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The impact of the COVID-19 pandemic on patients with migraine

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Abstract

Objectives: The aim of our work was to assess the impact of the COVID-19 pandemic and quarantine measures on migraine patients in regards to the activity of the disease, the psycho-emotional background of the patients and their quality of life.
Methods: his study included 133 patients with established diagnosis of migraine. All study participants were divided into two clinical groups: A—patients with chronic and episodic forms of migraine, who had a history of positive PCR test for COVID-19, and B—patients with chronic and episodic forms of migraine who did not have a history of coronavirus disease.
Results: We detected increase in the number of antimigraine medication ($p = 0.04$), frequency of headache attacks ($p = 0.01$), and the psycho-emotional state deterioration (increase in the Hamilton anxiety scale score) ($p = 0.002$) in patients after recovery from the coronavirus disease. There was no significant difference in the headache's intensity according to the VAS scale ($p = 0.51$) as well as in the dynamics of the Beck depression scale score ($p = 0.09$) before and after the COVID-19 infection.
Conclusion: Patients with a history of migraine who recovered from COVID-19 showed increased frequency of migraine headache attacks and anxiety.

Keywords
Migraine, COVID-19 pandemic, psycho-emotional state

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Introduction

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus, which usually manifests with respiratory symptoms, but can also affect the central and peripheral nervous systems.[1] The COVID-19 pandemic led to serious consequences for people's daily lives due to financial insecurity, social distancing, and various restrictive measures.[2] Therefore, the COVID-19 pandemic is considered to be a serious stressor that affects the majority of the world's population. The restrictions associated with the coronavirus pandemic lockdown influenced the mental health state of people, especially those with chronic diseases.[3–5]

The impact of coronavirus disease on the nervous system is still a matter of debate. There are several possible ways of the SARS-CoV-2 virus spreading in the human body: through the bloodstream with further dissemination in the neurons by using transsynaptic pathways after infection of the nerve terminals (direct or retrograde pathways), infection of endothelial cells within the blood-brain barrier, and through the lymphatic system.[6–8]

During the COVID-19 pandemic, an increase in the frequency of migraine attacks was discovered, which may be the result of a direct viral effect on the trigeminal vascular system.[9] Headache in patients with migraine is known to occur as a result of proinflammatory cytokine-mediated activation of trigeminal nerve endings, direct invasion of nerve endings by SARS-CoV-2, or vasculopathy in endothelial cells expressing angiotensin-converting enzyme 2. In particular, increased levels of Interleukin-1, transforming growth factor-β1 (TGF-β1), and Monocyte

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Chemoattractant Protein-1 were found in the cerebrospinal fluid of the patients with episodic tension-type headache and migraine.[10] The most common factors that provoke different forms of migraine, include light and sounds, stress and mental tension, inappropriate diet, lack of sleep, menstruation, weather changes, strong odors, and smoking.[11–14] The pandemic and subsequent quarantine caused changes in the habits and lifestyle of patients with migraine, which could increase the frequency and severity of headaches.[15,16] Changes in social behavior, labor activity, decreased accessibility of the health care system for routine medical care, and fear of the coronavirus disease, caused significant psychosocial changes that dramatically increased the exacerbation of chronic neurological diseases, including migraine headaches.[17–19] However, there is lack of data regarding the impact of the consequences of the coronavirus disease on the frequency and nature of migraine headaches.[20] The aim of our work is to assess the effect of the COVID-19 pandemic and quarantine measures on migraine patients in regards to the activity of the disease, the psycho-emotional background of the patients and their quality of life.

Methods

This study included 133 migraine patients, among them 103 women and 30 men, aged from 18 to 55 years (39.5 ± 6.3). All study participants were divided into two clinical groups: A—chronic and episodic forms of migraine, who had confirmed COVID-19 with a positive PCR test ($n = 95$; 72 women and 23 men with an average age of 36.8 ± 7.9 years), and B—chronic and episodic migraine who did not have a history of coronavirus disease ($n = 38$; 31 women and 7 men with average age of 44, 2 ± 5.6 years). The retrospective nature of the study was conducted from March 2020 to April 2022 years. All patients were examined on an outpatient basis at the polyclinic in Kyiv, Ukraine. For group A, patients were those with chronic and episodic forms of migraine, with a positive test for COVID-19; all studies were conducted using telemedicine.

The examination began with a clinical and neurological examination, based on the results of which patients were selected into the main group according to the inclusion and exclusion criteria. Before the start of the examination, each subject signed an informed voluntary consent for diagnosis, treatment, and processing of personal data.

Inclusion criteria:

- Age over 18 and under 55 years.
- Migraine headache that meets the criteria of Headache Classification Committee of the International Headache Society.[21]
- For women of childbearing age—absence of pregnancy and taking oral contraceptives.
- Signing informed consent for participation in the study.

Exclusion criteria:

- Presence of severe somatic pathology.
- Presence of drug abuse.
- The presence of organic pathology of the nervous system.
- Age of patients under 18 and over 55 years.

The Identity Migraine (ID Migraine) test was used to differentiate migraine from headaches of other etiology.[22]

Diagnostic criteria for migraine according to ichd3 criteria:

A. At least five attacks, evaluated by criteria B–D.

B. Duration of attacks 4–72 hours (without treatment or with ineffective treatment).

C. A headache has at least two of the following characteristics:
   1. Unilateral localization.
   2. Pulsating character.
   3. Intensity of pain from average to significant.
   4. Headache worsens with usual physical activity or requires cessation of usual physical activity (walking, climbing stairs).

D. The headache is accompanied by at least one of the following symptoms:
   1. Nausea and/or vomiting.
   2. Photophobia or phonophobia.
   3. Not related to other reasons (violations).

Patients with an attack frequency of at least 15 days per month for more than 3 months, provided that there was no fact of drug abuse.[21]

All participants underwent standard clinical examination, including neurological examination and neuropsychological questionnaires. In group A, the frequency, intensity, and character of headache attack were determined, as well as psycho-emotional status characteristics, quality of patients' life, and the number of antimigraine drugs used before and after the coronavirus disease. The same parameters were determined in the group B, taking into account the introduction of lockdown restrictions in Ukraine. Headache intensity was assessed using a visual analog scale (VAS).[23] On a numerical scale, the patient determined the intensity of pain in points from 0 to 10 (0—no pain; 10—unbearable pain). The Beck Depression Inventory (BDI) was used to screen for the presence and assess the severity of depression. This scale consists of 21 items that capture the core symptoms of depression according to the Diagnostic and Statistical Manual of Mental Disorders diagnostic criteria. Each answer was evaluated

Table 1. Clinical characteristics of patient groups before the COVID-19 pandemic.

Different subscales	Group A ($n=95$)	Group B ($n=38$)	p
Number of antimigraine drugs used during the last 3 months	15.3 ± 2.7	8.9 ± 1.6	0.039*
VAS score	7.5 ± 2.5	6.1 ± 3.9	0.89
HARS score	18.3 ± 5.7	16.8 ± 6.2	0.09
BDI score	15.3 ± 6.5	18.8 ± 4.3	0.13
Frequency of attacks during the last 3 months	8.09 ± 4.1	5.3 ± 2.6	0.67
MIDAS score	10.7 ± 3.8	13.1 ± 4.1	0.06

*$p < 0.05$.

from 0 to 3 points. An average score of 0–9 indicates no depression, 10–18—mild depression, 19–29—moderate depression, and 30–63—severe depression.[24] The Hamilton Anxiety Rating Scale (HARS) was used to assess the severity of perceived anxiety symptoms. The scale consists of 14 items and measures both mental anxiety (mental and psychological arousal) and somatic anxiety (physical complaints related to anxiety). Each item of the HARS was scored from 0 (absent) to 4 (severe) points with a total score range of 0–56, where 0–13 means no anxiety, 14–17—mild anxiety, 18–24—moderate anxiety, and ⩾25 corresponds to strong anxiety.[25] The MIDAS (Migraine Disability Assessment) scale was used to study the quality of life and the degree of social and household maladjustment. According to the number of days, the degree of maladaptation was determined as: I—0–5 days; II—6–10 days; III—11–20 days; IV—⩾21 days.[26] Also, we assessed the number of antimigraine drugs used in both clinical groups. Antimigraine drugs included drugs for the treatment of an acute migraine attack, such as triptans, nonsteroidal anti-inflammatory drugs, but did not include preventive drugs for migraine therapy. All study participants gave written informed consent, and the study was approved by the Institutional Ethics Committee.

Statistical analysis

Statistical data were processed using Graph Pad Prism version 9. A value of $p < 0.05$ was considered statistically significant. Student's *t*-test (*t*) was used to assess the reliability of the mean of two samples.

Results

The results of the ID Migraine screening test confirmed the diagnosis of migraine in all study participants, among them in group A: 73 (76.8%) patients had three positive answers out of three and 22 patients (23.2%)—two positive answers out of three. Group B had the following findings: 23 (60.5%) patients had three positive responses out of three and 15 patients (39.5%) had two positive responses out of three. The average number of participants with a high frequency and intensity of migraine headache was not significantly different between the groups ($p > 0.05$) before the COVID-19 pandemic. In group A the average score on the Hamilton anxiety and Beck depression scales were 18.3 ± 5.7 and 15.3 ± 6.5 points respectively; in group B the average score on the above-mentioned scales were 16.8 ± 6.2 and 18.8 ± 4.3 points respectively. According to the MIDAS scale data no significant difference was found between both groups ($p = 0.06$). Before the COVID-19 pandemic, the number of antimigraine drugs used in group A for the treatment of migraine attacks was significantly higher when compared to the group B participants ($p = 0.039$) (Table 1).

In those patients who had a history of the coronavirus disease the number of antimigraine medications increased significantly ($p = 0.04$), the frequency of headache attacks was also remarkably elevated ($p = 0.01$) and the psycho-emotional state of patients significantly worsened with the increase of anxiety level according to Hamilton anxiety scale score ($p = 0.002$). There was no significant difference in the intensity of headaches according to the VAS scale ($p = 0.51$) before and after the coronavirus disease, as well as the dynamics of the Beck depression scale score ($p = 0.09$). The average MIDAS scale score increased from the II degree of maladaptation 10.7 ± 3.8 to the III degree 15.1 ± 2.4 ($p = 0.046$) after the coronavirus infection (Table 2).

Patients of the group B used significantly lower amounts of antimigraine drugs ($p = 0.033$) and had a remarkable decrease in the Beck depression scale score and the MIDAS score ($p = 0.003$, $p = 0.07$ respectively) after COVID-19 lockdown.

Discussion

The clinical course of migraine worsened after COVID-19 infection according to subjective impressions and most patients experienced significant changes in their lifestyle in such a short period of time. The changes influenced patient's habits, sleep, food consumption, financial and work problems, increased general anxiety associated with the pandemic due to the fear of infection, quarantine, social isolation, and an overload of information. The data obtained while comparing the characteristics of headache before and after the coronavirus infection history are consistent with the results of Al-Hashel and Ismail.[27] The high level of stress in addition to overuse of acute migraine medications are known

Table 2. Clinical characteristics of the patient groups after the COVID-19 pandemic.

Different subscales	Group A ($n = 95$)		p	Group B ($n = 38$)		p
	Before COVID-19	After COVID-19 infection recovery		Before COVID-19 lockdown	After COVID-19 lockdown	
Number of antimigraine drugs use during the last 3 months	15.3 ± 2.7	18.2 ± 3.9	0.04*	8.9 ± 1.6	6.9 ± 3.2	0.03*
VAS score	7.5 ± 2.5	8.1 ± 1.9	0.51	6.1 ± 3.9	5.6 ± 2.5	0.89
HARS score	18.3 ± 5.7	21.7 ± 4.9	0.002*	16.8 ± 6.2	14.1 ± 7.3	0.09
BDI score	15.3 ± 6.5	15.5 ± 3.6	0.09	18.8 ± 4.3	13.7 ± 6.1	0.003*
Frequency of attacks during the last 3 months	8.09 ± 4.1	12.09 ± 3.1	0.01*	5.3 ± 2.6	7.3 ± 5.2	0.67
MIDAS score	10.7 ± 3.8	15.1 ± 2.4	0.04*	13.1 ± 4.1	8.5 ± 2.4	0.07

*$p < 0.05$.

to be risk factors for chronic migraine.[28,29] The increased frequency of headaches is associated with an increase in anxiety level, which underlines stress as the most common patient-reported trigger of migraine attacks.[30,31] It should be noted that migraine attacks can act as a stress factor, creating a vicious circle that increases both the severity and frequency of migraine attacks.[30] The COVID-19 pandemic itself is perceived to be a serious stressful event. Fear of death from COVID-19 was the most common concern among patients, followed by fear of worsening of their headache.[32]

In a recent study of Rodríguez-Rey et al.[33] more than 40% of the participants reported moderate to severe stress following the coronavirus illness with the majority suffering from depression and more than 20% experiencing anxiety. In our study a significant increase in the anxiety level in the group A patients was detected. It was established that migraine is closely related to both depression and anxiety that coincides with the data obtained in other studies.[34,35] According to our results, patients after total lockdown demonstrated a significant decrease in the level of depression and an improvement in the quality of life, that may be related to a reduction in work pressure, as well as a possible improvement in sleep quality and eating habits. Our findings are consistent with the results of Parodi et al.[36] that explain these findings with a reduction in the number of triggers as a result of decreased work and social activity. We did not find any difference in the headache intensity after experiencing the coronavirus disease. Corresponding data concerning the pain intensity was obtained in the retrospective study of Gonzalez-Martinez et al.[37]

Limitations of the study

Our study has some limitations. First, the retrospective nature of this study prevented us from a detailed follow-up through the COVID-19 illness and lockdown. Sample size/power analysis was not performed for this study. Number of antimigraine drugs used during the last 3 months before COVID-19 was different in both groups. Furthermore, the answers from the patients might have led to inaccuracies in few answers, because our patients can remember their former state as better or worse than it actually was. One of the limitations is whether exposure to the coronavirus actually affects migraine or whether it was a possible trigger factor. This lack of details about lifestyle habits and the nature of the study makes it difficult to establish clear causal relationships. We did not include more detailed variables evaluating lifestyle habits to avoid an excessively long survey. During COVID-19 pandemic, the clinical management of migraine as well as mental health should not be neglected.

Conclusion

Patients who recovered from COVID-19 showed increased frequency of headache attacks as well as increased levels of anxiety. COVID-19 led to an increase in the antimigraine drugs use in patients with migraine. After total lockdown restrictions, patients suffering from migraine showed a decrease in depression rate. As far as current health crisis is likely to have long-term effects, further research is needed to clarify the extent of the psychological impact of COVID-19 on patients with migraine.

Author contributions

OH: concept and design of the paper, data collection and analysis, responsibility for statistical analysis, writing the paper. OK: concept and design of the paper, writing the paper, critical review, final approval of the paper. MK: writing the paper, critical review, final approval of the paper. KS: writing the paper, statistical analysis, final approval of the paper.

Declaration of conflicting interests

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Ethics approval

Ethical approval for this study was obtained from Bioethics Commission of the Kyiv Medical University (APPROVAL NUMBER 10 of 18.12.2020)*.

Informed consent

Written informed consent was obtained from all subjects before the study.

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Supplemental material

Supplemental material for this article is available online.

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