

RESEARCH SUBMISSIONS

Characteristics of migraine in patients with headache disorders: A clinic-based study from Central American and Caribbean countries

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Abstract

Objective: The objective of the study was to measure the proportion of patients who consulted for headache and of those who had a final diagnosis of migraine. We also assessed the proportion and characteristics of patients with migraine and the impact of migraine on the daily activities and the professional and social lives of patients visiting private/public medical centers in Guatemala, Costa Rica, Panama, and the Dominican Republic.

Background: Underdiagnosis of migraine is high in Central America and Caribbean urban communities. However, there is limited knowledge on characteristics of headache disorders for the appropriate classification of migraine, which is a prerequisite for targeted treatment. Hence, there is a need to improve migraine awareness among patients and medical professionals in this region.

Methods: Central America and Caribbean countries epidemiology study of Migraine (CALM) was a non-interventional, cross-sectional, multinational study in adults aged 18–65 years with a history of or current headache. The primary outcome was the proportion of patients with migraine visiting medical centers due to headache disorders. Using a specially designed migraine survey questionnaire, patients self-reported migraine characteristics, duration, and severity of attacks and impact on work and social life.

Results: Of the 313 enrolled patients, 308 (98.4%) completed the study. Approximately 75.3% (232/308) of patients with headache visiting medical centers had migraine, with episodic migraine being the most common (193 [83.2%]). Overall, 34/308 (11.0%) patients had a new diagnosis of migraine. Among patients with migraine, 66 (28.4%) had a history of migraine for ≥ 20 years and 59 (25.4%) experienced severe pain. Overall,

Abbreviations: ADLs, activities of daily living; CAC, Central American and Caribbean; CALM, Central America and Caribbean countries epidemiology study of Migraine; CI, confidence interval; CM, chronic migraine; EM, episodic migraine; SD, standard deviation; USD, US dollar; YLD, years lived with disability.

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52.2% (121/232) of patients reported that migraine affected their professional life and 78.4% (182/232) reported an impact on social life.

Conclusion: The CALM study establishes that a high proportion of patients with migraine had a long duration and high severity of migraine attacks, leading to a direct impact on work/social life as well as on costs incurred by patients in these countries.

KEYWORDS

headache, migraine, quality of life, social impact, work productivity

INTRODUCTION

According to the 2016 Global Burden of Disease survey, migraine was the leading cause of years lived with disability (YLD) in the Central American and Caribbean (CAC) region (i.e., Guatemala, Costa Rica, Panama, and the Dominican Republic).¹

Individuals with migraine report a reduction in quality of life and an increase in disease disability and socioeconomic burden with an increase in the frequency of headache attacks.^{2,3}

Although migraine is a common disorder in urban communities in Latin America, underdiagnosis of migraine is high in this region.^{4,5,6} Despite the high prevalence of migraine and YLD in the CAC region,¹ data on the characteristics of migraine that classify patients according to the number of migraine or headache days per month (episodic migraine [EM] or chronic migraine [CM]), medical specialties attending to these patients, preventive treatments used for migraine, and the impact of migraine on the social or professional life of individuals are scarce.^{5,6}

Central America and Caribbean countries epidemiology study of Migraine (CALM) was the first clinic-based study of its kind on migraine and its classification in the CAC region. This study assessed the proportion of patients with migraine who sought medical attention for headache in the CAC region and the sociodemographic characteristics of patients with migraine visiting the main medical centers in Guatemala (three private centers), Costa Rica (three private centers), Panama (two public and one private center), and the Dominican Republic (two private centers). This study also assessed the effect of migraine on the quality of life of patients. This study was mainly conducted in secondary health-care centers recognized as reference sites for headache/migraine treatment (a combination of public and private sites). Findings from this study would provide insights for further research in this field and may be taken as a logistical pilot to what could be done in the CAC region.

METHODS

Study design

CALM was a non-interventional, multicenter, multinational, cross-sectional study conducted between January 3, 2019 (first patient, first visit) and November 8, 2019 (last patient, last visit) in the CAC

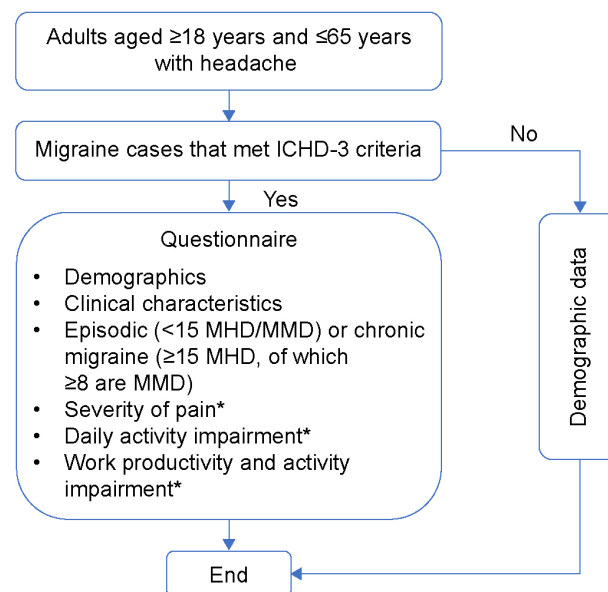


FIGURE 1 Study design. *Collected using standardized questionnaires. ICHD-3, International Classification of Headache Disorders third edition; MHD, monthly headache days; MMD, monthly migraine days.

region (Figure 1). The sites selected in each country were considered reference centers for the treatment of headache or migraine (the referrals were not quantified). Primarily, patients were referred to neurologists from other health-care practitioners. Patients attending the medical centers (the study had only one visit) for the treatment of headache or migraine were invited to participate in the study. There was no screening phase in the study, and only patients who accepted the invitation and met the eligibility criteria were included. Investigators at all participating sites were neurologists, with only one site having an algologist. Patients were assessed on an ongoing basis.

The study was conducted in accordance with the International Conference on Harmonization Good Clinical Practice regulations/guidelines, Guidelines for Good Pharmacoepidemiology Practices of the International Society for Pharmacoepidemiology,⁷ Strengthening the Reporting of Observational Studies in Epidemiology guidelines,⁸ and the ethical principles in the Declaration of Helsinki. All centers complied with the local regulations (see supporting information).

Patient eligibility criteria

Adults aged 18–65 years who had visited any medical center (i.e., hospitals, clinics, or private medical offices) at any time during the study period due to headache disorders, with or without a previous diagnosis of migraine, were enrolled in this study. Patients who were residents of the respective country where the study was conducted, who were willing to complete the self-administered questionnaires, and who provided written informed consent were enrolled.

Patients with any medically unstable condition that precluded appropriate diagnosis, as assessed by the primary treating physician; with headaches related to trauma or other systemic diseases; with acephalgic migraine; with current drug or alcohol use or dependence; or who were unable to complete the survey due to physical or mental disability or were unable to follow instructions or comply with follow-up procedures were excluded.

Data collection

Anonymous patient medical history and baseline data were collected from the medical records and/or patients' interviews at study centers in the participating countries. Patient interviews were conducted for those patients with no previous medical history at the study center. Standardized electronic case report forms were used to extract information from patients' medical records in a strictly anonymized manner. Patients completed a self-administered migraine survey questionnaire that collected data on characteristics of migraine, intensity of pain, duration of attacks, duration of the disease, and prior treatments.

Patients who were diagnosed with migraine as per International Classification of Headache Disorders-3 (ICHD-3) beta criteria⁹ during their visit to the medical center were considered "new cases" and those with a confirmed diagnosis prior to the study were reassessed by the investigator at the medical center. The confirmation of EM and CM was determined using a case report form in which patients were asked to report the monthly migraine days and headache days they have experienced over the last 3 months. After updating this data in the database, the software automatically classified them as having EM or CM.

Parameters evaluated

The key parameters assessed included the proportion of patients with migraine in the CAC region. Among those, the proportions with EM or CM were assessed. Other parameters assessed included:

- The percentage of new migraine cases, and of those the proportion of patients with EM or CM
- The sociodemographic characterization of patients with migraine (association of gender, age, and race)

- Description of the medical history (time elapsed from the first consultation to diagnosis and migraine history)
- Medical specialties involved in migraine diagnosis and treatment
- Migraine management (duration, symptoms, and degree of pain during attacks)
- Utilization of preventive treatments
- Quality of life according to the survey (difficulties in carrying out daily activities as a result of a migraine attack and work productivity and activity impairment as measured by a self-administered questionnaire)
- Overall costs (doctors' fees, emergency room visits, cost of health insurance, and other costs) of migraine treatment, which were analyzed descriptively using a questionnaire completed by the patient
- The intensity of pain was measured on a numeric rating scale ranging from 0 to 10, with 0 indicating no pain, 1–3 indicating mild pain (nagging, annoying, or interferes a little with activities of daily living [ADLs]), 4–6 indicating moderate pain (interferes significantly with ADLs), and 7–10 indicating severe pain (disabling; unable to perform ADLs)¹⁰

Statistical analysis

As this was the primary analysis of migraine data in the CAC region, no historical data were available. Data from clinical trials indicate that the prevalence of migraine is approximately 14.7% in Western European countries among the general population.¹¹ A sufficient sample size was required to estimate proportion of patients with migraine. Hence, the approximate lower limit of confidence interval (CI) of prevalence rate was set at 72% based on the real-time data. This is the first time the questionnaire has been created and used. A sample size of 313 patients was required in the study by considering a 2% dropout rate for 307 evaluable patients across all four countries, which produced a two-sided 95% CI with a width equal to 0.10, considering a margin of error of 5% with a CI of 95% using the Wilson (score) method.

Patients who sought medical attention for headache disorders were potential study participants. The treating physician included those who met the inclusion/exclusion criteria and accepted the invitation to participate.

All investigator-level data, patient demographics, medical history, and other baseline characteristics are presented using standard descriptive statistics. Continuous variables are presented as the mean, standard deviation (SD), 25th percentile, median, 75th percentile, and minimum and maximum values of the distribution. Categorical variables are presented as raw numbers and percentages. All analyses related to the data are presented by the overall population and by migraine types (i.e., EM and CM). Additionally, all analyses related to the data are presented by country and by the nature of the centers (public or private) wherever applicable. All collected data are listed, and the data analysis was performed using SAS® version 9.4 (SAS Institute Inc.). The full analysis set included all patients who had enrolled from medical centers in the CAC region; however, patients who

had protocol deviations were excluded from the full analysis set based on the severity of the protocol deviation as per medical judgment.

For the primary analysis, descriptive summaries are presented for the numbers and percentages of overall patients with migraine and by migraine types. The percentages are reported along with the Agresti–Coull 95% CIs.

For the secondary analysis, the proportions of new migraine cases diagnosed, and migraine subtypes were estimated with a binomial sample proportion and the Agresti–Coull 95% CI for this estimated proportion.

RESULTS

A total of 313 patients with headache disorders were enrolled across the four countries (Guatemala [$N = 94$], Costa Rica [$N = 76$], Panama [$N = 79$], and the Dominican Republic [$N = 64$]). Of these, 308 (98.4%) patients completed the study; four patients were excluded from the final analysis due to protocol deviations and one patient from Costa Rica did not complete the study because of the physician's decision. The study population comprised a pool of patients from both public and private practice.

Sociodemographic characteristics

The demographic characteristics were similar between the countries and with the overall study population. The mean (SD) age of the enrolled patients was 38.6 (10.9) years, the majority were of mixed race or Hispanic (276 [89.6%]) and women (250 [81.2%]), and about half had a family history of migraine diagnosis (148 [48.1%]; [Table 1](#)). More than half (166 [53.9%]) of the patients possessed a bachelor's degree. The proportion of patients with migraine among women and men was 85.3% (198) and 14.7% (34), respectively ([Table 1](#)).

In total, 239 (77.6%) patients had at least one instance of either relevant medical history or current medical condition. The most frequently (>20% of patients) reported historic or current medical conditions were psychiatric disorders (96 [31.2%]) and metabolism and nutrition disorders (78 [25.3%]).

Headache disorder characteristics and migraine

Migraine was diagnosed as the main reason for headache disorders among 232 (75.3%) patients (95% CI: 0.7–0.8) with headache disorder, with EM being the most common type of migraine (193 [83.2%]; 95% CI: 0.78–0.87). Among the patients with EM, the median (range) headache days and migraine days prior to enrollment to the study were 9.5 (0–40) days and 3.0 (0–31) days, respectively. The three most common characteristics and symptoms experienced by patients during a migraine attack were moderate to severe pain (244 [79.2%]), severe pain only on one side of the head (201 [65.3%]), and sensitivity to light and sound (199 [64.6%]).

Of the 232 patients with migraine, 66 (28.4%) had a history of migraine diagnosis for ≥ 20 years, 30 (12.9%) had migraine for

TABLE 1 Demographic characteristics (full analysis set)

Characteristics	All patients (N = 308)	Patients with Migraine (N = 232)
Age, years, mean (SD)	38.6 (10.9)	38.0 (10.7)
Gender		
Women	250 (81.2)	198 (85.3)
Men	58 (18.8)	34 (14.7)
Race		
Caucasian (White)	21 (6.8)	19 (8.2)
Black	11 (3.6)	9 (3.9)
Mixed race/Hispanic	276 (89.6)	204 (87.9)
Country of residence		
Guatemala	94 (30.5)	55 (23.7)
Costa Rica	74 (24.0)	56 (24.1)
Panama	76 (24.7)	68 (29.3)
Dominican Republic	64 (20.8)	53 (22.8)
Family history of migraine		
Yes	148 (48.1)	148 (63.8)
No	84 (27.3)	84 (36.2)
Missing	76 (24.7)	0
Educational qualification		
Primary education	11 (3.6)	5 (2.2)
Secondary education	49 (15.9)	29 (12.5)
Tertiary education	58 (18.8)	45 (19.4)
Bachelor or equivalent	166 (53.9)	132 (56.9)
Master or equivalent	18 (5.8)	15 (6.5)
Doctoral or equivalent	5 (1.6)	5 (2.2)
Missing	1 (0.3)	0

Note: Data are n (%) unless specified otherwise.

Abbreviations: n , number of patients; N , total population; SD, standard deviation.

16–20 years, 31 (13.4%) had migraine for 10–15 years, and 33 (14.2%) had migraine for 5–10 years; 63 (27.2%) patients had a migraine history of <5 years. The distribution of patients across countries in different migraine-affected period categories was similar to that in the overall study population. The proportion of patients who had migraine for ≥ 10 years was 61.2% (104) in private clinics and 37.1% (23) in public clinics, while the proportion of patients with <5 years of migraine history in public clinics was 35.6% (22) and 24.1% (41) in private clinics.

In 99 (42.7%) patients, the duration from first consultation to diagnosis of migraine was about 1 month. For a considerable proportion of patients (34 [14.7%]), the diagnosis of migraine took >5 years from the first consultation, and this was similar across the four participating countries (Guatemala: 11 [20.0%], Costa Rica: 9 [16.1%], Panama: 7 [10.3%], Dominican Republic: 7 [13.2%]). The proportion of patients for whom the diagnosis took >5 years in public clinics was 9.7% (6) and 16.5% (28) in private clinics.

Overall, 34 of 308 (11.0%) patients had a new diagnosis of migraine; of these patients, 27 (79.4%) had EM. The mean (SD) headache

days and migraine days for newly diagnosed patients prior to enrollment to the study were 13.1 (10.8) days and 9.6 (8.9) days, respectively.

Migraine as the reason for headache disorder was reported in 89.9% (62) patients visiting public clinics and in 71.1% (170) patients visiting the private clinics, with EM being the most common type. Country-wise data revealed that Guatemala had the lowest proportion (55 [58.5%]; 95% CI: 0.5–0.7) while Panama had the highest proportion (68 [89.5%]; 95% CI: 0.8–1.0) of patients in whom migraine was reported as the reason for a headache disorder, with EM being the most common type.

Medical specialties attending patients with migraine

The initial diagnosis of migraine was primarily done by general physicians (107 [46.1%]), but a majority of the patients received treatment for migraine from neurologists (154 [66.4%]). Overall, 58.6% (136/232) of patients were required to visit multiple medical professionals and had multiple consultations (144/232 [62.0%]; see supporting information) until diagnosis. Medical specialties attending patients with migraine in the CAC region were similar to those in the overall population, except in the Dominican Republic, where migraine was first diagnosed by neurologists (32 [60.4%]), followed by general physicians (9 [17.0%]). In private clinics, neurologists primarily diagnosed the majority of cases and prescribed treatment to patients.

Duration of migraine attacks

In the study sample, approximately one quarter of the patients (54 [23.3%]) reported a migraine attack of a full day in duration. Similar results were observed among the participating countries, except in Panama, where approximately one quarter of the patients had a migraine attack of between 2 and 4 days in duration (16 [23.5%]) and 15 (22.1%) patients had a migraine attack that lasted for a full day. About 24% of younger patients (aged 18–39 years) reported a migraine attack of a full day in duration that continued as a long-lasting attack of >4 days. Migraine attacks that lasted between 2 and 4 days were reported more often by the older group (aged 40–65 years) of patients (23%; [Figure 2A](#)). Overall, the duration of a migraine attack was longer among women than among men ([Figure 2B](#)). The mean (SD) number of migraine attacks within 7 days before patient enrollment was 2.2 (2.6). In private clinics, almost one quarter of the patients (40 [23.5%]) reported a migraine attack of a full day in duration as opposed to public clinics where a similar number of patients (16 [25.8%]) reported a migraine attack in a duration of more than 2 to 4 days.

The intensity of pain during migraine attacks was measured on a numeric rating scale of 0–10, as described earlier.¹⁰ Among the patients categorized by different pain scale categories, a severe degree of pain was observed in 59 (25.4%), 24 (10.3%), 44 (19.0%), and 39 (16.8%) patients at a score of 10, 9, 8, and 7, respectively ([Figure 3](#)).

Acute and preventive treatments for migraine

In total, 215 (69.8%) patients reported using either previous or ongoing migraine or headache-related medications. Of these, 203 (94.4%) patients received migraine-specific medication and the majority (198 [92.1%]) were receiving ongoing migraine-specific treatment. Overall, 127 (62.6%) patients had received preventive treatment and 158 (77.8%) patients had received acute treatment (see supporting information). Patients had to change treatments a mean (SD) of 1.1 (1.9) times to prevent migraine attacks.

Impact on daily activities, work productivity, and social life

The most common difficulties reported by all patients, regardless of the nature of the center (private or public) they had visited, was that migraine interfered with daily activities. Migraine led to cessation of activities by patients to rest, and patients felt tiredness or fatigue (sometimes) while performing daily activities ([Table 2](#)). Among the four participating countries, 16 patients (30.2%) from the Dominican Republic reported that migraine constantly interfered with daily activities (see supporting information).

Overall, 121 (52.2%) patients reported an impact of migraine on their professional/work life, and the three major impairments included inability to concentrate at work (72 [31.0%]), inability of colleagues to understand the patient's condition (31 [13.4%]), and missing too many workdays (26 [11.2%]; [Table 3](#)).

In all, 182 (78.4%) patients reported that migraine affected their social life, with the three most common impairments being inability to participate in all previous activities or hobbies (120 [51.7%]), inability to participate in social events (76 [32.8%]), and inability to participate in sport or exercise activities (66 [28.4%]; [Table 3](#)).

Among the four countries, the Dominican Republic had the highest proportion (62.3% [33]) and Panama had the lowest proportion (45.6% [31]) of patients in whom migraine had an impact on their professional or work life (see supporting information). The proportion of patients who felt an impact on professional or work life due to migraine was 55.9% (95) among those visiting private clinics and 41.9% (26) in those visiting public clinics.

Cost of migraine treatment

Among the four participating countries, the mean (SD) cost of migraine treatment was highest in the Dominican Republic (225.8 [310.2] US dollar [USD]), followed by Costa Rica (181.6 [179.7] USD), Guatemala (128.6 [125.7] USD), and Panama (53.9 [79.0] USD). A negligible proportion of patients received a disability-related allowance (Guatemala [0.9%], Costa Rica [1.3%], Panama [1.7%], and Dominican Republic [0.4%]).

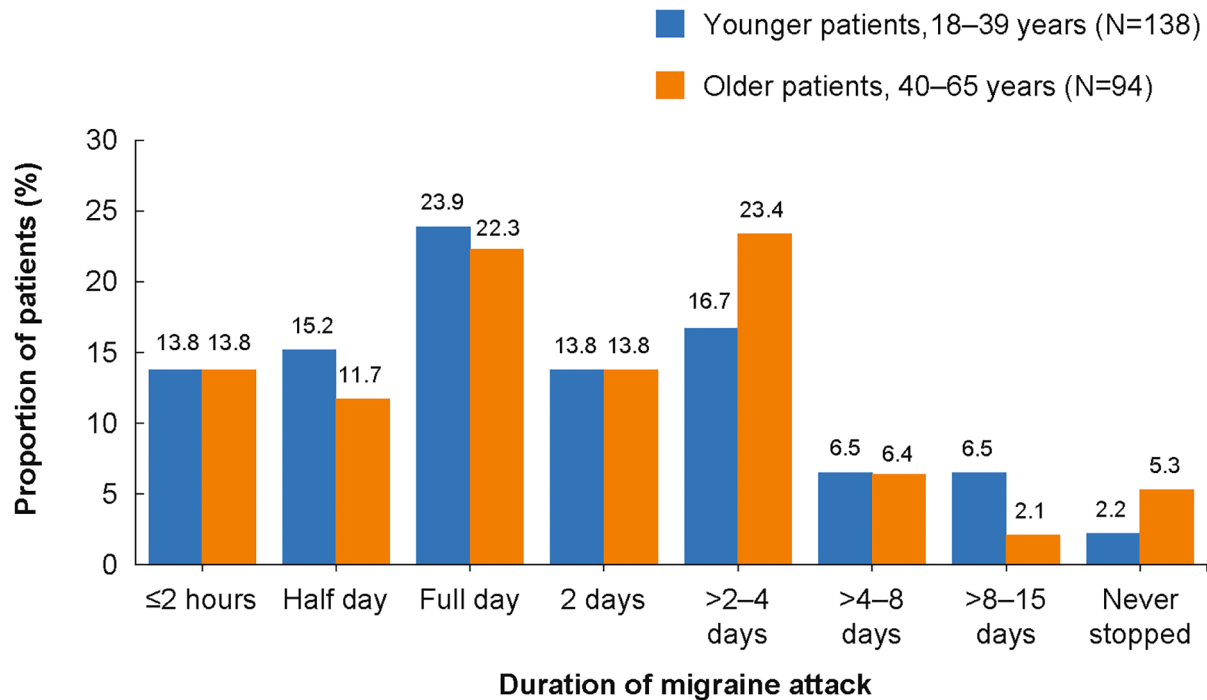
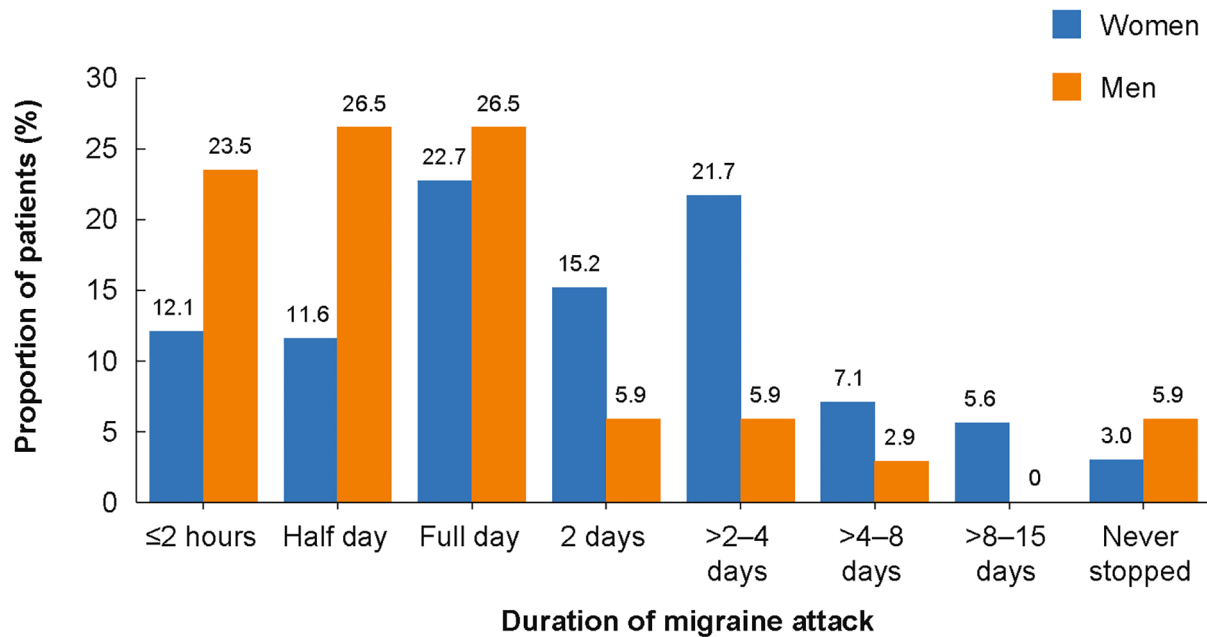
(A) Age***(B) Gender***

FIGURE 2 Distribution of duration of migraine attacks by (A) age* and (B) gender*. *Data missing for three patients. N: number of patients with migraine in the analysis set.

DISCUSSION

This is the primary analysis of the first clinic-based study describing the proportion of patients with migraine and the frequency of new migraine cases among patients with headache disorders as well as the characteristics of migraine and its impact on daily activities

and the professional and social life of patients by using a specially designed migraine-specific questionnaire in patients visiting medical centers in the CAC region.

Consistent with the global population,¹² migraine was more prevalent among women than men, and women in the CAC region reported a longer duration of migraine attacks.¹² Results from this

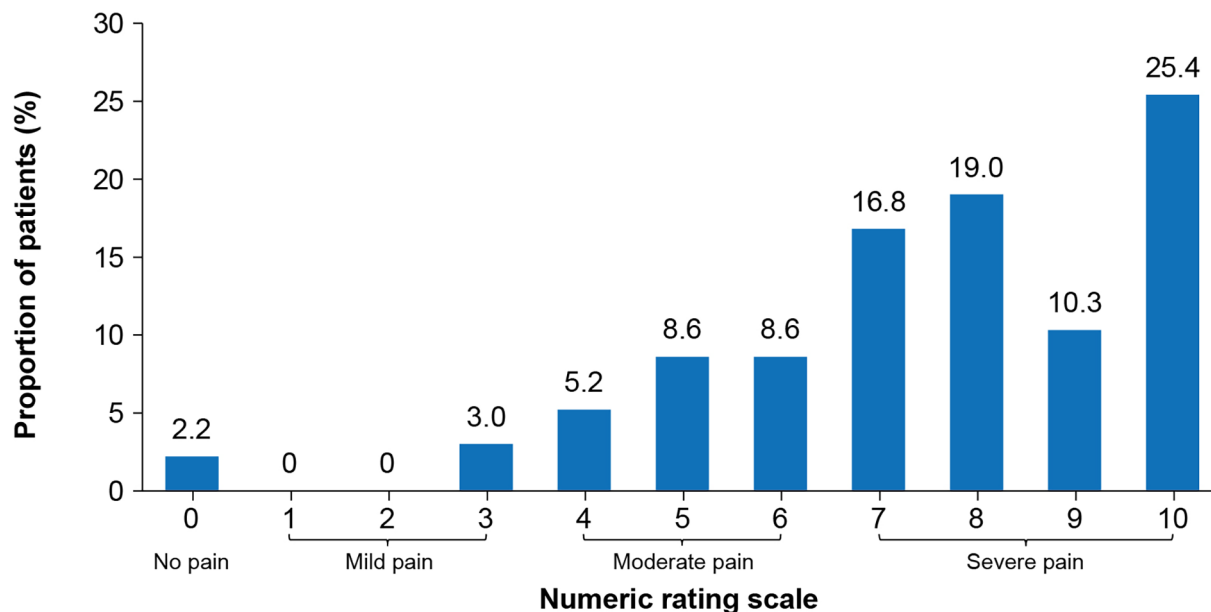


FIGURE 3 Degree of pain (full analysis set).

study also confirmed earlier reports¹³ that the duration of migraine attacks lasts between a few hours to days. In accordance with previous studies,¹⁴⁻¹⁶ moderate to severe pain was reported by 94% of patients visiting medical centers in the CAC region, and other symptoms affecting patients' daily activities, social participation, and work were also reported.

Evidence from previous studies shows that most patients with migraine (CM and EM) visited primary care physicians for their treatment.^{17,18} Consistent with this, migraine was predominantly diagnosed by general physicians in the participating countries, except in the Dominican Republic, where the diagnosis was predominantly made by neurologists. In the Dominican Republic, patients could directly visit a specialist without appointment or referral from general physicians across public and private centers. In Costa Rica, Panama, and Guatemala, patients need to be referred to specialists by a general physician but can consult them directly in private centers. These findings emphasize the need for appropriate referrals.^{19,20}

Owing to the duration of attacks, degree of pain, and symptom burden, there is a considerable impact on the quality of life and physical functioning of patients with migraine.²¹ In this study, a majority of the patients experienced interference in daily activities, cessation of daily activities, fatigue, and the need to rest due to migraine. Migraine affected the professional life of >50% of patients, indicating a substantial burden on work life for these patients. An equal number of patients also reported no impact of migraine on their work life or chose not to answer the question. A possible explanation for reporting "no impact" could be the patients' unwillingness to report the extent of time lost at work.²² Such patients may have adopted a coping strategy or may have worked through migraine headaches but with reduced productivity.²³ In this study, patients reported a mean loss of productivity due to migraine of 4.4 h per week on average. This was similar to the loss of productivity of 4.7 h per week

due to migraine reported in a population-based study (the American Migraine Prevalence and Prevention), indicating a substantial impact on the work life of patients with migraine.²⁴

Migraine also impaired social life in about 78% of patients, leaving them unable to attend social events or perform leisure activities. No studies have critically evaluated the effect of migraine on social life in the CAC region despite its significant impact on family life, relationships, and pursuit of hobbies or interests. The findings from the CALM study in the CAC region indicated that 33% of patients had to stop attending social events, 28% were unable to take part in sports/exercise activities, and 17% had to cancel going on a holiday. A population-based study conducted in the United States and the United Kingdom showed that 45% of patients with migraine missed family, social, and leisure activities; 32% avoided making plans for fear of cancellation due to headaches; and one half believed they were likely to argue with their partners (50%) and children (52%).²⁵ In another study, 17% of patients canceled family or social activities due to migraine.¹⁴ These findings suggest a substantial impact of migraine on social life, which should be accounted for when treating patients with migraine and prescribing medication in the CAC region. Use of validated questionnaires (general health and disease-specific) to evaluate the burden of disease and its impact on social and professional life could help health-care professionals to customize treatments for patients with migraine in these countries;²⁶⁻²⁹ however, further investigation is warranted to make more relevant conclusions.

In this study, the mean direct costs of migraine treatment varied among the four participating countries, being the highest in the Dominican Republic and the lowest in Panama. These differences in the costs incurred due to migraine could directly relate to the differences in the existing health-care systems and reimbursement policies in the four countries. The higher costs in the

TABLE 2 Daily activity impairment due to migraine (full analysis set)

Difficulties in carrying out daily activities ^a	All patients (N = 232)
Interfered with daily activities	
Did not interfere with activities of daily living at all	22 (9.5)
Interfered a little with activities of daily living	35 (15.1)
Interfered somewhat with activities of daily living	69 (29.7)
Interfered a lot with activities of daily living	58 (25.0)
Constantly interfered with activities of daily living	41 (17.7)
Missing	7 (3.0)
Needed to stop daily activity and rest	
Patients did not have to stop their daily activities and rest at all	44 (19.0)
Patients had to stop their daily activities and rest a few times	85 (36.6)
Patients had to stop their daily activities and rest sometimes	59 (25.4)
Patients had to stop their daily activities and rest a lot of the time	26 (11.2)
Patients always had to stop their daily activities and rest	17 (7.3)
Missing	1 (0.4)
Felt fatigue	
Patients had enough energy to complete all their activities of daily living	26 (11.2)
Patients had almost enough energy to complete all their activities of daily living	55 (23.7)
Patients sometimes did not have energy to complete all their activities of daily living	91 (39.2)
Patients often did not have energy to complete all their activities of daily living	40 (17.2)
Patients did not have any energy to complete all their activities of daily living	19 (8.2)
Missing	1 (0.4)

Note: Data are presented as n (%) unless specified otherwise.

"n" represents the number of patients in each category; "N" represents the total number of patients with migraine in the specified analysis set. Percentages are calculated using "N" as the denominator.

^aPatients were asked to recall the impact of migraine on daily activities in the past month for the self-administered questionnaire.

Dominican Republic are likely related to direct costs incurred by the patients, as most of them visited private clinics. In contrast, the lower costs in Panama, where patients mainly accessed the public health-care system (social security and public hospital), do not take into account the indirect financial burden on the public health-care system as these costs are not perceived directly by the patient on an ongoing basis, and hence were probably not reported in their responses to the survey. Patients from Costa Rica benefited from a mixed system, where a private practice physician could prescribe a drug and the patient could then claim the drug through their social security. Further pharmacoepidemiology

TABLE 3 Work productivity and activity impairment due to migraine (full analysis set)

Work productivity and activity impairment	All patients (N = 232)
Impact of migraine on professional life	
Patients with impact of migraine on professional/work life	121 (52.2)
Patients with no impact of migraine on professional/work life	54 (23.3)
Patients with missing information	57 (24.6)
Patients who missed too many days of work	26 (11.2)
Patients who felt that their colleagues did not understand their condition or take it seriously	31 (13.4)
Patients who felt they became more flexible and could cope better	22 (9.5)
Patients who felt judged for taking days off work	11 (4.7)
Patients who could not concentrate at work	72 (31.0)
Patients who believed that migraine did not impact their professional/work life	42 (18.1)
Other	26 (11.2)
Number of days unable to work due to migraine in the past month, mean (SD)	1.2 (2.4)
Number of paid sick days in the past month, mean (SD)	0.9 (2.2)
Number of work hours missed in the past 7 days, mean (SD)	4.4 (11.2)
Number of work hours completed in the past 7 days, mean (SD)	40.5 (28.9)
Impact of migraine on social life	
Patients who could not take part in all activities/hobbies that they used to	120 (51.7)
Patients who could not take part in sports/exercise	66 (28.4)
Patients who felt socially isolated	21 (9.1)
Patients who stopped going on a holiday	40 (17.2)
Patients who stopped going to social events	76 (32.8)
Patients who did not stay out for very long	25 (10.8)
Patients who believed that their migraine did not hold them back	42 (18.1)
Other	12 (5.2)

Note: Data are presented as n (%) unless specified otherwise.

"n" represents the number of patients in each category; "N" represents the total number of patients with migraine in the specified analysis set. Percentages are calculated using "N" as the denominator.

Abbreviation: SD, standard deviation.

analyses are needed to establish the true burden or cost for the health-care system and patients.

Limitations

This study has several notable limitations. It was not a population-based study and was of a short duration. The study did not have a

screening phase and the number of referrals from primary care were not quantified. As the cohort numbers were small among the countries, direct comparisons were not done. Specific questionnaires that are used to assess the impact of migraine on the patient's overall well-being were not used. Further, responses to the self-administered questionnaire used in the study were dependent on patient recall and, hence, could have led to biases. Completion of the self-administered questionnaires generally took 30–45 min, which could have led to patient fatigue and, therefore, unreliable or low-quality data. The collection of data was also impacted due to social determinants of health and inequities in some public health-care centers such as people living in rural areas, lack of access to health-care, level of education, lack of systematic arrangement of the data at medical centers, storage of data in paper format, and lack of a digital system to store medical records. We had missing data on the questionnaire but not on the proportions of migraine and its characteristics. This study evaluated the proportion of patients with migraine and the frequency of new migraine cases in a population that visited specialized medical centers for headaches and thus cannot be extrapolated to the general population without further evidence. Given the limited resources in these countries, and the practical and logistical obstacles encountered, findings from this study could be used as a methodological pilot that will help in defining specific objectives in future studies, which will allow us to fully understand the epidemiology and burden of migraine in the CAC region.

In conclusion, the CALM study showed that a high proportion of patients with migraine in the CAC region have a long duration and high severity of migraine attacks, which have a direct impact on the work/social life as well as on the costs incurred by the patients similar to that of the global population. The findings from this study will provide preliminary understanding of migraine characteristics and will help researchers to further explore the burden of disease and associated health-care costs in larger patient populations in these countries.

AUTHOR CONTRIBUTIONS

Study concept and design: Jeanine Obage, Diego Luna, Wilfran Pertuz. *Acquisition of data:* Priscilla Monterrey, Mónica González, Deyanira Ramírez, Fernando Gracia, Freddy Henríquez, Eka Pérez-Franco, Alejandro Díaz, Juan F. Vásquez, Aarón Benzádon. *Analysis and interpretation of data:* All listed authors contributed in interpretation of the data; data analysis was performed by NBS CONNEXT, which is a Novartis division specialized in this service. *Drafting of the manuscript:* All listed authors contributed to the drafting of the manuscript and outline with corrections, comments, and proposing statements based on data analysis and local context. *Revising it for intellectual content:* All listed authors contributed; also, specialized medical writing services provided by NBS CONNEXT. *Final approval of the completed manuscript:* All authors provided final approval before submission.

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CONFLICTS OF INTEREST

PM, MG, DR, FG, FH, EP-F, AD, JFV, and AB report no conflicts of interest. JO, DL, and WP are full-time employees of and hold stock in Novartis.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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