Original Article

Paradigm shift in migraine management impacted by COVID-19 pandemic and the role of confounding factors inflicting the change

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ABSTRACT

الأهداف: تقييم تأثير جائحة COVID-19 على نوعية حياة الصداع النصفي والعوامل الخارجية.

المنهجية: أجريت هذه الدراسة الجماعية القائمة على الملاحظة في مستشفى راشد، هيئة الصحة بدبي، الإمارات العربية المتحدة. أجرينا دراسة لتقييم مؤشرات الصداع النصفي في فترة ما قبل جائحة COVID-19، وفترات ما قبل الجائحة والوباء ولتقييم التحول النموذجي الناجم عن الوباء في إدارة الصداع النصفي.

النتائج: من بين 840 مصاباً بالصداع النصفي، اخترنا 201 مريض، الأغلبية من الإناث (78%). وجدنا صداع نصفي بدون الهالة في 70% وصداع نصفي مع الهالة في 29.9%. متوسط درجات MIDAS خلال الفترة الأولى والثانية والثانية كان 22.78 و 18.58 و 17.92 على التوالي مما يشير إلى درجة معينة من التحسن وليس التدهور أثناء الجائحة (p=0.001). ومن المثير للاهتمام، لوحظ انخفاض كبير في تواتر وشدة الصداع النصفي من فترة ما قبل الجائحة وفترة الجائحة (p=0.01). كما تراجعت معايير مثل أيام الصداع/الشهر، واستخدام العلاج المُجهض وزيارات الطوارئ. أظهر الصداع النصفي المزمن (CM) تحسنًا أكبر من الصداع النصفي العرضي (EM). أدت العوامل المربكة مثل العمل عن بعد والافتقار إلى الضغط الاجتماعي/المهني إلى هذا التغيير بشكل أساسي. يمكن أن تضمن الإستراتيجية المعدلة للتعامل مع الصداع أثناء أي جائحة/أزمة إدارة الجودة للصداع النصفي.

الخلاصة: كان لدى مرضى الصداع النصفي سلوك مرن خلال جائحة COVID وأظهروا تحسنًا ملحوظًا في جميع المؤشرات. لعبت العوامل الخارجية مثل العمل عن بعد الدور الأكثر ملاءمة.

Objectives: To assess the impact of the COVID-19 pandemic on migraineur's quality of life and confounding factors.

Methods: This is an observational cohort study conducted in Rashid hospital, Dubai Health Authority, UAE. Study was plotted to assess migraine indices in pre-COVID period, pre-pandemic and pandemic periods and to evaluate the pandemic induced paradigm shift in migraine management.

Results: Out of 840 migraineurs 201 patients were selected, with an obvious female predominance (78%). Migraine without Aura was found in 70% and Migraine with Aura in 29.9%. Mean MIDAS score during period I, II and II was 22.78, 18.58 and 17.92 respectively indicating certain degree of improvement rather than deterioration during pandemic (p=0.001). Interestingly significant reduction in both migraine frequency and severity from pre-COVID to COVID period was noticed (p=0.01). Parameters like headache days/month, use of abortive therapy and Emergency visits also declined. Chronic migraine (CM) showed more improvement than episodic migraine (EM). Confounding factors like distance working and lack of social/professional stress mainly rendered this change. A modified strategy to handle headache during any pandemic/crisis can ensure quality management of migraine.

Conclusion: Migraine patients had a resilient behavior during the COVID pandemic and showed significant improvement of all indices. Confounding factors like distance working played the most favorable role.

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Coronavirus disease 2019 (COVID-19) mainly exerts its effect by binding to receptors in the pulmonary epithelium and blood vessels with a special affinity to ACE2 receptors; release of inflammatory cytokines like IL-6 and TNFα ; dysregulation of the immune response; dysregulation of the renin–angiotensin–aldosterone system (RAAS); thrombo-inflammation; and direct viral toxicity.[1] Awareness of its clinical manifestations has developed over couple of years and thousands of researchers have reported their experiences to illuminate the world about this novel disease.

A systemic review on neurological manifestations has shown up a wide spectrum of symptoms, including smell disorders (59%), taste disorder (56%), headache (20%), ischemic stroke (5%), encephalopathy (8.8%), intracerebral hemorrhage (0.45%), encephalitis/meningitis (1.4%), myelitis (1.2%), neuropathy (acute like Guillain-Barre-syndrome) (1.2%) and rhabdomyolysis.[2] Headaches are encountered mainly in neurology clinics, reportedly these make 33% of neurology clinic visits.[3] With a serious concern, headaches are a major symptom reported during the COVID-19 pandemic. Headache-related issues can be segregated into 2 main categories: (i) already existing headaches that are affected by COVID or (ii) new headaches introduced by the infection itself or protective gadgets. For instance, frontline healthcare workers in all hospitals were mandated to wear personal protective equipment (PPE) while handling COVID-19 patients. Wearing the N95 mask during severe acute respiratory distress syndrome (SARS) epidemic in Singapore (2003) resulted in the occurrence of novel onset face-mask-associated headaches with a prevalence of 37.3%.[4] Similarly, amongst medical professionals using the N-95-mask and protective eyewear for an average of 5.7 hours/day, 81% reported de-novo PPE induced headaches and 91% stated aggravation in their pre-existing headaches. However, certain trigger factors, such as sleep deprivation (60.9%), physical stress (29.3%), emotional stress (13.0%), irregular mealtimes (15.2%), and inadequate hydration (39.1%) contributed too.[5] Of the primary headaches, migraine is highly prevalent and is the second leading cause of years-lost-to-disability worldwide.[6] Pandemic induced changes in the healthcare model impacted considerably on headaches and other chronic disorders.[7]

Management protocols, patient consultancy, clinic visit frequency, emergency visit criteria, and all other management protocols were modified during the pandemic. Consequentially, individuals' suffering from migraines intensified. Certain factors, such as stress, infection, fear of catching infection, isolation, limited options of recreation, altered sleep cycle, and wearing PPE, rendered notable changes in the frequency and severity of migraine. However, there were certain factors which positively impacted on migraineurs' lives.

Our objective in this study was to assess the impact of the COVID-19 pandemic on migraineur's quality of life and confounding factors. Such studies can play a leading role in devising new protocols for migraine management during any crisis in future.

Methods. This is an observational cohort study based on retrospective record review and interviews of patients via telemedicine correspondence, conducted in the Neurology Department, Rashid Hospital under the umbrella of the Dubai Health Authority (DHA) from January to August 2020. We included all patients who fulfilled the international classification of headache disorders (ICHD) criteria for migraine[8] and followed up in Neurology and headache clinics. All the patients who had certain details pertaining to our questionnaire available in the hospital computer system were selected.

On 29th January 2020, the first COVID-19 case was reported in UAE, which transformed into a visible disease load by March 2020. A night-time curfew was imposed on 26th March followed by a full curfew on 4th April 2020.[9] Our study compared migraine status before and during the pandemic. The first period (also called period-I) was from 1st September 2019 to 30th November 2019 and it was COVID-free period. The second period (period-II) was from 1st December 2019 to 28th February 2020, which covered the time when COVID-19 started in UAE and there were fewer cases. The third period (period-III) was from 1st March 2020 to 31st May 2020 and it was pandemic period with plenty of COVID cases.

Data for period-I were collected from the hospital incorporated computer system (digital electronic records). Data for period-II and -III were collected through telemedicine-based interviews. The main variables were the Migraine Disability Assessment (MIDAS), mean number of headache days per month, mean headache severity, number of abortive therapies used per month, and emergency visits per month due to migraines. Confounding factors were COVID-19

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Table 1 - Indicating migraine assessment indices and contributory factors during 3 periods.

Migraine indices	Period -I 1st Sep-30th Nov 2019	Period -II 1st Dec,19- 28th Feb 2020	Period -III 1st March - 31st May 2020	Statistical significance
MIDAS (mean)	23.68	18.52	17.85	p=0.02
Headache free pts (No/month)	2	8	9	p=0.002
Headache days/month	6.76	5.67	6.41	p=0.47
Mean severity	7.06	6.61	6.47	p=0.02
Abortive Rx/ month	5.30	4.73	5.11	p=0.24
ED visits/ month	1.06	0.78	0.80	p=0.05
Triggered headache majorly	85%	56.8%	78%	
Top 3 trigger factors	Sleep dis, Stress, Excessive light/ sound	Sleep dis, Stress, Excessive light/ sound	Sleep dis, Stress, Excessive light/ sound	
Migraine induced by COVID Stress	8%	21%	36%	
Infection (proximity)	0	1%	13%	

MIDAS - Migraine Disability Assessment, ED - Emergency Department

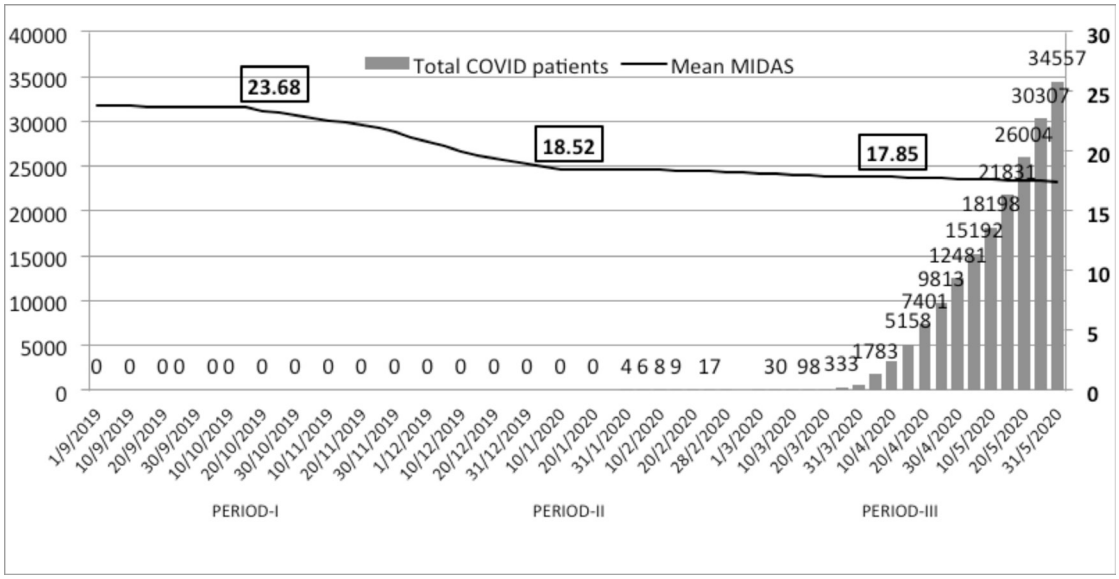

Figure 1 - Mean MIDAS score plotted with number of COVID positive cases in Dubai, showing 3 different periods of study. MIDAS - Migraine Disability Assessment

related stress, trigger factors, compliance, exposure to infection (especially COVID-19), and distant working.

Our minimal target sample size was 78, calculated with WHO calculator considering prevalence of migraine to be 3.8% in a cross-sectional population based study[10] and 95% confidence interval. Means and medians of quantitative variables and frequencies of qualitative variables were measured. The mean values of all parameters in period-I, II and III were compared using the paired t-test. Univariate and multivariate analysis were conducted to examine the relationship between various factors and their impact on migraine indices. To ascertain the association between changes in MIDAS score and confounding factors bivariate correlation and linear regression methods were studied as well.

Results. We reviewed the records of 840 migraine patients from our neurology/headache clinics. Out of these, 201 patients had complete data suitable to the designated variables. Females predominated this sample (78%), with a M:F ratio of 1:3.5. The age of our patients ranged from 13–71 years with a mean age of 36.5 (±2.5) years. Half of our patients belonged to the young age group (26–45 y). To ascertain the association of pandemic with longevity of migraine, duration

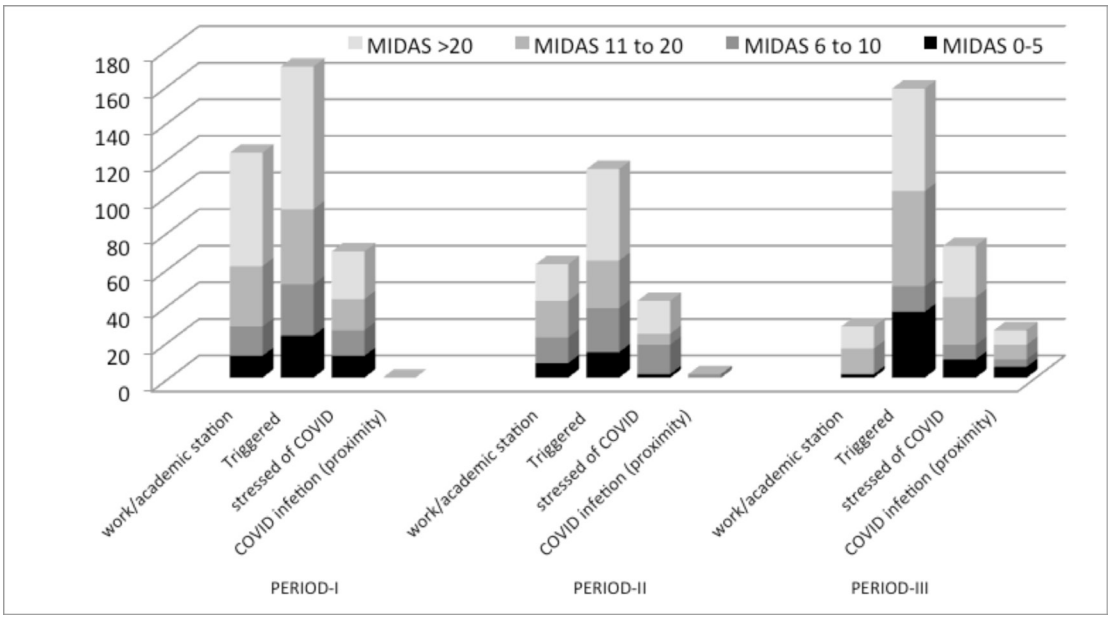

Figure 2 - Number of patients with confounding factors of migraine plotted against the MIDAS score in 3 periods. (First column shows only those patients who worked/ studied in institutions, second column is for pts having triggered headache with trigger factors other than COVID stress, third column for the patients who triggered with COVID stress, fourth column for those who had COVID infection in friends or family). MIDAS - Migraine Disability Assessment

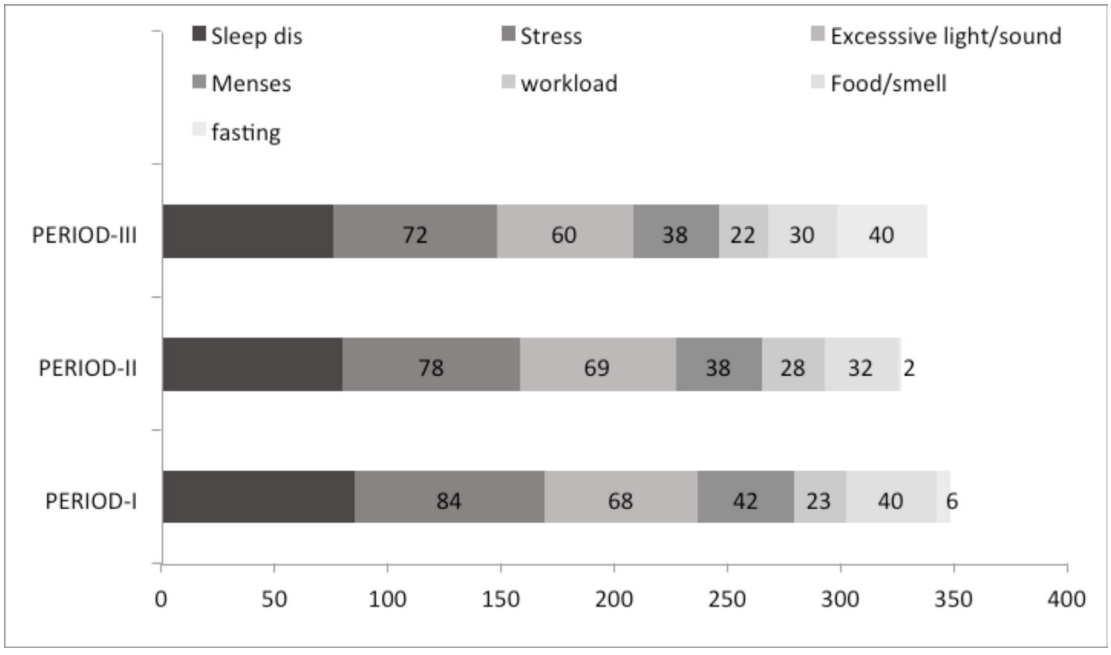

Figure 3 - Showing number of the migraine patients plotted with trigger factors during 3 periods of study.

since onset was also noted, which delineated that the patients who suffered from migraines >10years were 30.3%, 4–10years were 37%, and <3years were 32.7%. However, migraine frequency and management were noticed to be equally affected by COVID irrespective of its longevity.

The ethnic distribution showed a predominance of patients from UAE (86%), followed by other Arab

countries (7%), the Indian subcontinent (4%), and the Far East (2%). Migraine was classified according to ICHD-3 criteria;[9] 141 (70.1%) patients experienced migraines without aura (common migraine) and 60 (29.9%) patients experienced migraines with aura (classic migraine). Based on the frequency 10% patients suffered from chronic migraine and the rest had episodic migraine.

To quantify the impact of migraine on daily life, the MIDAS score was compared between these periods. This revealed a significant improvement in MIDAS score during the pandemic periods. The mean MIDAS scores during period-I, II and III were 22.78, 18.58 and 17.92, respectively (**Figure 1**). Paired t-test showed a significant improvement in MIDAS score from period-I to period-II (p=0.02) and period-III (p=0.001), which deliberately indicated that the pandemic had a positive impact on migraineurs. In order to explore the reason for changes in MIDAS scores, we looked for the factors by applying one-way ANOVA test and discovered that main factor contributing to this change was distance working/studying (p=0.004).

Certain other parameters were also improved during pandemic. The number of headache days per month is a prominent component in this context. Patients with up to 3 headache days/month transformed from 35.3% (in period-I) to 49.3% (during the pandemic period). Patients having frequent headaches (4–15days /month) declined from 52.7% to 40.8% during the pandemic period. Similarly, chronic migraine (>15 days per month) reduced from 11% to 10% in the pandemic period.

Headache severity undoubtedly has a deep impact on quality of migraineurs' life. A comparative analysis of Severity of migraine attack, frequency, emergency visits and average consumption of abortive pills during these periods was conducted. In the questionnaire, a simple pain score (0–10) was used and patients were instructed to narrate their headache magnitude. As a matter of fact, a significant improvement in migraine severity was demonstrated from Period-I to period-III (**Table 1**). Interestingly, the frequency and mean severity were significantly reduced from Period-I to period-II (p=0.01, CI 95%). (**Table 1**).

Out of 201 patients, 185 (90%) were using prophylactic migraine management; 55 used Propranolol, 48 used Amitriptyline, 44 used Topiramate, and 38 used calcitonin gene-related peptide (CGRP) inhibitors as a preventive therapy. Out of these, 58% of patients demonstrated good compliance, defined as taking medicine >90% of the days every month. Amongst the non-compliant patients (31.8%), approximately two thirds ran out of medicine during the COVID-19 pandemic due to logistic issues. Before the pandemic they reported being complaint. Patients using monotherapy did much better than combination therapies (p<0.05). Segregating the efficacy of preventive therapies and assessing their isolated role in MIDAS score reduction during pandemic period by using multiple regression indicated the peculiarly efficient role of Propranolol, Amitriptyline and CGRP-inhibitors (p=0.034). Noncompliance during the pandemic periods was a common issue encountered for all the preventive therapies, which may have interfered in this grading.

The confounding factors were interrogated in detail as trigger factors of migraine. Work-related stress can be a major burden that exacerbates migraine; hence, patients were questioned about their working circumstances during all the periods. Similarly, students were questioned about their distance vs school/college learning. Univariate and multivariate analysis were conducted to examine the relationship between various factors and their impact on migraine control. We found that 61.7% of patients worked/studied at their institutions in period-I, which were reduced to 31% and 14% in period-II and -III, respectively. This represented a decline in 'on-location' work and a gradual increase in distance working/learning. Statistical correlation by chi-square test between work place (during COVID pandemic) and migraine indices showed a decline in headache frequency (p=0.02) and MIDAS score (**Figure 2**). Application of Linear regression analysis ascertained significant cause effect relationship (p <0.01). Similarly, the existence of stressors (professional, social, and logistic) was evaluated as triggers during the 3 periods and correlated with the headache frequency and intensity. These results showed that stressors (other than stress of COVID) were reduced during the pandemic, which led to reduced headache frequency and intensity (p=0.03). The chi-square test was applied to establish an association between the trigger factors and trends in migraine indices. Further confirmation by bivariate correlation and linear regression methods confirmed a positive relationship between stressors and MIDAS scale. There was a positive association between other trigger factors and migraine burden; however, these did not reach to significance (**Figure 2**).

The use of abortive therapy for acute migraine attacks was assessed as it is one of the control predictors. The mean number of abortive pills used per month reduced from 5.3 (period-1) to 4.73 (period-II) and 5.1 (period-III). Paired t-test indicated a significant improvement from period I to II (p=0.001, CI 95%).

Thorough analysis of reduction in abortive therapy consumption in relation to confounding factors via bivariate analysis showed a significant positive correlation of stressors to abortive therapy (chi-square *p*-value=0.005). Additionally, distance working during period-III showed a significant association with reduced abortive therapy consumption (p=0.03).

The extreme forms of migraine were indirectly assessed using the number of emergency visits for injectable therapy or admission, regardless of contributory factors. Similarly, this also revealed downward trends during pandemic period. The mean visits dropped from 1.19/month in period-I to 0.8/month in period-III. The number of patients visiting the Emergency Department (ED) very frequently (>10 visits/month) were noticed to be 6, 4 and 4 in period-I, II, and III, respectively. Comparing means of high frequency visits resulted in significant difference (p<0.05) for all period transitions; however, frequency of ED visits (as a whole) failed to establish any significant association to contributing factors on linear regression. There was concern that the turnout of patients would have been reduced during the COVID-19 pandemic as a result of preventive precautions; however, this was nullified by the fact that mean ED visits in period II (pre-pandemic) was also reduced (0.78 per month), when a full lockdown had not been invoked and precautions were preliminary.

The effect of infections, including COVID-19, on migraine patients was also studied. Patients were interrogated about the history of infection in them and their relatives or people in close proximity. None of the patients sustained any particular infection. Two of the patient's relatives in period-II and 26 in period-III were infected with COVID-19. We presumed that in the presence of infected relatives, patients' migraine should have worsened because of stress or COVID phobia. Surprisingly, this was disregarded by the fact that patients' migraine parameters improved during period-III. None of the quantitative parameters, including MIDAS score, headache days, consumption of abortive therapy, severity grade of headache or ED visits had a significant relationship with infection on bivariate analysis.

Discussion. According to the global disease burden (GDB) survey 2016, 1.04 billion people worldwide experience migraines. This is responsible for 45.12 million years of life lived with disability (YLD), with peak prevalence in women between 15 and 49 years. YLD due to migraine has increased from 1990 to 2016 and is higher than those due to tension-type headache, which is a more prevalent disorder amongst primary headaches.[11] Since the worldwide COVID-19 pandemic, health care systems have focused on providing additional testing services, therapeutic coercion, isolation, and preventive measures. This has adversely affected economies worldwide and so has a negative impact on healthcare system.

Migraine prevalence in our region is 23% in Kuwait,[12] 7.9% in Qatar,[13] 10.1% in Oman,[14] 5.0 % in Saudi Arabia,[15] 25.2% in Pakistan,[16] 20.8% in Russia,[17] 25.6 in India,[18] and 29% in Turkey.[19] A major share of healthcare budget in these countries has been utilized for management services of migraine and other headaches. During the COVID-19 pandemic, headache clinicians continued to work to support migraineurs and prevent hospital visits, while also minimizing face-to-face visits and procedural treatments. This is crucial to protect the safety of our patients and limit their exposure to COVID-19. Additionally, this is critical challenge to prevent the infection of healthcare workers and minimize additional demands on hospital infrastructure.

Migraine attacks are triggered by stress and infection, which are commonly faced during pandemics. Therefore, we hypothesized that suffering due to migraine would escalate during this period. Contrarily, all studied parameters measuring migraine severity declined during COVID-19. Data showed a reduction in professional, logistic, and social stressors during the pandemic, which led to the optimal migraine control. It is noteworthy that despite increased COVID-related stress, migraineurs had improved quality of life during the pandemic periods, suggesting that professional and logistic stressors exerted a stronger impact on migraine than COVID-related stress. Parodi et al[20] evaluated 49 patients for migraine burden via the global assessment of migraine severity (GAMS) and visual analogue scale (VAS) using phone interviews. Additionally, they quantified depression and anxiety via the Beck depression inventory (BDI) and Zung Self-Rating Anxiety Scale (SAS). Migraine and depression scores calculated 2 months immediately before lockdown compared to those calculated during quarantine period established a significant improvement during the quarantine period (p=0.001). This indicated that during quarantine, individuals had fewer migraine attacks despite a moderate level of depression.

The Italian Registry of Headache (Registro Italiano delle Cefalee, RICe) endorsed an observational registry signifying a greater improvement in headache frequency and analgesic consumption in patients with chronic migraine comparative to episodic migraine. Alcohol use, smoking, eating, and subjective perception of sleep quality did not affect headache frequency or

intensity, whereas use of symptomatic drugs and working conditions did adequately. The improvement of headache frequency was correlated with the number of stay-at-home days and this bivariate correlation was significant ($p<0.0001$),[21] also projected by our data. However, their data showed episodic migraines in 76% patients and remaining had chronic migraine, comparatively our data contained 90% patients with episodic migraine.

Another multicentric Italian cohort, compared monthly migraine days (MMD), monthly painkiller intake (MPI) and headache impact test-6 (HIT-6) in migraineurs receiving CGRP inhibitors, during pre-COVID and COVID periods indicated improvement in MMDs whilst MPI remained unchanged.[22] Their statistical evaluation suggested significant improvement in case of chronic migraine (CM) rather than episodic migraine (EM) and males obviated more pronounced improvement in comparison to females. Likewise, our data showed significant improvement in CM in comparison to EM. Contrary to Italian cohort, all variables in our data like MIDAS score, monthly headache days, rescue medication usage improved worthwhile and females showed more improvement in MIDAS score rather than males ($p=0.23$).

Our results revealed that patients experienced significant improvements from period-I to period-II. However, improvement during period-III was not equally substantial. As a critical analysis we looked into the reasons why improvement in period-II was more obvious contrary to period-III, despite all the confounding factors being more favorable in period-III. We found that certain factors played a peculiar role in increasing the suffering of migraineurs during period-III. Telemedicine-based patient interviews revealed that 31.8% patients were noncompliant and two thirds out of them had run out of medicine during period-III. Furthermore, COVID phobia led to them being unable to collect medications from the hospital pharmacy. Although frequent telephonic clinics and home delivery services were incorporated but unfortunately, they could not avail them.

This issue was managed by many of the headache specialists and neurologists by switching the preventive therapies to long-acting therapies, for instance CGRP-receptor antagonists, and replacing CGRP antagonist with procedures like Botulin toxin. To break the long pain cycle, a bridging strategy has been successfully availed in a few places.[23] Secondly, fasting in the holy month of Ramadan was a significant trigger factor (this occurred in April-May 2020), which decelerated the improvement graph in period-III. This was reported by 40 patients (20%) (**Figure 3**). The lifetime prevalence of fasting-induced headaches was approximately 4%. The mechanism of how fasting triggers migraines is not well established; however, certain factors like hypoglycemia, dehydration, caffeine withdrawal, free fatty acids, sympathetic nervous system activation, hypothalamic dysfunction, insulin, and several other hormonal factors may serve as potential headache triggers.[24]

A thorough review of confounding factors established that working environment was the most effective factor for reducing the frequency and severity of migraine during the pandemic periods. A critical analysis raised some quarries about MIDAS score, for instance first 2 questions are related to work. These don't apply on housewives, unemployed and retired individuals. Presumably, this factor did not alter the results because we compared the MIDAS scores of the same patients with similar profile at different periods. As the patients' employment status did not change during any period and so this factor did not alter the MIDAS score. Also, the other factor that could have influenced the results was the fact that during the COVID-19 pandemic (period-III), there were no social gatherings/activities, so question 5 lost its validity. Certain arbitrary modifications were formulated to reduce this impact i,e we took the percentage of the response to question 5 in Period-I and II and added this to the total score in period-III for each patient. Factually, in addition to MIDAS score few more variables were studied as well like headache days/month, headache severity scale and number of abortive pills used. These were also reduced, indicating a true improvement rather than a bias.

Certain limitations may have influenced the results. First, we encountered 840 migraine patients; however, missing data in the incorporated computer system limited our study to 201 patients. This may affect the strength of study. Secondly, fasting and compliance issues during period-III affected the results. Without these factors, we could have measured a well-demarcated impact of solely the pandemic on migraine. All indices were markedly improved from period-I to period-II, this improvement did not continue with the same robustness in period-III. Such studies may enable us to establish management protocols and therapeutic policies for migraine management and other clinical disorders, which may lead us to handle healthcare issues during any crisis in a smarter way.

Conclusion. Despite of all the risks and stressors, migraineurs showed resilient behavior against pandemic distress, with a reduction in migraine severity indices. The maintenance of habitual lifestyles and social distancing during the pandemic further supported

such resilience, which was less evident in people with a limited stay at home. Improvement in the early phase of COVID-19 was more pronounced than later period, likely because of the decelerating impact of compliance and other confounding factors.

Taken together, this paradigm shift has meant that it is possible to upgrade the therapeutic approach of migraine management by structuring telemedicine clinics, establishing home delivery systems, and counselling of patients to alleviate their stress. This will certainly lead to a better therapeutic outcome.

References

1. Gupta A, Madhavan MV, Sehgal K, Nair N, Mahajan S, et al. Extrapulmonary manifestations of COVID-19. ***Nature Medicine*** 2020; 26: 1017-1032.
2. Nepal G, Rehrig JH, Shrestha GS, Shing YK, Yadav JK, Ojha R et al. Neurological manifestations of COVID-19: a systematic review. ***Critical Care*** 2020; 24: 421.
3. Baykan B, Ertas M, Karli N, Akat-Aktas S, Uzunkaya O, Zarifoglu M, et al. The burden of headache in neurology outpatient clinics in Turkey. ***Pain Pract*** 2007; 7: 313-323.
4. Lim EC, Seet RC, Lee KH, Wilder-Smith EP, Chuah BY, Ong BK, et al. Headaches and the N95 face-mask amongst healthcare providers. ***Acta Neurol Scand*** 2006; 113:199-202.
5. Ong JJ, Bharatendu C, Goh Y, Tang JZ, Sooi KW, Tan YL, et al. Headaches associated with personal protective equipment–A cross-sectional study among frontline healthcare workers during COVID-19. ***Headache*** 2020; 60: 864-877.
6. GBD 2016 Headache Collaborators. Global, regional, and national burden of migraine and tension-type headache, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. ***Lancet Neurol*** 2018; 17: 954-76.
7. Silvestro M, Tessitore A, Tedeschi G, Russo A. Migraine in the Time of COVID-19. ***Headache*** 2020; 60: 988-989.
8. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). ***Cephalalgia*** 2013, 33: 629-808.
9. Coronavirus: Dubai announces two-week 24-hour curfew as disinfection continues". Al Arabiya English. 4 April 2020. Retrieved 13 April 2020. from URL: https://english.alarabiya.net/News/gulf/2020/04/04/Coronavirus-Dubai-extends-sterilization-enforces-strict-restrictions-on-movement
10. Bener A, Swadi H, Qassimi EM, Uduman S. Prevalence of headache and migraine in schoolchildren in the United Arab Emirates. ***Ann Saudi Med*** 1998; 18: 522-524.
11. GBD 2016 Headache Collaborators. Global, regional, and national burden of migraine and tension-type headache, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. ***Lancet Neurol*** 2018; 17: 954-976.
12. Al-Hashel JY, Ahmed SF, Alroughani R. Burden of migraine in a Kuwaiti population: a door-to-door survey. ***J Headache Pain*** 2017; 18: 105.
13. Bener A. Frequency of headache and migraine in Qatar. ***Neuroepidemiology*** 2006; 27: 61-66.
14. Deleu D, Khan MA, Al Shehab TA. Prevalence and clinical characteristics of headache in a rural community in Oman. ***Headache*** 2002; 42: 963-973.
15. Lipton RB, Bigal ME. Migraine: epidemiology, impact, and risk factors for progression. ***Headache*** 2005; 45: S3-S13.
16. Herekar AA, Ahmad A, Uqaili UL, Ahmed B, Effendi J, Alvi SZ, et al. Primary headache disorders in the adult general population of Pakistan – a cross sectional nationwide prevalence survey. ***J Headache Pain*** 2017; 18: 28.
17. Ayzenberg I, Katsarava Z, Sborowski A, Chernysh M, Osipova V, Tabeeva G, et al. The prevalence of primary headache disorders in Russia: a countrywide survey. ***Cephalalgia*** 32: 373-381.
18. Kulkarni GB, Rao GN, Gururaj G, Stovner LJ, Steiner TJ. Headache disorders and public ill-health in India: prevalence estimates in Karnataka state. ***J Headache Pain*** 2015; 16: 67.
19. Ertas M, Baykan B, Orhan EK, Zarifoglu M, Karli N, Saip S, et al. One-year prevalence and the impact of migraine and tension-type headache in Turkey: a nationwide home-based study in adults. ***J Headache Pain*** 2012; 13: 147-157.
20. Parodi IC, Poeta MG, Assini A, Schirinzi E, Del Sette P. Impact of quarantine due to COVID infection on migraine: a survey in Genova, Italy. ***Neurol Sci*** 2020; 41: 2025-2027.
21. Delussi M, Gentile E, Coppola G, Prudenzano AM, Rainero I, Sances G, et al. Investigating the Effects of COVID-19 Quarantine in Migraine: An Observational Cross-Sectional Study from the Italian National Headache Registry (RICe). ***Front Neurol*** 2020; 11: 597881.
22. Altamura C, Cevoli S, Aurilia C, Egeo G, Fofi L, Torelli P, et al. Locking down the CGRP pathway during the COVID-19 pandemic lockdown: the PandeMig study. ***Neurol Sci*** 2020; 41: 3385-3389.
23. Chowdhury D, Datta D. Managing migraine in the times of COVID-19 pandemic. ***Ann Indian Acad Neurol*** 2020; 23: S33-S39.
24. Dalkara T, Kılıç K. How does fasting trigger migraine? A hypothesis. ***Curr Pain Headache Rep*** 2013; 17: 368.