0.4 (0.2–0.8)
15–29 years	92 (22)	40 (32)	2.3 (1.8–2.8)
30–45 years	171 (41)	45 (36)	3.8 (3.2–4.4)
45–59 years	118 (28)	16 (13)	7.3 (6.1–8.8)
Over 60 years	29 (7)	2 (2)	14.5 (9.7–20.8)
Overall	419 (100)	124 (100)	3.3 (3.0–3.7)
Migraine with aura			
Less than 15 years	13 (3)	8 (7)	1.6 (0.8–2.7)
15–29 years	110 (22)	38 (35)	2.8 (2.3–3.4)
30–45 years	194 (39)	46 (42)	4.2 (3.6–4.8)
45–59 years	151 (31)	14 (13)	10.7 (9.1–12.6)
Over 60 years	26 (5)	4 (4)	6.5 (4.2–9.5)
Overall	494 (100)	110 (100)	4.4 (4.1–4.9)

RR, risk ratio

Table 4 Comorbidity of migraine (*n*=1147)

Disease	Females, *n* (%) (*n*=921)	Males, *n* (%) (*n*=226)	*p*	Total, *n* (%) (*n*=1147)
Cardiovascular problems (overall)	139 (15)	9 (4)	0.001	147 (13)
Hypertension	113 (12)	7 (3)	0.06	120 (10)
Raynaud phenomenon	5 (1)	0 (0)	0.56	5 (0.4)
Mitral valve prolapse	3 (0.3)	0 (0)	0.19	3 (0.2)
Ischaemic cardiopathy	7 (1)	0 (0)	0.47	7 (0.6)
Other cardiovascular problems	11 (1)	1 (0.4)	0.11	12 (1)
Neurological problems (overall)	62 (7)	10 (4)	0.20	72 (6)
Epilepsy	15 (2)	3 (1)	0.15	18 (2)
BPPV	25 (3)	3 (1)	0.38	28 (2)
Stroke	1 (0.1)	0 (0)	0.16	1 (0.08)
Other neurological problems	21 (2)	4 (2)	0.14	25 (2.1)
Gastrointestinal problems (overall)	214 (23)	19 (8)	0.001	233 (20)
Functional bowel disorders	164 (18)	16 (7)	0.56	180 (16)
Peptic problems	13 (1)	2 (1)	0.57	15 (1)
Others	37 (4)	1 (0.4)	0.17	38 (3)
Psychiatric problems (overall)	283 (31)	40 (18)	0.001	323 (28)
Depression	191 (21)	21 (9)	0.06	212 (18)
Anxiety disorders	64 (7)	10 (4)	0.73	74 (6)
Other psychiatric problems	28 (3)	9 (4)	0.01	37 (3)

BPPV, benign paroxysmal positional vertigo

Table 5 Comparison between patients with and without aura

	Without aura (*n*=543)	With aura (*n*=604)	*p*
Age, mean±SD	37.3±13.8	37.9±13.3	0.4
Age of onset of migraine, mean±SD	20.0±10.1	18.9±10.9	0.08
Height, mean±SD	158.5±11.8	150.1±8.6	0.08
Weight, mean±SD	64.0±14.1	65.4±13.3	0.33
Body mass index, mean±SD	25.2±4.4	25.4±4.7	0.07
Females, *n* (%)	494 (91)	419 (69)	0.20
Headache in the family, *n* (%)	334 (62)	383 (63)	0.85
Migraine disability (Grade IV), *n* (%)	269 (50)	331 (55)	0.17
Nausea, *n* (%)	451 (83)	542 (90)	0.01
Vomiting, *n* (%)	285 (52)	412 (68)	0.00
Phonophobia, *n* (%)	270 (50)	392 (65)	0.00
Photophobia, *n* (%)	237 (44)	351 (58)	0.00
Cardiovascular problems, *n* (%)	67 (12)	78 (13)	0.92
Neurological problems, *n* (%)	29 (5)	43 (7)	0.27
Gastrointestinal problems, *n* (%)	101 (19)	131 (22)	0.26
Psychiatric problems, *n* (%)	141 (26)	177 (29)	0.29
Food, *n* (%)	35 (6)	66 (11)	0.01
Menstruation, *n* (%)	181 (33)	238 (39)	0.06
Stress, *n* (%)	52 (10)	55 (9)	0.76

age of onset was earlier in males (Table 1). Other observations such as the larger height and weight of the Mexican males with migraine are expected observations according to previous studies in the Mexican population [17].

MA is a primary headache disorder that affects about 30% of migraine sufferers. In some patients MA is associated with attacks of migraine without aura and this coexistence has sparked a debate as to whether these forms of migraine are actually clinically distinct entities [18]. The

IHS diagnostic criteria provide a clinical description of the aura; aura consists of transient, unilateral or bilateral visual, sensory or motor symptoms considered to arise from a recurrent reversible, idiopathic dysfunction of the cortex or brainstem. One of the most important findings in our study was the high frequency of MA. In the majority of studies performed in the general population the frequency varies from 15% to 30%. We consider that this finding could be explained by a reference bias. Both institutions are national reference centres for complex neurological conditions and this could be the reason for the high prevalence of MA. On the other hand it is worth noting the high frequency of accompanying symptoms in patients with aura; this observation could be explained in the same way as the high frequency of patients with aura. It is possible that the most complicated patients are referred to specialised centres in Mexico. This preponderance of patients with MA with more complications and more symptoms has been seen in studies of epilepsy clinics and tertiary centres in other populations [19, 20].

Migraine and epilepsy are comorbid. Andermann reported a median epilepsy prevalence of 5.9% (range 1%–17%) in migraineurs, which greatly exceeds the population prevalence of 0.5% [21, 22]. Perhaps an altered brain state increases the risk of both migraine and epilepsy and thus accounts for the comorbidity of these disorders [22]. Genetic or environmental risk factors may increase neuronal excitability or decrease the threshold for both types of attacks. A reduction in brain magnesium [23] or alterations in neurotransmitters provide plausible potential substrates for this increase in neuronal excitability [24]. In our study the frequency was 2%, which is in the range of reported frequencies.

The comorbidity of migraine with psychiatric conditions is well established [25]. As for affective disorders, the lifetime prevalence of major depression is 34.4% in patients with migraine and 10.4% in patients without migraine. The lifetime prevalence of anxiety disorders in migraine is significantly increased in comparison to controls with panic disorders (10.9% *vs*. 1.8%), generalised anxiety disorders (8.6% *vs*. 1.8%) and phobic disorders (39.8% *vs*. 20.6%). In our study the most frequent disorders were depression and anxiety disorders. The main bias in this observation is the source of the information. As we comment in methods, we obtained the information from the clinical charts and a general interview with the patients. It is possible that if we had done a direct evaluation of psychiatric comorbidity we would have obtained a higher frequency of these alterations. For this reason the frequency of depression is lower in our population than that reported in the literature.

The ascertainment of chronic conditions varies in the different studies performed in several countries. In our study we used the information contained in charts and the information supplied by the patient; this being the main weakness of our study because we could over- or underestimate the prevalence of the different medical conditions. Even so, many researchers have found a good correlation between the different methods of measuring comorbidity and our method is a widely accepted methodology to ascertain many chronic medical conditions including hypertension, coronary heart disease, cancer, arthritis and other cardiovascular diseases. On the other hand the lack of a control group does not permit the estimation of the prevalence of these chronic medical conditions in the general population to perform a comparison with migraineurs [10, 26, 27].

Many environmental factors and physiologic influences may provoke a migraine attack or increase its severity. Menstruation is a common migraine trigger or enhancer. Changes in body rhythm such as sleep deprivation, too much sleep or fasting may provoke an attack. Minor head trauma and changes in weather may trigger migraine. In approximately 15%–20% of patients with migraine, foods may be a provocative factor; foods that are related to migraine are chocolate, strong cheeses, citrus fruits and sometimes the sweetener aspartame; they may all trigger a migraine attack. Excessive use of caffeine-containing foods and caffeine withdrawal may trigger both migraine and tension headaches [28]. In our study the main trigger was stress in 36%, followed by menstruation and food, which are classically described as the principal triggers.

In this study we described the clinical characteristics of a large sample of patients with migraine in Mexico City. The majority of characteristics of our sample are similar to other reports, except that in our sample the frequency of MA was higher. This finding could be explained by a reference bias of the participating institutions, but it could be explained by genetic and race variations.

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