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Epidemiology and clinical characteristics of headache among COVID-19 patients in Lebanon: a retrospective cohort study

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Abstract

Background With the spread and rise in the number of infections of COVID-19 globally, patients experienced neurologic manifestations such as headache and dizziness, along with other serious medical conditions such as stroke and seizures. Many reported cases highlighted headache to be one of the most common COVID-19-related neurological symptoms. With the evolution of the pandemic, broad studies are needed to better understand the mechanism of headache with COVID-19. The aim of this study is to recognize the epidemiology, characteristic and progression of headache among patients with COVID-19 in Lebanon.

Methods A retrospective cohort study was done to assess 439 patients for headache during the course of COVID-19. The Statistical Package for Social Sciences (SPSS) version 26 was used for descriptive analysis.

Results A confirmed COVID-19 Infection by PCR test was confirmed among 86% of the participants. Tension-like headache was the most common type of headache experienced by participants during COVID-19. Pain was mainly diffuse (48.7%), and compressing in nature (77.0%). Moreover, about 29% required a physician consultation and 7.7% had emergency visits. Partial relief by analgesics was reported in 54.9%, and mainly by paracetamol (64.6%). Those who reported having a history of primary headache before contracting COVID-19 were 46.7%. Among them, 36.7% patients reported a change in the type of headache and about 49.6% reported increased severity.

Conclusion Headache accompanied with COVID-19 is a common symptom during the early stages of illness. COVID-19 related headache was characterized as mainly involving the whole head region, pressuring, and partially relieved by analgesics. Thus, headache should raise early concern for the probability of being infected by COVID-19.

Keywords COVID-19, Virus, Headache, SARS-CoV-2

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Introduction

The year 2019 witnessed the emergence of a novel Corona virus (COVID-19) in Wuhan, China, leading to a global pandemic by March 2020 [1]. By July 7, 2023, a total of 691 million confirmed COVID-19 cases and 6.9 million deaths were reported [2]. The clinical symptoms of COVID-19 were mainly fever, sore throat, cough, myalgia, fatigue, diarrhea, shortness of breath, and anosmia [1, 3, 4]. In addition, several studies highlighted the neurological manifestations of COVID-19 such as headache, epilepsy, myalgia, and Guillian–Barre syndrome (GBS), encephalitis, anosmia, and others [1, 3, 5]. These neurological symptoms are caused by three main mechanisms. These mechanisms include direct nervous system involvement, immune system-mediated problems, or secondary to a systemic disease or lung damage [6]. A study done in Spain reported that the occurrence of headache reached about 22.7% in patients whose age ranged between 18 and 49 years old [7]. According to the American Headache Society, around 47.1% patients during the acute phase of COVID-19 reported having headache [8].

Many studies focused on the characteristics and location of the headache, whether unilateral/bilateral or diffuse, occipital or fronto-temporal, and the associated symptoms such as photophobia, phonophobia, conjunctival injection, nausea and vomiting [9]. In Lebanon, no studies have been conducting to study the prevalence and characteristics of headache associated with COVID-19 infection. The aim of this study is to recognize the epidemiology, characteristic and progression of headache among patients with COVID-19 in Lebanon.

Methodology

Sampling and methods

To study the characteristics and epidemiology of headache during COVID-19 pandemic in Lebanon, a retrospective cohort study was conducted, preceded by a pilot study which included 15 participants. The questionnaire was developed by 2 neurologists, which included a total of 32 multiple choice questions focused around headache characteristics, progression, and severity experienced during the course of the disease (Additional file 1). Data were gathered between December 20, 2020 and 1 February, 2021. Data collection was done following the snowballing technique, where participants between the ages of 18 and 70 years old were invited by means of social media, using a web-based link suitable for smart phones or paper based for those who preferred using paper, as lockdown restrictions were limiting face-to-face interaction.

Inclusion and exclusion criteria

Participants between the ages of 18 and 70 living in Lebanon, who exhibited symptoms of COVID-19 infection or tested positive on a polymerase chain reaction (PCR) test, and reported experiencing headaches throughout the duration of the illness were included. Pediatric population, participants above 70 years of age and those who reported active acute illnesses other than COVID-19 were excluded from the study.

Sample size

The World Bank organization estimates that the total Lebanese population is approximately 6,848,952 [10].

Sample size was calculated using the following formula: $n = ((Z \alpha/2)^2 (p) (1-p))/\delta^2$, with a confidence interval of 95%, and level of significance “ α ” equals 5%, which corresponds to $Z \alpha/2 = 1.96$ [11].

An estimation on the variation of the results of this study from the actual proportion (δ) at 0.05.

The estimation of the knowledge among the population “ p ” due to lack of literature was unknown, so an estimate of 50% was considered.

Therefore, a sample of 384 participants was required.

In order to attain better representability and better results, more responses were considered.

Results

Demographics and clinical characteristics of study population

The study population involved a total of 439 participants, including 71.8% females and 28.2% males with a mean age of 39 years. Majority of participants had a Lebanese nationality (91.8%), and were living in Beirut area (49.7%). A total of 18.5% of the participants had a history of chronic disease, mainly hypertension (63%). The majority of the participants (77.7%) were educated, and 55.1% were employed. Other clinical characteristics of the study group are summarized in Table 1.

History of COVID-19 infection

Among the participants, 86.0% had a PCR confirmation of COVID-19 infection, while 14.0% did not. Headache was the most common reported symptom among participants during COVID-19 infection (92.8%).

Headache characteristics during COVID-19 infection

As regarding headache, 62.8% of the participants reported a mild intermittent headache, while 29.5% reported a migraine type of headache. Other types of headache were reported by participants such as cluster (6.0%), and trigeminal neuralgia (1.7%) (Table 2).

Table 1 Demographic and clinical characteristics of those who had headache during COVID infection ($n = 439$)

	<i>n</i> (%)
Gender	
Male	124 (28.2%)
Female	315 (71.8%)
Residency	
Beirut	218 (49.7%)
North	48 (10.9%)
South	47 (10.7%)
Bekaa	41 (9.3%)
Mount Lebanon	85 (19.4%)
Nationality	
Lebanese	403 (91.8%)
None Lebanese	36 (8.2%)
Marital status	
Single	189 (43.1%)
Married	232 (52.8%)
Divorced	13 (3.0%)
Widowed	5 (1.1%)
Education level	
Lower than high school	35 (8.0%)
High school	45 (10.3%)
University	341 (77.7%)
Vocational diploma	18 (4.1%)
Employment	
Employed	242 (55.1%)
Unemployed	39 (8.9%)
Student	95 (21.6%)
Housewife	57 (13.0%)
Retired	6 (1.4%)
Age (years)	
18–30	216 (49.2%)
31–40	126 (28.7%)
41–50	67 (15.3%)
51–60	23 (5.2%)
61–70	7 (1.6%)
Have chronic diseases	
No	358 (81.5%)
Yes	81 (18.5%)
Hypertension	51 (63.0%)
Diabetes	28 (34.6%)
Cardiac disease	15 (18.5%)
Kidney disease	9 (11.1%)
Pulmonary disease	14 (17.3%)

Headache usually occurred during the first 2 days of infection (53.3%) and lasted less than 3 h (31.9%). Accordingly, 38% participants reported the severity of headache to be between 4 and 6 over a scale of 10. Only 4.8% of the patients needed emergency admission,

Table 2 Headache characteristics during COVID infection

	<i>n</i> (%)
Had headache before COVID infection	
No	205 (46.7%)
Yes	234 (53.3%)
Type of headache before COVID-19	
Migraine	69 (29.5%)
Clusters	14 (6.0%)
Trigeminal neuralgia	4 (1.7%)
Slight intermittent pain (tension)	147 (62.8%)
Headache initiation after infection	
First 2 days	233 (53.1%)
Third to 7th day	149 (33.9%)
Eight to fourteen days	38 (8.7%)
Fourteen days to 2 months	19 (4.3%)
Headache severity	
1–3	59 (13.4%)
4–6	167 (38.0%)
7–9	166 (37.8%)
10	47 (10.7%)
Analgesic consumption	
No	27 (6.2%)
Yes	412 (93.8%)
Paracetamol	266 (64.6%)
NSAID or equivalent	35 (8.5%)
Paracetamol and NSAID	111 (26.9%)
Effectiveness of analgesics	
Complete pain relief	144 (35.0%)
Partial pain relief	226 (54.9%)
No pain relief	42 (10.2%)
Headache very severe needed ED	
No	405 (92.3%)
Yes	34 (7.7%)
Headache led to consulting a physician	
No	310 (70.6%)
Yes	129 (29.4%)
Headache was one of three annoying symptoms during COVID infection	
No	89 (20.3%)
Yes	350 (79.7%)
Headache location	
Half	67 (15.3%)
Diffuse	214 (48.7%)
From front	131 (29.8%)
From back	27 (6.2%)
Headache characteristics	
Pressure in head	338 (77.0%)
Beating	46 (10.5%)
Burning	21 (4.8%)
Stabbing	34 (7.7%)
Headache duration	
Less than 3 h	140 (31.9%)

Table 2 (continued)

	n (%)
3–12 h	111 (25.3%)
12–24 h	20 (4.6%)
1–2 days	54 (12.3%)
3–7 days	68 (15.5%)
More than 7 days	46 (10.5%)
Headache accompanied with other symptoms	
No	75 (17.1%)
Yes	364 (82.9%)
Nausea and/or vomiting	152 (41.8%)
Noise intolerance	169 (46.4%)
Light intolerance	128 (35.2%)
Neck pain	135 (37.1%)
Eye pain	115 (31.6%)
Headache increased	
No	155 (35.3%)
Yes	284 (64.7%)
Headache increased with	
Fever	116 (40.8%)
Cough	115 (40.5%)
Regular movement	129 (45.4%)
Other symptoms	
No	19 (4.3%)
Yes	420 (95.7%)
Myalgia	349 (83.1%)
Gastrointestinal symptoms	156 (37.1%)
Loss of taste and smell	287 (68.3%)
Loss of consciousness	52 (12.4%)
Nerve injury	29 (6.9%)
COVID severity	
Did not need oxygen	392 (89.3%)
Needed oxygen at home	17 (3.9%)
ED admission	21 (4.8%)
Hospital admission	7 (1.6%)
ICU admission	2 (0.5%)
Headache treatment other than analgesics	
No	368 (83.8%)
Yes	71 (16.2%)
Headache before COVID changed during or after infection	
No	187 (57.4%)
Yes	139 (42.6%)
Type changed	51 (36.7%)
Increased severity	69 (49.6%)
Increased duration	40 (28.8%)
Response to analgesic consumption changed	29 (20.9%)
Increased episodes	41 (29.5%)
Took treatment other than analgesics before COVID	
No	397 (90.4%)
Yes	42 (9.6%)
Stopped during COVID infection	25 (65.8%)

Table 2 (continued)

	n (%)
Stopped after COVID infection	13 (34.2%)
Family history of headache	
No	234 (53.3%)
Yes	205 (46.7%)

intensive care unit (ICU) admission (0.5%), hospitalization (1.6%), physician consultation (29.4%), and oxygen supplementation at home (3.9%). Analgesics were the mainstay treatment during headache episodes (83.8%), however, they only partially relieved the pain episodes (54.9%). Paracetamol alone (64.6%), paracetamol with non-steroidal anti-inflammatory drugs (NSAID) (26.9%), and NSAID alone (8.5%) were the analgesics used. Most participants did not take any treatment other than analgesics before COVID (90.4%). Headache before COVID changed during or after infection (42.6%). Headache localization was mainly diffuse (48.7%) and frontal in location (29.8%). Headache was increased with regular movement (45.4%), fever (40.8%), and cough (40.5%). Headache associated symptoms reported by patients were noise intolerance (46.4%), nausea and vomiting (41.8%), neck pain (37.1%), light intolerance (35.2%), and eye pain (31.6%). Participants experienced other important symptoms related to COVID-19 such as myalgia (83.1%), loss of taste and smell (68.3%), gastrointestinal symptoms (37.1%), loss of consciousness (12.4%), and nerve injury (6.9%) (Table 2).

Up to 47% of patients reported to have a previous history of headache. Among them 49.6% patients reported an increase in severity as well as increase in duration (28.8%), more frequent episodes (29.5%), a change in the type of headache (36.7%), and a change in the response to analgesic consumption (20.9%).

Discussion

The study conducted targeted and evaluated the prevalence of headache related to COVID-19.

Although headache is a prominent symptom, studies did not focus on its importance but rather focused on the respiratory, and intensive care aspects that were much more prominent during the course of the disease [12]. For this, the primary focus of this study was to categorize and specify headache intensity, duration, exacerbating factors, and any change in the previous type of headache prior to COVID-19 infection.

Several types of headache has been classified, for which we are going to discuss 3 of them. For instance, migraine is characterized as a stabbing, pulsatile unilateral

headache that lasts between 4 h and 3 days. Migraine is often associated with nausea, vomiting, photophobia and phonophobia. Migraine can be familial, or can be associated with hormonal imbalances, psychological disorders, smoking, environmental factors, epilepsy, and others [13].

Cluster headache is another type, characterized as an excruciating unilateral pain of short duration (15 min to 3 h), and associated with autonomic features such as ptosis, lacrimation, rhinorrhea, sweating and conjunctival injection. Cluster headache is more common among males and smokers [13, 14].

Trigeminal neuralgia is characterized by a unilateral electric shock-like pain along the trigeminal nerve branches. It is caused by irritation to the trigeminal nerve, and often stimulated by brushing hair and teeth, smoking, shaving, talking, eating, drinking, or even a light breeze or water splash to the face. Trigeminal headache is more common among females, and can either occur spontaneously, or as a result of head trauma and dental procedures [15].

There are many possible mechanisms of headache related to COVID-19, however, virus invasion through nasal or oral cavity by the trigeminal nerve is the most rational mechanism especially that our results show a close association between headache and loss of taste and smell (68.3%) [3]. The involvement and alteration of angiotensin converting enzyme (ACE2 and ACE) in the regulation of blood pressure can indirectly cause headache as well [16]. Another mechanism could be due to increase in inflammatory cytokines including tumor necrosis factor (TNF α), Interleukins (IL-1, and IL-6) known as the cytokine storm [12, 16, 17]. The headache that appears after the 7th and 10th day of illness are usually provoked by this cytokine storm [12]. In our study, 87% of the participants reported headache in the first week of infection which could be due to viral illness itself and not due to cytokine storm. Infection of cerebral tissue, or intracerebral hypoxia could be other potential causes of headache during COVID-19 infection [16]. However, hypoxia was absent in about 89% of patients in our study.

Many studies reported headache as a clinical manifestations of COVID-19 [5, 12, 17]. In our study, tension headache (62.8%) and migraine (29.5%) were commonly encountered as well. The location of headache in our study shows diffuse involvement (48.7%) predominantly with pressuring character (77%), and only partially relieved with analgesics (54.9%), with a duration of less than 12 h (57%). This is also shown in other studies where pain was mainly moderate to severe bilateral, frontal, and characterized by pressuring quality [4, 5, 7, 17, 18]. Intensity of headache was reported to be equally moderate >4/10 (38%), to severe >7/10 (37.8%) in our study.

Similarly, a study done showed that 89% of participants reported headache to have an intensity >5, and 60% having an intensity of >7/10 in severity [5]. Approximately 53% of participants in our study reported headache initiation during the first 2 days of COVID-19 infection. Other studies reported a more severe course of headache occurring during the 7th and 10th day of infection correlated to the cytokine storm, with the need of analgesic use exceeding 3 days among 72.2% of participants [4, 12]. Although other studies showed a more severe course of headache, only 7.7% of the participants necessitated emergency admission, and 29.4% required a consultation from a physician in our study. The milder symptoms found in our population could be suggested by the possible developed immunity among our participants, as the data were collected 1 year after the pandemic started [19].

About 43% of participants reported a change of the previous headache during or after COVID-19 infection. The changes reported were increasing severity of headache (49.6%), type changed (36.7%), increasing episodes (29.5%), increasing duration (28.8%), and change in response to analgesics (20.9%). A retrospective study published in 2023, showed that headache was one of the earliest neurological symptoms reported among patients with COVID-19, and hence people who had primary headache would experience an increase in severity [20].

There are several other features reported in our study along with headache during COVID-19 such as myalgia (83.1%), loss of taste and smell (68.3%), gastrointestinal symptoms (37.1%), loss of consciousness (12.4%), and nerve injuries (6.9%). These are considered systemic symptoms and were reported in 98% of participants in a study done in Spain [7]. In a study done in Beijing, China, 262 cases reported fever, cough, fatigue, and dyspnea [18]. Another study interestingly confirmed 11.4% COVID-19 cases attributed with gastrointestinal symptoms and showed that 21.62% among them were associated with higher rates of headache compared to patients without gastrointestinal symptoms. This is mainly attributed to the presence of high fever and alteration in electrolyte balance [18]. In addition, participants reported nausea and vomiting (152, 41.8%), photophobia (128, 35.2%), and phonophobia (169, 46.4%) along with COVID-19 headache in our study. These symptoms are also directly correlated with symptoms of migraine. These features are important to consider in order to determine the severity of the illness. Headache that is due to meningitis or encephalitis during the course of illness will be predominantly associated with neck stiffness, nausea and vomiting, light sensitivity, and fever [18]. This proves how headache can play a role in the prognosis and spectrum of COVID-19 disease. Our study showed a low incidence

of nerve injuries as well as loss of consciousness associated with headache among participants diagnosed with COVID-19, since the mean age of our patients was 39 years with low frequency of associated medical conditions. Thus, patients who usually complained of headache during COVID-19 did not have a viral central nervous system (CNS) infection, but rather a systemic viral infection in accordance to our study.

Limitations and strengths of the study

There are several notable limitations to this study. Based on the considered time period, the number of participants is considerably low with a total of 439. Therefore, the prevalence may not represent a global scale and thus cannot easily generalize findings. Given that it is an online questionnaire, younger individuals were able to easily participate more than the elderly where they preferred a hard copy (more than 70% of participants filled the soft copy). Moreover, not all participants were tested for COVID-19 by PCR, and some may be lacking symptoms of COVID-19. Furthermore, patients who had a severe course of illness could not be included, so study mainly assessed milder forms of the disease. Lastly, CSF analysis and neuroimaging were not done to rule out secondary causes of headache.

There are several strengths in our study, the questionnaire provided was a very detailed, meticulous, and devoted one that investigated several aspects of previous and current headaches in relation to COVID-19 (Additional file 1: Questionnaire). The answers were carefully examined to minimize any inconsistencies. In addition, a neurologist specialist was directly involved in data collection which made data, history, and characteristics of headache more reliable.

Conclusion

Headache is one of the most frequent and primary symptom associated with COVID-19 within the first 2 days of infection. COVID-19-related headache was characterized mainly as diffuse, pressuring, and partially relieved by analgesics. Headache was associated with photophobia, phonophobia and myalgia. Moreover, patients with previous headache reported an increase in pain severity, duration, more frequent episodes and a change in the headache type. Thus, headache should raise early concern of probability of being infected by COVID-19.

Abbreviations

COVID-19	Corona virus
SPSS	Statistical Package for Social Sciences
PCR	Polymerase chain reaction
GBS	Guillain–Barre syndrome
ICU	Intensive Care Unit
ACE	Angiotensin converting enzyme
TNF	Tumor necrosis factor

IL	Interleukins
CNS	Central nervous system
CSF	Cerebro spinal fluid
NSAIDs	Non-steroidal anti-inflammatory drugs

Supplementary Information

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Additional file 1. Questionnaire.

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Author contributions

HEJ and SA worked on the questionnaire development. NS, HK and JH worked on data collection. HK worked on data analysis. NS, JH and CB worked on manuscript write-up. HEJ, SA and CB revised the paper.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

IRB approval provided from Makassed General Hospital, Beirut, Lebanon, on June 22, 2021.

Consent for publication

Not applicable.

Competing interests

There is no potential conflict of interest with respect to research.

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