Clinical Neurology: Research Article

Clinical Course of Migraine during Strict Quarantine due to SARS-CoV-2: Effect of Psychiatric Comorbidities in a Clinical Cohort

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Abstract

Objective: During the SARS-CoV-2 pandemic, there has been a significant increase in the prevalence of anxiety and depression. This study sought to establish the probability of migraine progression by comparing data from week 0 with week 12 of quarantine. ***Methods:*** A retrospective cohort study. Three hundred ten patients were included, 238 with episodic migraine and 33 with chronic migraine; they all completed a self-administered questionnaire with demographic, clinical, and psychiatric symptom information. A multivariate statistical analysis was conducted to identify factors associated with the progression of migraine. ***Results:*** This study demonstrated a 22.5% progression probability from episodic migraine to chronic migraine with an RR 2.7 and CI (1.92–3.95, $p < 0.001$). The increase in depression scores ($p < 0.005$), anxiety ($p < 0.001$), and alteration in sleep quality ($p < 0.003$) were associated with the worsening of migraine. ***Conclusion:*** During the SARS-CoV-2 pandemic, depression, anxiety, and the deterioration of sleep quality influenced the probability of progression from episodic migraine to chronic migraine.

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Introduction

Migraine is a multifactorial medical condition in which psychiatric disorders play a relevant role. Among these disorders, depression, anxiety, and the association with sleep disorders have been determined as determining factors for clinical progression [1–3]. The SARS-CoV-2 pandemic has been a health emergency with significant level of mortality and a considerable probability of physical and emotional sequelae [4]. To reduce the pandemic effects, governments worldwide resorted to quarantine as the main measure to reduce the rate of infections and their consequences. This strategy generated collateral effects such as fear of contagion, financial crisis, social isolation, excess of information, and uncertainty [5]. These effects have been associated with a significant increase in anxiety and depression levels in quarantined populations during the pandemic [6]. In Colombia, the strict quarantine lasted 12 weeks from March 19, 2020, to June 10, 2020, and only health workers, military and security forces, and those working in food and communications were given unrestricted mobility. During this period of strict quarantine, our workgroup noted a clinical deterioration of our cohort members, which prompted the objective of this study: to establish the probability of
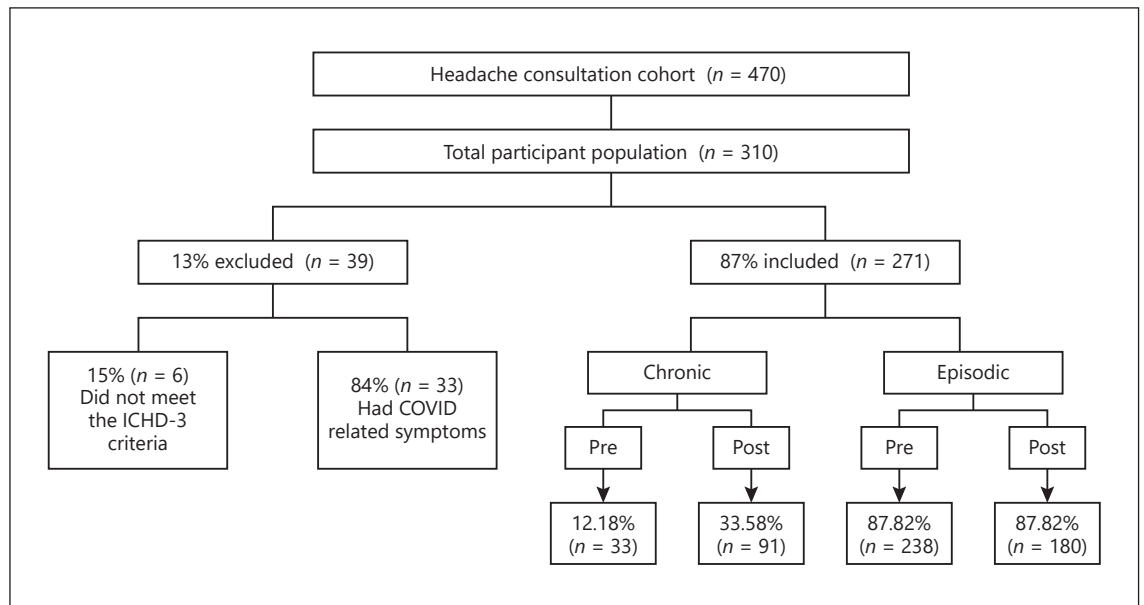
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Fig. 1. Flowchart of the study.

migraine progression by comparing the information obtained in week 0 of the quarantine to that of week 12, under the hypothesis of deterioration due to the increase in psychiatric symptoms.

Methodology

Study Design and Participants

A retrospective cohort study was carried out comparing week 0 with week 12; the data corresponded to patients of the specialized program of headache consultation. Follow-up was carried out for a period of 3 months, with data collection in the second week of June, the date on which the first strict quarantine ended in Colombia.

Data Collection

Through email, patients registered in the institution's headache program were invited to complete a self-administered survey. A response rate of 42% was obtained. Those patients who did not meet the self-administered International Classification of Headache Disorders (ICHD) criteria [7] and those who reported symptoms suggestive of SARS-CoV-2 in the survey during the period of strict quarantine were excluded. The survey included sociodemographic data and clinical information on headache, psychiatric symptoms, and those related to sleep. Anxiety was evaluated with the "General Anxiety Disorder-7" (GAD-7) scale, Spanish version [8]. This scale evaluates 7 items: (A) feeling nervous, anxious, or on edge; (B) not being able to stop or control preoccupation; worrying too much about different things; (C) trouble relaxing; (D) being so restless that it is difficult to stay still; (E) getting angry or irritated easily; and (F) feeling scared as if something terrible could happen. Four alternatives are offered: (1) not at all, (2) several days,

(3) more than half the days, and (4) almost every day. Scores can range from 0 to 21. The scale has a Cronbach alpha of 0.92, a sensitivity of 89%, and a specificity of 92% [9]. Depression was calculated with the "Patient Health Questionnaire-9" (PHQ-9) scale Spanish version [10], which has 9 items: (1) anhedonia; (2) depressed mood; (3) difficulty sleeping; (4) feeling tired; (5) change in appetite; (6) guilt, self-blame, or worthlessness; (7) difficulty concentrating; (8) feeling slowed down or restless; and (9) thoughts of being better off dead or hurting oneself. Symptoms are rated using a 4-point scale (0 – never, 1 – several days, 2 – more than half the time, and 3 – almost every day). General scores range from 0 to 27. The Scale has a Cronbach alpha of 0.35, a sensitivity of 92%, and a specificity of 89% [11].

Sleep disturbances were determined with the Pittsburgh Sleep Quality Index (PSQI) Spanish version [12]. The PSQ scale is a 19-item questionnaire designed to measure 7 component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction. Scores are graded from 0 (no difficulty) to 3 (severe difficulty); when added together, they produce an overall score ranging from 0 to 21. Scores >5 indicate significant sleep disturbance. The scale has a Cronbach alpha of 0.81, a sensitivity of 88.6%, and a specificity of 74.0% [13]. It was defined as an increase in the scores for anxiety, depression, and alteration in sleep quality, which is 1 step away from the absence of these disorders, to a mild/moderate or severe stage or to a change from mild/moderate to severe in the corresponding scales.

The impact of the headaches was calculated with the "Headache Impact Test" (HIT-6) scale, a self-administered questionnaire used to measure the negative impact of headaches on normal daily activity. It comprises 6 items that measure the frequency with which recent headaches resulted in severe pain, the frequency with which they affected daily activities, and the frequency with which they resulted in the desire to lie down, headache-related fatigue,

Table 1. Sociodemographic characteristics

Variable	%	n
Mean age (SD) (range)	35.6 (11.82) (15–75)	
Sex		
Female	87.1	236
Male	12.9	35
Civil status		
Single	42.8	116
Married	30.6	83
Divorced	3.3	9
Common-law marriage	22.5	61
Widow/er	0.7	2
Migraine type (week 0)		
Chronic migraine	12.18	33
Episodic migraine	87.82	238
Migraine (week 12)		
Chronic migraine	33.6	91
Episodic migraine	66.5	180
Monthly income		
Low	34.3	93
Medium	53.5	145
High	12.2	33
Occupation		
Health worker	12.9	35
Office work	27.3	74
Housewife	17.7	48
Student	12.5	34
Unemployed	12.9	35
Others	16.6	45

irritability, or difficulty concentrating. Each item is scored using 5 response categories (never, rarely, sometimes, very often, or always); each category is associated with a numerical value (6, 8, 10, 11, and 13, respectively), which generates a range of possible added total scores from 36 to 78. It has a Cronbach alpha of 0.73, a sensitivity of 68%, and a specificity of 74.0% [14].

Statistical Analysis

The data were analyzed using IBM SPSS (IBM Corporation, Armonk, NY, USA) Version 21. The normality distribution of the data was tested using the Shapiro-Wilk test. Nominal (categorical) variables were presented as frequencies (percentages), and constants were presented as medians with standard deviation. Evaluation of the statistical significance of the categorical variables in relation to migraine and its progression was done using Pearson's χ^2 stage, analyzing the level of independence (H0 = $p > 0.05$) or association (H = $p < 0.05$) of the different variables with their corresponding classifications. For the comparative analysis of samples, a bilateral test (2-tailed) was established. The Wilcoxon rank test was performed for related samples, analyzing the differences between the GAD, PSQI, and PHQ scale scores from week 0 to week 12, determining differences between the 3 variables.

Finally, a multivariate multiple correspondence analysis was carried out to determine each variable's categories associated with episodic migraine progression to chronic migraine. An analysis of matrices of expected and residual values in relation to the variables sex, occupation, diagnosis of depression, anxiety, sleep problems, and Headache Impact Test (HIT-6) scale was done. The probability of change between episodic to chronic migraine was presented as relative risk (RR) and 95% confidence intervals (CI). The data are considered statistically significant with a p value <0.05. Figure 1 shows a flowchart with the data obtained from the study.

Results

Out of 310 patients interviewed, 6 were excluded for not meeting the criteria for migraine and 33 were excluded due to manifesting symptoms suggestive of the SARS-CoV-2 infection during the study period, for a final study population of 271 participant patients (87.4%) (Fig. 1). The mean age was 35.6 (SD 11.8), range 15–75, years, where the female gender predominated (87.1%) (Table 1).

The self-perception evaluation comparing week 0 versus week 12 showed that in the episodic migraine patient group, 10.5% improved, 34.5% remained the same, and 55.3% worsened. In the chronic migraine group, the percentages were 1.3, 22.9, and 75.8%, respectively. 67.1% of patients did not seek a consultation, while 25.1 and 7.7% sought medical attention in outpatient and emergency services, respectively (Fig. 2).

The analysis of the change of migraine-type diagnosis according to the frequency between exposed and not exposed showed that patients with episodic migraine with deteriorating anxiety, depression, and sleep disorders had a 22.5% probability of evolving to chronic migraine: RR: 2.75 (95% CI: 1.92–3.95), $p > 0.001$.

The report of the depression symptom scores on the PHQ-9 scale showed a greater probability of deterioration when comparing week 0 with week 12. This behavior was similar when analyzing the probability of worsening anxiety, GAD-7 scale, and quality sleep index, PSQI. The measurement of migraine impact using the HIT scale at week 12 showed that 83.0% experienced a severe impact, 2.6% important impact, 5.1% experienced a certain impact, and 2.2% experienced little or no impact.

The analysis of variables showed a statistically significant association between the change from episodic migraine to chronic migraine with deterioration in the scores for depression – PHQ, anxiety – GAD, and Sleep Quality PSQ at week 0 versus week 12; this association was also statistically significant with the HIT-6 scale scores, female sex, and unemployment status at the beginning of the pandemic. The analysis for the variables anxiety scores, depression, and sleep scale at week 0 did not
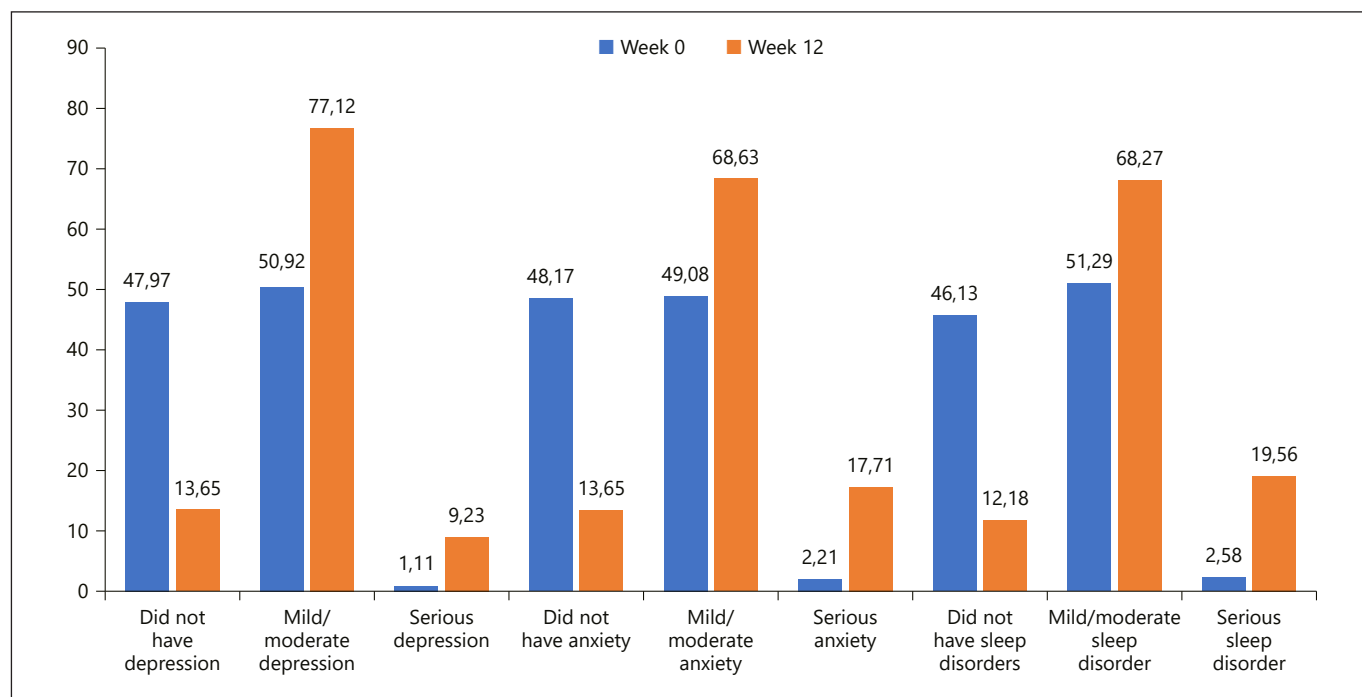
Fig. 2. Comparison of the proportion (%) of individuals and the severity of symptoms of anxiety, depression, and quality of sleep at week 0 versus week 12 of the pandemic.

show statistical significance, nor was this relationship demonstrated when analyzing the variables change in economic income, physical activity changes, and being in medical treatment or not (Table 2).

Discussion

This study demonstrates an association between depression, anxiety, and sleep disorder in patients with migraine, data widely confirmed in several investigations [15–17]. A 22.5% probability of progression from episodic migraine to chronic migraine was also evidenced when comparing week 0 versus week 12 of strict quarantine at the beginning of the SARS-CoV-2 pandemic in Colombia. This deterioration was correlated with an increase in the scores for depression, anxiety, and deterioration in sleep quality, with a higher proportion of patients with severe depression, anxiety, and quality of sleep disorders being observed, and a decrease in the percentage of patients with mild disorders or who did not manifest any of said variables when comparing week 0 versus week 12. This finding, in which there is a direct correlation between the severity of psychiatric symptoms and the progression of migraine, coincides with what was reported in several studies

Table 2. Factors related to migraine progression

Variables	χ^2	p value
Female gender	8.224	0.016
Loss of work activity	53.736	<0.001
Decrease in economic income	1.045	0.903
Practicing a physical activity	2.113	0.715
Receiving preventive treatment	1.550	0.461
Depression week 0	5.642	0.687
Increased level of depression week 12	38.004	<0.001
Anxiety week 0	3.228	0.780
Increased level of anxiety week 12	18.476	0.005
Sleep quality index week 0	2.113	0.909
Deterioration sleep quality index week 12	19.636	0.003
HIT-6 scale week 12	20.117	0.016

of the general and clinical population. The study American Migraine Prevalence and Prevention (AMPP) reported, by means of an analysis adjusted for variables corresponding to sociodemographics, BMI, the intensity of pain, allodynia skin, excessive use of painkillers, and anxiety, the severity of depression as a predictor factor of progression to chronic migraine, moderate stage (OR = 1.77, 95% CI: 1.25–2.52), moderately severe (OR = 2.35, 95% CI: 1.53–3.62), and severe (OR = 2.53, 95% CI: 1.52–4.2)

without generating the same impact when it was compared with the group of patients in a mild stage or without depression [18]. Similarly, the Migraine in America Symptoms and Treatment (MAST) study compared the probability of psychiatric comorbidities diagnosed by a health professional in 15,133 patients with migraine, finding a higher risk of depression in those with >21 days of headache per month OR 2.26 (1.91, 2.69) compared to those with a frequency of 4–9 days per month OR 1.31 (1.2, 1.44). This difference was also statistically significant in this study when comparing the probability of anxiety, taking into account the same frequency ranges, OR 2.13 (1.8, 2.53) and OR 1.33 (1.22, 1.46), respectively [19]. In a clinical population, a study of psychiatric comorbidities with 100 patients and an 8-year follow-up showed a greater probability of a stationary clinical course or deterioration of migraine in those who were diagnosed with depression and anxiety during follow-up [20]; a similar design, after a period of 10 weeks of observation, demonstrated the opposite effect when directly correlating an improvement of migraine with low levels of depression [21].

The aforementioned studies support the dose-response theory in the 2-way relationship between migraine and psychiatric disorders, in which the greater the severity of the affective component, the greater the progression of migraine. These data, together with the results of our study and the methodological structure used, in which a group of patients with a baseline level of migraine frequency is subjected to a "controlled environment" of adverse emotional factors inherent to quarantine, allow us to consider that the 2-way relationship leans toward a greater influence of psychiatric disorders on migraine instead of the opposite. This approach can also be supported when analyzing the effect of migraine on psychiatric disorders. Under this approach, a study with 290 patients analyzed the 10-year influence of migraine in patients with major depression and anxiety, showing us that although migraine affected the quality of life of this group of patients, there was no consistent effect on the severity of these psychiatric disorders when comparing people with migraine versus controls [22]. Our study had a higher proportion of young and female patients; this finding can be explained by the epidemiology of the conditions studied, by the prevailing incidence of psychiatric symptoms in women during the pandemic, and by the greater probability of access in this age group to the media, a potentially enhancing factor for the appearance of affective symptoms [5–24].

This study's main strength is obtaining information on the clinical course of a group of patients with migraine undergoing adverse psychological conditions derived from quarantine due to the SARS-CoV-2 pandemic. The main weaknesses are the methodological limitations of conducting a study under urgent parameters, the memory bias associated with the retrospective nature of the information at week 0, and the increased probability of obtaining more responses from those patients with clinical deterioration during the period of analysis.

In conclusion, this study provides information that suggests a greater impact of psychiatric disorders on migraine rather than the opposite. Additionally, it offers elements for designing policies when facing similar public health situations in the future.

Statement of Ethics

Written informed consent was obtained from each study participant. The study was reviewed and endorsed by the Ethics Committee of Del Rosario University, record DVO005 13–49 CV 12–93. The study design followed the requirements of the Declaration of Helsinki and other international regulations.

Conflict of Interest Statement

The authors declared that they had no potential conflicts of interest in regard to the research, authorship, and/or publication of this article.

Author Contributions

J.M.-C. participated in the design of the study, the collection and interpretation of data, and the writing of the manuscript. L.G. participated in the design of the study, the collection and interpretation of data, data analysis, and the writing of the manuscript. J.S. participated in the design of the study and the writing of the manuscript. All authors read and approved the final manuscript.

Data Availability Statement

The authors report that the data sets used and/or analyzed during the current study are available on reasonably appropriate request.

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