



Poor patient awareness and frequent misdiagnosis of migraine: findings from a large transcontinental cohort

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Background and purpose: Although migraine is the second most disabling condition worldwide, there is poor awareness of it. The objective was to assess the awareness of migraine and previous diagnostic and therapeutic consultations and treatments in a large international population of migraineurs.

Methods: This was a multicentre study conducted in 12 headache centres in seven countries. Each centre recruited up to 100 patients referred for a first visit and diagnosed with migraine. Subjects were given a structured clinical questionnaire-based interview about the perceptions of the type of headache they suffered from, its cause, previous diagnoses, investigations and treatments.

Results: In all, 1161 patients completed the study. Twenty-eight per cent of participants were aware that they suffered from migraine. Sixty-four per cent called their migraine 'headache'; less commonly they used terms such as 'cervical pain' (4%), tension headache (3%) and sinusitis (1%). Eight per cent of general practitioners and 35% of specialists (of whom 51% were neurologists and/or headache specialists) consulted for migraine formulated the correct diagnosis. Before participating in the study, 50% of patients had undergone X-ray, computed tomography and/or magnetic resonance imaging of the cervical spine and 76% underwent brain and/or cervical spine imaging for migraine. Twenty-eight per cent of patients had received symptomatic migraine-specific medications and 29% at least one migraine preventive medication.

Conclusions: Although migraine is a very common disease, poor awareness of it amongst patients and physicians is still an issue in several countries. This highlights the importance of the promotion of migraine awareness to reduce its burden and limit direct and indirect costs and the risk of exposure to useless investigations.

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Introduction

Migraine is the third most frequent disorder worldwide with a 1-year prevalence of 14.7% [1] and is the second most disabling disease globally [2,3].

Until recent years, migraine remained underdiagnosed and undertreated [4–7]. This is probably due to the facts that patients choose to self-diagnose or not seek professional care for a number of reasons [8,9], and non-specialized professionals often misdiagnose migraine with other diseases. The most frequent alternative misdiagnoses are ‘sinusitis’ [10,11], ‘allergy’ [11], ‘cervical pain syndrome’ [12] and tension-type headache [7,8]. Importantly, a large proportion of patients who believe they suffer from one of the latter conditions undergo unnecessary medical imaging including radiation exposure in 40% of cases and receive inappropriate treatments [10,12].

In this study, the aim was to assess whether patients belonging to a large population of migraineurs seen at tertiary headache centres in seven countries were aware they were suffering from migraine, and to document prior specific diagnostic and therapeutic consultations and treatments.

Methods

This was a multicentre study conducted at 12 headache centres in seven countries worldwide (Table 1). One of the main requirements for selecting researchers was good translation capabilities. The study was approved by local ethics committees of each participating centre. All patients gave informed consent before taking part in the study.

The study was conducted between 1 July 2015 and 31 October 2016. Each centre was asked to recruit 100 consecutive patients, with the lowest acceptable number set at 50 subjects.

Inclusion criteria were (i) subjects aged 18–75 years referred to the headache centre/clinic for a first visit; (ii) diagnosis of episodic migraine with aura and/or migraine without aura and/or chronic migraine according to the International Classification of Headache Disorders 3rd edition (ICHD-III beta) criteria [13]. Exclusion criteria were (i) subjects who were not native speakers for the national language and (ii) subjects with a headache onset within the previous year.

Procedures

At each site patients were evaluated by a neurologist certified as a headache specialist, who diagnosed the type of headache via ICHD-III beta criteria [13] during a regular consultation. All consecutive patients diagnosed with migraine and willing to participate were recruited after obtaining informed consent.

Included patients were asked nine questions by the treating neurologist. The following topics were covered: (i) the names the patients gave their headache before the visit; (ii) what patients thought was/were the cause(s) of their headaches; (iii) what diagnosis(es) they received from their general practitioner (GP) or other medical professionals; (iv) which visits and para-clinical exams they performed/underwent for migraine; (v) which treatments (either pharmacological or non-pharmacological) they tried specifically for migraine; (vi) if they had first and/or second degree relatives affected with migraine. The neurologist

Table 1 Number of participants recruited by centre per country

Country	Headache centre	No. of participants per centre	No. of participants (total per country out of the whole population) (%)
Brazil	Medicine School of Barbacena (FAME/FUNJOB) and Hospital Foundation of Minas Gerais	101	101 (8.7)
Italy	Mondino National Neurological Institute, Pavia	102	602 (51.9)
	Interdepartmental Center for Headache and Drug Abuse, Padua University, Padua	104	
	University of Florence and Headache Center, Careggi University Hospital, Florence	85	
	Headache Center, Azienda Ospedaliera ‘Pugliese – Ciaccio’ Catanzaro	100	
	Headache Center, Department of Neurology and Psychiatry, Sapienza University, Rome	102	
	Headache Center, Policlinico Universitario di Palermo, Palermo	109	
Moldovia	National Headache Center, Republic of Moldova	100	100 (8.6)
Mexico	Clínica de Cefaleas y Dolor Crónico No Oncológico, Hospital Universitario, Monterrey	100	100 (8.6)
Argentina	Centro de cefaleas, Hospital de Clínicas José San Martín, Buenos Aires	100	143 (12.3)
	Servicio de Neurología, Hospital Alemán, Buenos Aires	43	
Chile	Dipreca Headache Center, Santiago	56	56 (4.8)
Uruguay	Headache Center, Hospital Maciel, Servicio de Neurología, Montevideo	59	59 (5.1)

conducting the consultation read the questions from a questionnaire to the patients in the official language spoken in each participating country (Italian, Portuguese, Romanian, Spanish).

The questionnaire was developed in English (Appendix S1)) and subsequently translated to the national language by a panel of researchers for each country. Guidelines reported in 'Translation protocol for hybrid documents' [14] were followed to ensure a high quality of translation. The first version of the questionnaire in the four languages was back-translated into English by a translator to check for appropriateness of translation, finally creating the back-checked consensus-based translation for each of the four languages.

Following completion, each researcher uploaded the patients' answers, socio-demographic data (age, gender, country region, educational and socio-economic level) and clinical data (pain characteristics, presence of associated symptoms such as nausea, vomiting, photo/phonophobia) on a structured form on a dedicated web platform (<http://www.protocolliweb.com/themigrainequestionnaire>).

All the open-text answers (OTAs) were translated into English by researchers before being inserted into the database. A second independent review performed by another researcher belonging to the same language group was performed to ensure a correct translation of the OTAs. Two researchers (MV and FK) independently categorized the OTAs. Any disagreement between the two authors was resolved by consensus by involving a third person (CT).

The Coordinator Centre (Mondino National Neurological Institute, Pavia, Italy) performed the analysis of the data.

Statistic procedures

The Statistical Package for Social Sciences (SPSS) version 24 was used for the statistics. Data are presented as mean \pm SD (range) for continuous variables and as $n/\%$ for categorical variables. Analyses of variance (ANOVAS) were carried out to evaluate differences between subgroups of patients belonging to the same country ($n = 7$). Pearson's chi-squared tests were used for 2×7 tables in order to compare proportions amongst the seven groups. Comparison of the seven participating countries in the study was assessed by using univariate analysis. Due to multiple testing over 13 variables, adjusted P values based on the Bonferroni correction were considered. The significance level was therefore lowered to $P < 0.0038$ ($P = 0.05/13$).

Differences in socio-demographics and clinical variables were also compared by using univariate analysis between two groups: (i) migraine patients who were

aware they suffered from migraine and those who were not, and (ii) migraine patients who believed they suffered from 'cervical pain attacks' (CP) and those who did not. Following this, a multivariate analysis was carried out. In this analysis, only those variables that had a statistical significance of $P < 0.15$ in the univariate analysis were considered. As a multivariate analysis was applied for such variables, Bonferroni correction was not strictly required. Such analysis identifies variables that are independent risk factors. A value of $P < 0.05$ was considered significant. All P values were two-tailed.

Results

All participating centres enrolled at least 50 patients each, accounting overall for 1161 participants. The distribution of patients across headache centres/countries is reported in Table 1. Around half of participants ($n = 602$) were recruited from Italy. Nine hundred and thirteen (78.6%) patients were female, and the mean (SD) age was 39 ± 13 years. Seven hundred and seventy-five subjects (66.8%) had a high education level (high school or university). Other characteristics of the subjects and features of migraine attacks as well as migraine history are reported in Table S1.

Of 1161 patients, 326 (28%) were aware that they suffered from migraine whilst 64% of the whole population called their migraine 'a headache'. Other less commonly used terms were CP (4%, mostly in Italy), tension headache (3%, mostly in Mexico, Chile and Uruguay) and sinusitis (1%) (Table S2).

All patients had previously visited a GP for their migraine and only 28% of patients were correctly diagnosed with the disorder (Table S3). Eighty per cent of patients had visited at least one specialist for their migraine (Table S4). Of these, 51% were neurologists and/or headache specialists and 35% formulated the correct diagnosis (Table S3). Overall 13% of patients were accurately diagnosed by both their GP and another specialist. With respect to diagnostics, 50% of patients ($N = 577$) were prescribed with an X-ray and/or computed tomography (CT) and/or magnetic resonance imaging (MRI) of the cervical spine, whereas 76% of patients ($N = 890$) underwent imaging of the brain and/or cervical spine that exposed them to radiation (Table S4).

Three hundred and twenty-nine patients (28%) of our whole migraine population had previously received a symptomatic migraine-specific medication (triptans and/or ergots) (Table S5), of whom 64% ($N = 212$) reported having received a diagnosis of migraine by a GP. Twenty-nine per cent ($N = 342$)

had received at least one migraine preventive medication (Table S5) of whom 81% ($N = 276$) reported having received a diagnosis of migraine by a GP. Thirty-eight per cent ($N = 124$) of patients correctly diagnosed with migraine by their GP and 38% ($N = 161$) of those accurately diagnosed with migraine by another practitioner received migraine-specific medications.

When comparing characteristics of patients across different countries, it was found that subjects from Mexico had the highest rate of awareness of their migraine (51%) followed by Chile (39%), Argentina (34%), Brazil (30%), Italy (25%), Moldova (17%) and Uruguay (12%) (Table S6).

The highest rates of previous migraine diagnosis by another physician were seen in Argentina (68%, specialist MD), Mexico (66%, GP), Moldova (53%, specialist MD) and Uruguay (52%, specialist MD). Despite being differently prevalent across different countries, stress was reported as the most frequent trigger of headache by patients, including 68% and 29.4% of patients from Mexico and Italy respectively (Table S6).

On multivariate analyses, high educational level [odds ratio (OR) 1.97, 95% confidence interval (CI) 1.43–2.78, $P < 0.001$], number of family members with migraine (OR 1.17, 95% CI 1.04–1.31, $P = 0.005$), throbbing pain (OR 2.02, 95% CI 1.23–3.31, $P = 0.005$), lateralization of pain (OR 1.36, 95% CI 1.01–1.83, $P = 0.043$) and vomiting (OR 1.43, 95% CI 1.06–1.93, $P = 0.018$) independently increased the likelihood of being aware of the diagnosis of migraine, whilst a shorter duration of attacks decreased it (OR 0.98, 95% CI 0.97–0.99, $P = 0.001$). The output of the univariate analysis and the list of variables that were included in the multivariate analysis are reported in Table S7.

At univariate analysis patients who believed they suffered from CP ($n = 51$) more frequently experienced bilateral pain ($P = 0.001$) and pain located to the back of the head ($P < 0.001$). Only these two variables reached a P value of < 0.15 in the analysis and were therefore entered into the multivariate analysis. Only pain in the back of the head remained significantly associated with the self-diagnosis of CP on multivariate analysis (OR 2.53, 95% CI 1.22–5.23, $P = 0.012$).

Discussion

In this international multicentre study, the intention was to assess the current state of patient awareness of migraine in a large international population of migraineurs. It was found that only 28% of patients were

aware that they were experiencing migraine. This is quite surprising considering that these patients had already seen at least one doctor and 80% at least one head and neck pathology specialist before their visit to one of the study centres. Even more remarkably, about half of patients had specifically visited another neurologist/headache centre for their current headache, implying a previous incorrect or misunderstood diagnosis.

Accordingly, less than one-third of patients received migraine-specific symptomatic and migraine preventive medication. Previous studies on a US migraine population found that only 20% of patients treated their acute attacks with prescribed medications [15] and 12% of migraineurs used a daily preventive migraine medication [16].

More than half of our study population was Italian, and our results are in line with those of another Italian study showing that, amongst 2675 patients with migraine attending a headache centre for the first time, only 26.8% had been previously identified as migraineurs, although 62.4% of them had consulted their GP and 38.2% a headache specialist in the previous year [6]. In another prospective study involving over 77 000 Mexican women, migraine was identified by means of questionnaires in 19% of the population, 45.1% of these having received a correct diagnosis [17]. This figure is higher than ours overall; however, when stratifying patients according to different countries, the proportion was found to be as high as 66% in Mexico. The great variability of migraine misdiagnosis by GPs, but also neurologists and other specialists, across countries probably reflects different substrates that need to be separately addressed in future studies, possibly including issues related to different medical education and practice.

Sixty-seven per cent of patients termed their migraine simply a headache, and other names were used rather infrequently. Interestingly, the term CP was used by 4.4% of the overall population and by 90% of Italian patients, probably reflecting different cultural backgrounds. Similar to our findings, in a previous study 62.3% of migraine patients attending an Italian headache centre termed their headache CP [12]. The localization of pain to the back of the head increased the misbelief that it was CP by 2.5-fold according to multivariate analysis, and in line with previous findings [12].

At least 50% of patients were prescribed with an X-ray and/or CT and/or MRI of the cervical spine, suggesting that a large proportion of GPs suspected the diagnosis of cervicogenic headache, a rarer condition with a clear-cut phenotype [18].

A finding of concern is that 76% of patients underwent examinations that exposed them to radiation. These should only be prescribed by the practitioner in the case of 'red flags' or atypical phenotypes in clinical practice and it is unlikely that this was the case in such a high proportion of our participants [19]. Some studies highlight that even in paediatric patients the use of CT scan to diagnose headache remains high despite existing guidelines [20].

Subjects who were aware that they suffered from migraine had a high educational level (74.8% vs. 63.6%, $P < 0.001$), or had an affected family member (68.4% vs. 61.6%, $P = 0.032$), probably reflecting more rapid and efficient access to information and/or medical care in these conditions. Interestingly, lateral head pain, pain aggravation by physical activity and association with vomiting and phonophobia were also associated with awareness of migraine, suggesting that more specific clinical features help patients and/or physicians distinguish migraine from other causes of neck/head pain. These findings were not consistently replicated when stratifying patients by country, indicating that pain perception and interpretation is largely influenced by the different sociocultural backgrounds [21].

Overall, these results support the importance of campaigns to improve awareness of migraine amongst patients and practitioners. Such measures to improve migraine knowledge should be customized for each country to properly address the specific misbeliefs (with respect to types of misdiagnosis and wrong diagnostic and/or therapeutic paths). Considering a study published in 2013, which highlighted high rates of misdiagnosis and diagnostic and/or therapeutic errors in trigeminal autonomic cephalalgias and hemicrania continua [22], it is suggested that awareness campaigns should also include such disabling headache types.

The limitations of our study must be considered. First, it was performed on patients who had been referred to tertiary headache centres and therefore findings in our sample cannot be generalized to all migraine patients. Yet, it is likely that awareness of migraine would be even lower in the general population. Secondly, the questionnaire is based on the patient's report, and therefore it is possible that the number of misdiagnoses by previous physicians is overestimated due to lack of patient's understanding rather than incorrect diagnosis.

Furthermore, the questionnaire was administered by a specialist; therefore interviewer bias may have taken place. Similarly, the questionnaire was translated into four different languages as appropriate for each headache centre. Although there is confidence

with the translation of the questionnaire, the possibility that the translation of patients' answers from the native language into English could have led to some differences cannot be ruled out.

Moreover, our study used a non-validated questionnaire and is exposed to possible recall biases. However, it is believed that this type of questionnaire represents the best trade-off in this setting, i.e. collecting information on patient's perception in large populations, and unfortunately no similar questionnaires are available which have been validated so far. Finally, there was an unequal number of participants recruited from each country with more than 50% of participants being recruited from Italy, making other groups less representative of their respective countries.

Although variable across countries, it was found that poor awareness of migraine amongst sufferers and those doctors they sought consultation from led to unnecessary risk exposure and costs, and prevented or delayed access to appropriate treatments.

This is still occurring despite current international guidelines which have been translated into many languages. This suggests that different strategies need to be pursued to increase awareness of this medical condition.

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Disclosure of conflict of interest

The authors declare no financial or other conflicts of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Questionnaire.

Table S1. Socio-demographic and clinical data of the whole population ($n = 1161$).

Table S2. Patient perception of the cause of migraine ($n = 1161$).

Table S3. Prior diagnosis received by patients ($n = 1161$).

Table S4. Visits and para-clinical examinations performed for migraine ($n = 1161$ patients).

Table S5. Pharmacological and non-pharmacological treatments tried by the patients ($n = 1161$).

Table S6. Comparison of the seven participating countries in the study.

Table S7. Differences in socio-demographics and clinical variables between the subjects who were aware they suffered from migraine and those who were not.

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