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Effect of COVID-19 quarantine on patients admitted to neurosurgery outpatient

Eyüp ÇETİN*[®], Mehmet Edip AKYOL[®]

Department of Neurosurgery, Dursun Odabaş Medical Center, Van Yüzüncü Yıl University, Van, Turkey

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Abstract

Coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. Throughout the pandemic period, numerous countries around the world have implemented nationwide isolation measures to control the spread and transmission of COVID-19. During this period, the prevalence of some physical and mental diseases have increased due to prolonged home isolation measures. In the present study, we aimed to examine the effect of the COVID-19 isolation measures imposed in Turkey on patients admitted to our neurosurgery outpatient clinic.

Keywords: isolation, COVID-19, pandemic, low back pain, headache

1. Introduction

Coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, in December 2019 and then spread to the entire world and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the primary cause of COVID-19 (1). Throughout the pandemic period, numerous countries around the world have implemented nationwide isolation measures to control the spread and transmission of COVID-19 (2).

In Turkey, as of March 2020, the government has imposed nationwide restrictions to prevent the risk of COVID-19 infection, such as closing schools, bars, nightclubs, theaters, gyms, mosques, and all public gathering places. Additionally, a permanent isolation was declared for the elderly and individuals with chronic diseases. In later periods, weekend curfews were imposed and the people were ordered to stay at home, work remotely, and engage in distance learning (3). Of these measures, the stay-at-home order has been shown to be an effective way to prevent COVID-19 infection and reduce the mortality rates (4).

Nevertheless, although the voluntary and compulsory stay-at-home measures are highly effective for preventing exposure to COVID-19, they have been shown to have several disadvantages such as causing reduced physical activity, weight gain, behavioral addiction, and social problems (5). In turn, reduced physical activity may lead to an increased prevalence of musculoskeletal disorders and pain (6). Additionally, long-term inactivity during the COVID-19 pandemic has been associated with a number of health problems (7).

Despite technological advancements and new treatment methods, low back pain and related conditions remain an important health concern around the world, even in developed countries (8). The global incidence of low back pain is estimated to be between 1.4% and 20% (9). Low back is one of the most common sites of work-related pain and low back pain poses significant problems in both private and professional lives of individuals (10). These problems include sleep disturbances, physical and mental disability, work absenteeism, decreased work efficiency (11). Additionally, the economic impact of low back pain also represents a major concern worldwide. Of note, the cost of low back pain is estimated to represent 1-2% of the gross national product in Western countries (12). Low back pain is primarily associated with occupational exposures in awkward postures, such as heavy lifting and repetitive lifting, as well as trunk flexion, rotation and hyperextension, pushing, pulling, carrying, and whole-body vibrations (13). In addition, some factors such as age, gender, hypertension, smoking, ergonomics, job satisfaction, excessive body weight or obesity, lack of physical activity, and depression may intensify low back pain (14). However, the prevalence of low back pain may change depending on the alterations in individual habits and lifestyles. Accordingly, a number of measures have been taken in many countries to prevent the risk of COVID-19 transmission (15).

Following the outbreak of COVID-19, a number of innovations were introduced into working conditions. To



illustrate, many corporations introduced remote working models based on the use of technological devices in order to minimize the risk of contamination (16). Expectedly, the home environment has numerous differences when compared to the working environment. Of note, the absence of ergonomic office furniture at home may prevent a healthy posture and thus may lead to the onset of musculoskeletal disorders (17). Prolonged sedentary behavior increases the risk of spinal disorders such as neck and back pain (18). On the contrary, home working has several positive effects as well, such as reducing psychological stress, improving the family life, and increasing the work efficiency (19).

The pandemic has also changed the amount of time spent at home and the daily routine of most people. Due to the reduced face-to-face interaction opportunities during the COVID-19 pandemic, people have resorted to technological devices with internet-based services (20). Moreover, people have started to spend more time on the internet and social media via smartphones in order to overcome boredom, seek information, utilize educational services, and do research (21). Internet usage has also increased significantly during the pandemic period (22). There are many psychiatric and musculoskeletal disorders associated with excessive smartphone use (23), which mainly typically include discomfort and pain in various parts of the body, including the neck, shoulder, elbow, wrist, hand, and thumb (24).

In a study conducted with a home working population in Italy, it was found that the prevalence of existing neck pain increased in 50% of the workers and decreased in 8% of them (25).

Headache is one of the most common diseases worldwide. Moreover, tension-type headache and migraine are reported as the second and third most common diseases in the world, respectively (26). According to the international classification of headache disorders, 50.1-78.4% of headaches are associated with primary headaches, while 2.5-23% of the cases cannot be classified (27). Correct classification of headache disorders is a prerequisite for targeted therapy both for headache specialists and clinicians (28).

Belvis et al. evaluated more than 41,000 COVID-19 patients and detected headache in 8-12% of them (29). After an incubation period of 2 to 24 days, a clinical picture including fever, dry cough, and difficulty breathing may be seen. Additionally, various combinations of weakness, muscle aches, headache, nasal congestion, nausea, vomiting, diarrhea, hemoptysis, sore throat, myalgia, arthralgia, anosmia, and ageusia may occur. On the other hand, the initial clinical manifestations may be complicated by pneumonia, acute respiratory distress syndrome, and sepsis in some patients [30]. Additionally, headache has been shown to be the 5th most common symptom of COVID-19 after fever, cough, myalgia, fatigue, and shortness of breath (31). During the pandemic period, the loneliness caused by the isolation measures has led to an increased prevalence of many pain conditions and to a significant increase in the prevalence of headaches (32).

There are numerous mental health problems associated with the isolation measures imposed during the COVID-19 pandemic (33). A previous study compared clinical data of patients before and after the pandemic and showed an increase in the prevalence of average psychological disorders (34). Since the cure of the pandemic has not yet been found and the uncertainty continues, it has led to an increases prevalence of psychiatric disorders including panic, anxiety, and depression (35). Additionally, some other studies showed that the individuals forced to quarantine at home are at increased risk for depression and post-traumatic stress disorder symptoms (36).

To date, numerous studies have investigated the increased prevalence of psychological and physical disorders resulting from the sedentary lifestyle during the COVID-19 pandemic. However, to our knowledge, there has been no retrospective study evaluating the changes in patients admitted to neurosurgery outpatient clinics. In the present study, we aimed to examine the effect of the COVID-19 isolation measures imposed in Turkey on patients admitted to our neurosurgery outpatient clinic.

2. Materials and Methods

2.1. Study design and participants

The retrospective study reviewed pre- and post-pandemic clinical records of 4,950 patients aged 18-100 years who applied to our outpatient neurosurgery clinic over the 10-month period between April 1, 2020 and January 15, 2021. Patients with conditions associated with trauma, those with a history of surgery, and patients who regularly visited the clinic for postoperative follow-up were excluded from the study.

Age, gender, occupation, presence of chronic disease, duration and progression of pain, ongoing medication, history of psychiatric diseases, clinical examinations and treatments, duration of home stay, and complications associated with delayed hospital admission were recorded for each patient. Patients were divided into two groups according to the duration of home stay due to COVID-19: (i) group 1 (0-4 months; n=1,913) and (ii) group 2 (\geq 5 months; n=2,036).

The study was conducted in accordance with the principles of Helsinki Declaration and the study protocol was approved by Van Yuzuncu Yil University Ethics Committee.

2.2. Statistical analysis

Data were analyzed using SPSS for Windows version 27.0 (Armonk, NY: IBM Corp.). Variables were expressed as mean, standard deviation (SD), median, minimum-maximum, frequencies (n), and percentages (%). Normal distribution of continuous variables was assessed using Kolmogorov-

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Smirnov test. Continuous variables were compared using Mann-Whitney U test and categorical variables were

compared using Chi-square test. A p value of <0.05 was considered significant.

Table 1. Demographic and clinical characteristics

		Min-Max	Median		SD/n-%
Age (years)		17.0 - 92.0	43.0	44.0 ± 14.4 5.8 ± 2.5	
Duration of home stay (months)		0.5 - 9.5	6.0		
Duration of home stay	0-2 months			546	11.0%
	3-4 months			1367	27.6%
	5-7 months		1318	26.6%	
	≥ 8 months	1718	34.7%		
Gender	Male			2202	44.5%
	Female			2747	55.5%
Presenting complaints					
Low back pain				2989	60.4%
Headache				1523	30.8%
Neck pain				526	10.6%
Leg pain				364	7.4%
Arm pain				46	0.9%
Back pain				38	0.8%
Vertigo				12	0.2%
Carpal tunnel				7	0.1%
Cranial mass				4	0.1%
Hydrocephalus				2	0%
Comorbidity	(-)			4416	89.2%
Comorbidity	(+)			533	10.8%
LDH				169	31.7%
Cranial mass				136	25.5%
HT				59	11.1%
SDH				49	9.2%
DM				44	8.3%
Hydrocephalus				26	4.9%
Chiari malformation				21	3.9%
Spinal mass				7	1.3%
Epilepsy				6	1.1%
Other				34	6.4%
	(-)			4827	97.5%
Chronic diseases	(+)			122	2.5%
	(-)			4913	99.3%
Psychiatric disorders	(+)			36	0.7%
	(-)			4925	99.5%
Complications associated with delayed hospital admission	(+)			24	0.5%

LDH: Lactate dehydrogenase deficiency, HT: Hypertension, SDH: Subdural hematoma, DM: Diabetes mellitus

3. Results

No significant difference was found between the group with a duration of home stay of 0-4 months and the group with a duration of ≥ 5 months with regard to age and gender (p > 0.05 for both). Similarly, no significant difference was found between the two groups with regard to the prevalence of low back pain, headache, neck pain, arm pain, back pain, carpal tunnel, cranial mass, and hydrocephalus (p > 0.05), whereas the prevalence of leg pain was significantly lower and the prevalence of vertigo was significantly higher in patients with a duration of ≥ 5 months (p < 0.05 for both) (Table 2).

No significant difference was found between the two groups with regard to the prevalence of all comorbidities (p>0.05 for all) except for Chiari malformation, which was significantly higher in patients with a duration of ≥ 5 months (p<0.05). Similarly, no significant difference was found between the two groups with regard to the prevalence of chronic diseases and the complications associated with delayed hospital admission (p>0.05 for both). However, the prevalence of psychiatric diseases was significantly higher in patients with a duration of ≥ 5 months (p<0.05) (Table 2).

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		Duration of home stay (0-4 months)			Duration of home stay ≥ 5 months			
		Mean	Mean±SD/n-%		Mean±SD/n-%		Median	р
Age (years)		44.4	44.4 ± 14.8		43.8±14.1		42.0 7.5	0.272 m
Duration of home stay (months)		3.1	3.1 ± 1.1		7.4±1.4			
Gen Male der		883	46.2%		1319	43.4%		0.062 x ²
Female		1030	53.8%		1717	56.6%		
Presenting complaints								
Low back pain		1163	60.8%		1826	60.1%		$0.649 \mathrm{x}^2$
Headache		584	30.5%		939	30.9%		0.766 x ²
Neck pain		197	10.3%		329	10.8%		0.549 x^2
Leg pain		166	8.7%		198	6.5%		<i>0.005</i> x ²
Arm pain		15	0.8%		31	1.0%		0.398 x ²
Back pain		16	0.8%		22	0.7%		0.661 x ²
Vertigo		1	0.1%		11	0.4%		<i>0.031</i> x
Carpal tunnel		2	0.1%		5	0.2%		0.584 x
Cranial mass		1	0.1%		3	0.1%		1.000 x
Hydrocephalus		1	0.1%		1	0.0%		1.000 x ²
Comorbidity	(-)	1708	89.3%		2708	89.2%		
	(+)	205	10.7%		328	10.8%		0.923 x
LDH		35.1%		97	29.6%		0.180 x	
Cranial mass		22.4%		90	27.4%		0.198 x	
HT		12.7%		33	10.1%		0.348 x	
SDH		7.3%		34	10.4%		0.236 x	
DM		10.7%		22	6.7%		0.100 x^2	
Hydrocephalus		5.9%		14	4.3%		0.408 x ²	
Chiari malformation		1.0%		19	5.8%		0.005 x	
Spinal mass		0.5%		6	1.8%		0.186 x ²	
Epilepsy			1.0%		4	1.2%		0.795 x ²
Other			5.9%		22	6.7%		0.695 x
Chronic diseases	(-)	1858	97.1%		2969	97.8%		0.140 x ²
	(+)	55	2.9%		67	2.2%		
Psychiatric disorders	(-)	1905	99.6%		3008	99.1%		$0.042 x^2$
	(+)	8	0.4%		28	0.9%		
Complications associated	(-)	1908	99.7%		3017	99.4%		
with delayed hospital admission	(+)	5	0.3%		19	0.6%		0.072 x ²

^mMann-Whitney U test / X² Chi-square test, LDH: Lactate dehydrogenase deficiency, HT: Hypertension, SDH: Subdural hematoma, DM: Diabetes mellitus

4. Discussion

The world is looking to an uncertain future for the first time in long years and it seems extremely difficult to win the war against this virus. More importantly, it is expected that the globalization of the world, the emergence of repeated infections due to COVID-19 mutations, and the outlook for new types of pandemics will lead to the prolongation and continuity of isolation measures (37). Although the isolation measures are loosened from time to time, the consequences of the pandemic can be aggravated and thus require repeated isolation measures. Moreover, although isolation measures help prevent virus transmission, the order and nature of the epidemic remain uncertain, thereby causing social and economic deterioration by affecting the functioning of the health system (38).

Despite the ongoing efforts to develop an effective vaccine, many people are concerned about vaccine safety. Bogart et al. showed remarkably high rates of potential vaccine hesitancy in the general population (39). In the present study, we evaluated the effects of COVID-19

isolation measures on neurosurgical patients based on the assumption that these measures would be further prolonged.

In the present study, we evaluated a total of 4,950 patients who applied to our neurosurgery outpatient clinic over a period of approximately 10 months from the beginning of the COVID-19 isolation period. We excluded patients who were previously operated on in our clinic or had complications due to previous surgeries and those affected by the COVID-19 virus. In doing so, we aimed only to determine the effects of isolation measures on our patients. We divided the patients into two groups according to the duration of home stay due to COVID-19: (i) group 1 (0-4 months) and (ii) group 2 (\geq 5 months), and we analyzed the results statistically. The results indicated no significant relationship between the isolation measures and age and gender.

In our study, no significant correlation was found between the duration of isolation measures and the prevalence of regional pains such as low back pain, headache, neck pain, arm pain, and back pain. This finding contradicts with the findings reported in the literature and may be due to the relaxation of temporary isolation measures. In contrast, the prevalence of leg pain decreased significantly as the duration of isolation measures increased. This finding could be attributed to the relaxing effect of home isolation on spinal disc herniation. On the other hand, the prevalence of vertigo increased significantly as the duration of isolation measures increased. Although the occurrence of vertigo in patients with COVID-19 infection has been reported in the literature, to our knowledge, there is no meaningful research on the effect of isolation on vertigo (40). Literature indicates that organic vertigo syndromes are closely associated with psychiatric disorders (41). Accordingly, we considered that the increased prevalence of vertigo in our patients could be associated with the increased prevalence of psychiatric disorders.

In our patients, the prevalence of Chiari malformation increased significantly as the duration of isolation measures increased. In the literature, social isolation has been reported to be positively associated with interleukin (IL)-6 and it has also been shown that the methylation of RNA leads to increased proinflammatory responses, thereby leading to epigenetic effects that are known to have adverse effects on health (42). Reducing loneliness is associated with decreased pro-inflammatory gene expression, which further reinforces the relationship between loneliness and inflammatory responses (43). Studies have shown that the increased symptoms of Chiari malformation has significant effects on loneliness and stress factors (44).

In our study, no significant relationship was found between the duration of isolation measures and the prevalence of chronic diseases. Based on this finding, we assume that the elderly population with chronic diseases are not significantly affected by the isolation measures. Additionally, it was also observed that the prevalence of psychiatric disorders increased in line with the duration of isolation measures, which could be associated with the increased prevalence of loneliness caused by isolation measures and with the increase in stress factors (45)

.In line with the globalization of the world, infectious viral diseases pose the risk of turning into a pandemic. Despite technological advancements and scientific studies, pandemics cause negative effects on humans' lifestyles. During the COVID-19 pandemic, the restrictions imposed by governments around the world encourage people to perform voluntary and involuntary home isolation. Additionally, these restrictions further increase the sedentary behavior of people, which is a prevalent problem brought by the modern age, and thereby increase the prevalence of some physical and mental diseases, ultimately leading to serious individual and social problems.

Conflict of interest

None to declare.

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None to declare.

References

- Sohrabi C, Alsafi Z, O'Neill N, Kerwan A, Al-Jabir A, Iosifidis C, Agha R. "World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19)," Int. J. Surg., vol. 76, pp. 71–76, Apr. 2020, doi: 10.1016/j.ijsu.2020.02.034.
- Gostin LO, Wiley LF. "Governmental Public Health Powers during the COVID-19 Pandemic: Stay-at-home Orders, Business Closures, and Travel Restrictions," JAMA - J. Am. Med. Assoc., vol. 323, no. 21, pp. 2137–2138, Jun. 2020, doi: 10.1001/jama.2020.5460.
- Eroğlu Y. "Forecasting Models For COVID-19 Cases of Turkey Using Artificial Neural Networks and Deep Learning.," Endüstri Mühendisliği, vol. 31, no. 3, pp. 353–372, Dec. 2020, doi: 10.46465/endustrimuhendisligi.771646.
- Fowler JH, Hill SJ, Levin R, Obradovich N. "The effect of stayat-home orders on COVID-19 cases and fatalities in the United States," medRxiv, Apr. 2020, Accessed: Mar. 23, 2021. [Online]. Available: http://arxiv.org/abs/2004.06098.
- Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, Evaluation and Treatment Coronavirus (COVID-19). StatPearls Publishing, 2020.
- Holth HS, Werpen HKB, Zwart JA, Hagen K. "Physical inactivity is associated with chronic musculoskeletal complaints 11 years later: Results from the Nord-Trøndelag Health Study," BMC Musculoskelet. Disord., vol. 9, no. 1, pp. 1–7, Dec. 2008, doi: 10.1186/1471-2474-9-159.
- Lippi G, Henry BM, Bovo C, Sanchis-Gomar F. "Health risks and potential remedies during prolonged lockdowns for coronavirus disease 2019 (COVID-19)," Diagnosis (Berlin, Ger., vol. 7, no. 2, pp. 85–90, Apr. 2020, doi: 10.1515/dx-2020-0041.
- 8. Stanaway JD et al. "Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: A systematic analysis for the Global Burden of Disease Study 2017," Lancet, vol. 392, no. 10159, pp. 1923–1994, Nov. 2018, doi: 10.1016/S0140-6736(18)32225-6.
- **9.** Fatoye F, Gebrye T, Odeyemi I. "Real-world incidence and prevalence of low back pain using routinely collected data," Rheumatology International, vol. 39, no. 4. Springer Verlag, pp. 619–626, Apr. 10, 2019, doi: 10.1007/s00296-019-04273-0.
- 10. Meisha DE, Alsharqawi NS, Samarah AA, Al-Ghamdi MY. "Prevalence of work-related musculoskeletal disorders and ergonomic practice among dentists in Jeddah, Saudi Arabia," Clin. Cosmet. Investig. Dent., vol. 11, pp. 171–179, 2019, doi: 10.2147/CCIDE.S204433.
- Şimşek Ş, Yağci N, Şenol H. "Prevalence of and risk factors for low back pain among healthcare workers in Denizli Denizli'de sağlık çalışanlarında bel ağrısı prevelansı ve risk faktörleri PAIN A RI," Agri, vol. 29, no. 2, pp. 71–78, 2017, doi: 10.5505/agri.2017.32549.
- 12. Dutmer AL, Preuper HRS, Soer R, Brouwer S, Bültmann U, Dijkstra PU et al. "Personal and Societal Impact of Low Back Pain," Spine (Phila. Pa. 1976)., vol. 44, no. 24, pp. E1443– E1451, Dec. 2019, doi: 10.1097/BRS.00000000003174.
- 13. P. Coenen, On the origin of back pain.
- 14. Bento TPF, Genebra CVDS, Maciel NM, Cornelio GP, Simeao

SFAP, Vitta A. Journal of, and undefined 2020, "Low back pain and some associated factors: is there any difference between genders?," Elsevier, Accessed: Mar. 23, 2021. [Online]. Available:

https://www.sciencedirect.com/science/article/pii/S14133555183 10128?casa_token=lHW_ppi7Q7gAAAAA:K4Y6Dxj14t3fmGH OqjU_CBPlgULEAKURyrUQ21aU3WjIZ9hThO8eYhPj9oAdO SYxnlXrcaK3pg.

- Huang C, W Yeming, L Xingwang et al. "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China," Lancet, vol. 395, no. 10223, pp. 497–506, Feb. 2020, doi: 10.1016/S0140-6736(20)30183-5.
- **16.** Messenger J, Oscar VL, Lutz G, Simon B, Greet V, Mathijn Wilkens. "Working anytime, anywhere: The effects on the world of work," 2017, doi: 10.2806/425484.
- Will JS, Bury DC, Miller JA. "Mechanical Low Back Pain" Am Fam Fhysician, no. 98, pp. 421–428, 2018, Accessed: Mar. 23, 2021. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/30252425/.
- 18. Baker R, Coenen P, Howie E, Williamson A, Straker L. "The short term musculoskeletal and cognitive effects of prolonged sitting during office computer work," Int. J. Environ. Res. Public Health, vol. 15, no. 8, Aug. 2018, doi: 10.3390/ijerph15081678.
- Vittersø J, Akselsen S, Evjemo B, Julsrud TE, Yttri B, Bergvik S. "Impacts of Home-Based Telework on Quality of Life for Employees and Their Partners. Quantitative and Qualitative Results From a European Survey," J. Happiness Stud., vol. 4, no. 2, pp. 201–233, 2003, doi: 10.1023/A:1024490621548.
- 20. Mathew KVB, Walarine MT. "Neck pain among smartphone users: an imminent public health issue during the pandemic time," J. Ideas Heal., vol. 3, no. Special1, pp. 201–204, Sep. 2020, doi: 10.47108/jidhealth.vol3.issspecial1.65.
- 21. Király O, Potenza MN, Stein DJ, King DL, Hodgins DC, Saunders JB, et al. "Preventing problematic internet use during the COVID-19 pandemic: Consensus guidance," Compr. Psychiatry, vol. 100, p. 152180, Jul. 2020, doi: 10.1016/j.comppsych.2020.152180.
- **22.** Sun Y, Li Y, Bao Y, Meng S, Sun Y, et al. "Brief Report: Increased Addictive Internet and Substance Use Behavior During the COVID-19 Pandemic in China," Am. J. Addict., vol. 29, no. 4, pp. 268–270, Jul. 2020, doi: 10.1111/ajad.13066.
- Ding D, Li J. "Smartphone Overuse A Growing Public Health Issue," 2017, doi: 10.4172/2161-0487.1000289.
- 24. Matar Boumosleh J, Jaalouk D. "Depression, anxiety, and smartphone addiction in university students- A cross sectional study," PLoS One, vol. 12, no. 8, p. e0182239, Aug. 2017, doi: 10.1371/journal.pone.0182239.
- 25. Moretti A, Menna F, Aulicino M, Paoletta M, Liguori S, Iolascon G. "Characterization of Home Working Population during COVID-19 Emergency: A Cross-Sectional Analysis," Int. J. Environ. Res. Public Health, vol. 17, no. 17, p. 6284, Aug. 2020, doi: 10.3390/ijerph17176284.
- 26. Steiner TJ, Stovner LJ, Birbeck GL. "Migraine: The Seventh Disabler," Headache J. Head Face Pain, vol. 53, no. 2, pp. 227– 229, Feb. 2013, doi: 10.1111/head.12034.
- 27. Pedraza MI, Mulero P, Ruíz M, de la Cruz C, Herrero S, Guerrero AL. "Características de los 2.000 primeros pacientes registrados en una consulta monográfica de cefaleas," Neurologia, vol. 30, no. 4, pp. 208–213, May 2015, doi: 10.1016/j.nrl.2013.12.010.
- **28.** Albers L, Straube A, Landgraf MN, Heinen F von Kries R. "High diagnostic stability of confirmed migraine and confirmed

tension-type headache according to the ICHD-3 beta in adolescents," J. Headache Pain, vol. 15, no. 1, pp. 1–5, Dec. 2014, doi: 10.1186/1129-2377-15-36.

- **29.** Belvis R. "Headaches During COVID-19: My Clinical Case and Review of the Literature," Headache J. Head Face Pain, vol. 60, no. 7, pp. 1422–1426, Jul. 2020, doi: 10.1111/head.13841.
- 30. Adhikari SP, Meng S, Wu YJ, Ma YP, Ye RX, Wang QZ, Sun C, S Sean, Rozelle S, Raat H, Zhou H. "Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: A scoping review," Infectious Diseases of Poverty, vol. 9, no. 1. BioMed Central Ltd., p. 29, Mar. 17, 2020, doi: 10.1186/s40249-020-00646-x.
- 31. Borges do Nascimento IJ, Cacic N, Abdulazeem HM, von Groote TC, Jayarajah U, Weerasekara I, et al. "Novel Coronavirus Infection (COVID-19) in Humans: A Scoping Review and Meta-Analysis," J. Clin. Med., vol. 9, no. 4, p. 941, Mar. 2020, doi: 10.3390/jcm9040941.
- **32.** Yamada K, Wakaizumi K. "Loneliness, social isolation, and pain following the COVID-19 outbreak: data from a nationwide internet survey in Japan," doi: 10.21203/rs.3.rs-240504/v1.
- 33. Mahase E. "Covid-19: Mental health consequences of pandemic need urgent research, paper advises," BMJ, vol. 369, p. m1515, Apr. 2020, doi: 10.1136/bmj.m1515.
- 34. Pierce M, Hope H, Ford T, Hatch S, Hotopf M, John, et al. "Mental health before and during the COVID-19 pandemic: a longitudinal probability sample survey of the UK population," The Lancet Psychiatry, vol. 7, no. 10, pp. 883–892, Oct. 2020, doi: 10.1016/S2215-0366(20)30308-4.
- 35. Tsamakis K, Triantafyllis AS, Tsiptsios D, Spartalis E, et al. "COVID-19 related stress exacerbates common physical and mental pathologies and affects treatment (Review)," Exp. Ther. Med., vol. 20, no. 1, pp. 159–162, Apr. 2020, doi: 10.3892/etm.2020.8671.
- 36. Hawryluck L, Gold WL, Robinson S, Pogorski S, Galea S, Styra R. "SARS control and psychological effects of quarantine, Toronto, Canada," Emerg. Infect. Dis., vol. 10, no. 7, pp. 1206–1212, 2004, doi: 10.3201/eid1007.030703.
- **37.** Wang R, Hozumi Y, Yin C, Wei GV. "Mutations on COVID-19 diagnostic targets," Genomics, vol. 112, no. 6, pp. 5204–5213, Nov. 2020, doi: 10.1016/j.ygeno.2020.09.028.
- 38. Haider N, Yusuf Osman A, Gadzepko A, Akipede GO, Asogun D, Ansumana R, et al. "Lockdown measures in response to COVID-19 in nine sub-Saharan African countries," BMJ Publishing Group, Oct. 2020. doi: 10.1136/bmjgh-2020-003319.
- 39. Bogart LM, Ojikutu BO, Tyagi K, Klein DJ, Mutchler MG, Dong L, Lawrence SJ, et al. "COVID-19 Related Medical Mistrust, Health Impacts, and Potential Vaccine Hesitancy Among Black Americans Living With HIV," J. Acquir. Immune Defic. Syndr., vol. 86, no. 2, pp. 200–207, Feb. 2021, doi: 10.1097/QAI.00000000002570.
- 40. Almufarrij I, Munro KJ. "One year on: an updated systematic review of SARS-CoV-2, COVID-19 and audio-vestibular symptoms," Int. J. Audiol., pp. 1–11, Mar. 2021, doi: 10.1080/14992027.2021.1896793.
- 41. Eckhardt-Henn A, Best C, Bense S, Breuer P, Diener G, Tschan R, et al. "Psychiatric comorbidity in different organic vertigo syndromes," J. Neurol., vol. 255, no. 3, pp. 420–428, Mar. 2008, doi: 10.1007/s00415-008-0697-x.
- 42. Cole SW. "Social regulation of human gene expression: Mechanisms and implications for public health," Am. J. Public Health, vol. 103, no. SUPPL.1, Oct. 2013, doi:

10.2105/AJPH.2012.301183.

- 43. Creswell JD, Irwin MR, Burklund LJ, Lieberman MD, Arevalo JMG, Ma J, et al. "Mindfulness-Based Stress Reduction training reduces loneliness and pro-inflammatory gene expression in older adults: A small randomized controlled trial," Brain. Behav. Immun., vol. 26, no. 7, pp. 1095–1101, Oct. 2012, doi: 10.1016/j.bbi.2012.07.006.
- 44. Garcia MA, Li X, Allen PA, Delahanty DL, Eppelheimer M, Houston JR, et al. "Impact of Surgical Status, Loneliness, and

Disability on Interleukin 6, C-Reactive Protein, Cortisol, and Estrogen in Females with Symptomatic Type I Chiari Malformation," Cerebellum, pp. 1–15, Mar. 2021, doi: 10.1007/s12311-021-01251-w.

45. Varga TV, Bu F, Dissing AS, Elsenburg LK, Bustamente JJH, Matta J, et al. "Loneliness, worries, anxiety, and precautionary behaviours in response to the COVID-19 pandemic: a longitudinal analysis of 200,000 Western and Northern Europeans," Lancet Reg. Heal. - Eur., vol. 2, p. 100020, Jan. 2021, doi: 10.1016/j.lanepe.2020.100020.