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Investigation of the Relationship between Headache and Anxiety during the Late COVID-19 Pandemic Period: A Prospective Case-Control Study

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Abstract

Objective: The effects of the COVID-19 pandemic on both the physical and psychological well-being of individuals have not yet been clearly understood. Especially during the early period of the pandemic, the most prevalent psychological effects included fear, preoccupation with health, anxiety, and feeling of loneliness caused by a general sense of uncertainty. The incidence of headache was as high as 70% among the mild COVID-19 cases. Findings from the past coronavirus outbreaks indicated that neuropsychiatric symptoms might cause a significant health burden and adversely affect the patients' quality of life. The present study aimed to investigate the anxiety-related clinical conditions of the patients diagnosed with primary headache, who presented to the neurology polyclinic during the prolonged pandemic period.

Methods: The research was designed as a two-center, prospective case-control study. Patients diagnosed with primary headache, who presented to the neurology outpatient clinic, and healthy volunteers without a primary headache diagnosis were included in the study. Data collection tools included the sociodemographic data form, Headache Impact Test, Coronavirus Anxiety Scale Short Form, and COVID-19 Disease Perception Scale.

Results: Data collected from a total of 869 participants, including 408 (47%) patients diagnosed with headache and 461 (53%) healthy volunteers, were investigated. The results of the Headache Impact Test-6 suggested a severe effect on quality of life in 187 participants (45.8%) in the headache group and 73 participants (15.8%) in the Control Group (p=0.001). There was coronavirus anxiety in 59 (14.5%) participants with headache and 8 (1.7%) participants in the Control Group (p=0.001). Furthermore, the rate of coronavirus anxiety in participants that had and did not have COVID-19 was 44 (13.7%) and 22 (4.1%), respectively (p=0.001).

Conclusion: The study results revealed that patients with headache and COVID-19 presented with a higher rate of coronavirus anxiety than healthy controls and those not diagnosed with COVID-19. Further studies on larger samples are necessary for investigating the long term neuropsychiatric effects of COVID-19 in individuals.

Keywords: COVID-19, neuropsychiatry, headache, anxiety, HIT-6

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Geç Dönem COVID – 19 Pandemisinde Baş Ağrısı ile Anksiyete İlişkisinin İncelenmesi: Prospektif Vaka-Kontrol Çalışması

Öz

Amaç: Covid-19 pandemisi, bireylerin hem fiziksel hem de psikolojik sağlığını üzerine etkileri halen net olarak bilinmemektedir. Salgının özellikle ilk dönemlerinde belirsizliğin getirdiği korku, sağlık kaygısı, endişe ve yalnızlık hissi bu dönemin en sık görülen ruhsal etkileri arasında yer almıştır. Hafif seyirli COVID-19 olgularında baş ağrısı sıklığı %70 gibi yüksek oranda bulunmuştur. Geçmiş koronavirüs salgınlarından elde edilen bulgular, nöropsikiyatrik semptomların önemli oranda sağlık yüküne sebep olduğu ve bireylerin yaşam kalitesini olumsuz etkilediğini göstermiştir. Bu araştırmada, uzamış pandemi döneminde nöroloji polikliniğine başvuran primer baş ağrısı tanısı bulunan hastaların anksiyete ile ilişkili klinik özelliklerinin değerlendirilmesi amaçlanmıştır.

Yöntemler: Araştırma iki merkezli, prospektif vaka-kontrol çalışması olarak planlanmıştır. Nöroloji Polikliniği' ne başvuran primer baş ağrısı tanısı olan hastalar ve primer baş ağrısı tanısı olmayan sağlıklı gönüllüler dahil edildi. Katılımcılara sosyodemografik veri formu, Baş Ağrısı Etki Testi-6, Koronavirüs Anksiyete Ölçeği Kısa Formu ve COVID-19 Hastalık Algısı Ölçeği uygulandı.

Bulgular: Değerlendirmeye alınan hastaların 408' i (%47) baş ağrısı tanılı, 461' i (%53) ise sağlıklı gönüllü grubu olmak üzere toplam 869 katılımcının verileri incelendi. Baş ağrısı grubunda bulunan 187 katılımcıda (%45,8), kontrol grubunda ise 73 katılımcıda (%15,8) Baş ağrısı Etki Test-6'ya göre yaşam kalitesinde şiddetli etki görüldü (p=0.001). Baş ağrısı bulunan 59 (%14,5) katılımcıda, kontrol grubunda ise 8 katılımcıda (%1,7) koronavirüs anksiyetesi mevcuttur (p=0.001). Ayrıca COVID-19 geçiren grupta 44 (%13,7) katılımcıda, COVID geçirmeyen grupta ise 22 katılımcıda (%4,1) koronavirüs anksiyetesi tespit edildi (p=0.001).

Sonuç: Baş ağrısı bulunan ve COVID-19 geçiren hastaların, sağlıklı kontrollere ve COVID geçirmeyenlere göre daha yüksek oranda koronavirüs anksiyetesinin bulunduğu tesbit edilmiştir. COVID-19' un uzun vadede bireylerde oluşturabileceği nöropsikiyatrik etkilerin araştırılması adına bu konuda daha geniş örneklemlerle yapılmış ileri düzey çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: COVID-19, Nöropsikiyatri, Başağrısı, Anksiyete, HIT-6.

INTRODUCTION

The novel coronavirus (SARS-CoV-2), better known as COVID-19, is an infectious disease with fatal consequences that originated in the Chinese City of Wuhan in December 2019 and proliferated throughout the world. The virus with neurotropic and neuroinvasive capacity, may affect many systems, especially the respiratory system and the central nervous system[1]. Millions of people were quarantined and the national borders were closed with an aim to decrease contagion, and accordingly social and economic problems arose during the fight against the virus. Especially during the early period of the pandemic, the most prevalent psychological effects included fear, preoccupation with health, anxiety, and feeling of loneliness caused by uncertainty[2]. Several studies have been conducted on the psychological effects associated with the pandemic in the general population, at risk populations, and the healthcare workers[2-5]. Owing to the effects of quarantine, anxiety, depression, and suicide cases were reported from numerous countries[6].

The direct effects of COVID-19 on the central nervous system and the role of psychoneuroimmunity have not yet been substantially understood even though the psychosocial effects of the pandemic were investigated. Relevant studies reported that the neuropsychiatric manifestations of COVID-19 mostly included acute meningoencephalitis, demyelination, anosmia, manic-depressive disorder, delirium, and agitation[7]. Approximately, 11%–34% of the patients hospitalized for COVID-19 presented with symptoms of headache1. A study that investigated 409 patients with COVID-19 reported that the most common neurological

symptom was headache (16.%), followed by dizziness (13.9%) and altered consciousness (11.2%)[8]. Mao et al. retrospectively reviewed the files of 214 patients diagnosed with COVID-19 and reported that 36.4% of the patients developed neuropsychiatric symptoms. [9] Dizziness (16.8%) and headache (13.1%) were reported as the most prevalent symptoms associated with the central nervous system, wherein depression, anxiety, and delirium were the most prevalent psychiatric disorders[9].

The most prevalent types of headache in COVID-19 infection include tension-type headache (TTH), migraine, and cluster headache[10]. The reported headache cases were characterized by sudden onset, localization in the forehead or periorbital region, compressive effect, and partial response to analgesics[1]. Although the mechanism of headache in COVID-19 has not yet been fully elucidated, several hypotheses on the subject exist[1]. A number of factors, in particular the genetic, immunological, and environmental factors, influence the prognosis of this viral infection. The immune system is stimulated by cytokines that are produced upon intake of exogenous antigens and by other inflammatory mediator factors[11]. B cells that occur as a result of interleukin-6 release, differentiate into the plasma cells, thereby increasing the antibody production. In addition, secondary lymphoid organs are known to be stimulated by T lymphocytes. The permeability of the blood–brain barrier increases and polymorphonuclear leukocytes and lymphocytes migrate to the central nervous system as a result of the activation of chemokines, including monocyte chemoattractant protein-1, which induces monocyte migration through interleukin-8. Eventually, COVID-19 infection invades the central nervous system owing to its neurotropic capacity[12]. Furthermore, it was suggested that COVID-19 infection caused an increase in circulating proinflammatory cytokines as a result of the stimulation of trigeminal nerve, which affected the pain-sensitive areas of the brain and induced headache[1]. Vasoactive amines, including glutamate, calcitonin gene-related peptide, substance P, serotonin, and neurokinin cause vasodilation in the meninges. Activation of pain-sensitive C and A-δ fibers may contribute to the pathogenesis[13]. Headaches may also occur secondary to hypoxemia developing in the alveolar tissues during COVID-19 infection[14].

Reportedly, epidemics have resulted in the occurrence of anxiety, stress, fear, anger, insomnia, and depressive symptoms in individuals[3]. An increased incidence of mental disorders including primarily the anxiety disorders, depression, and obsessive-compulsive disorders were reported, whereas the COVID-19 pandemic was associated with worsening of pre-existing psychiatric disorders in vulnerable populations[15]. Whether these findings are due to the psychosocial problems as induced by the pandemic or the direct effects of the virus on the central nervous system remains unclear. Previously, a study suggested that hypoxemia, a prevalent condition in COVID-19, might cause mental illnesses[16]. Studies on experimental animals showed that the animals had behavioral problems and poor performance in maze-solving, mating, and social plays subsequent to nasal inoculation of the coronavirus[17].

In the light of the above inferences, headache and anxiety are the two neuropsychiatric symptoms that are closely associated with each other. Findings from coronavirus outbreaks in the past indicated that neuropsychiatric symptoms caused a significant health burden and adversely affected the quality of life of individuals, although the main focus of treatment in the COVID-19 pandemic are the pulmonary symptoms[18]. To the best of our knowledge, there was no study that investigated the two neuropsychiatric symptoms together during the prolonged

pandemic period, despite the fact that there were many studies in the literature on headache and anxiety. The present study, we aimed to investigate the anxiety and related clinical traits of the patients, who presented to the neurology outpatients clinic with the Primary Headaches according to third edition of the International Classification of Headache Disorders (Migrain, tension-type headache, trigeminal autonomic cephalalgia and other primary headache disorders) in the late pandemic period. Furthermore, we aimed to contribute in the relevant literature and shed light on future studies.

METHODS

Study Sample

Present research was designed retrospective and case-control study. This study was conducted between August 10, 2021 and October 10, 2021 in Malatya Training and Research Hospital and Yeşilyurt State Hospital, located in the Eastern Anatolia region of Turkey. The study was approved by the Ministry of Health and the local Ethics Committee (Decision No. 2021/46) and performed pursuant to the criteria stipulated in the Declaration of Helsinki. Patients diagnosed with primary headache, who presented to neurology outpatient clinic and healthy volunteers without primary headache diagnosis were included in the study. The inclusion criteria included literate patients aged 18–80 years, who volunteered to participate in the study. Patients were excluded from the study according to following exclusion criteria: patients with a condition that might affect their cognitive functions, including dementia, and thereby hindering the completion of the scale and sociodemographic data; and patients with a psychiatric condition. A total of 905 people participated in the study. Thirty-six people has diagnosis of psychiatric conditions were rejected from the study. The Control and Patient Groups were constructed to ensure a strong directly proportional intergroup correlation in terms of sex and age. The sociodemographic data form, Headache Impact Test-6 (HIT-6), Coronavirus Anxiety Scale Short Form (CAS-SF), and COVID-19 Disease Perception Scale (CDPS) were used to collect patient data. Written informed consent was obtained from all participants. The scales were applied to the patient and control groups in the form of online (Google Documents®) and paper survey. In power analysis, effect size; 0.8, α:0.05 (type-1 error) and β-1; 0.80 were calculated. At least 52 (n:29/23) subjects should be included in order for the difference between the two groups to be 0.5 according to CAS-SF/1 between the headache group and the control group.

Sociodemographic Data Form

The participants' information, including age, sex, level of education, type of headache, and whether they had COVID-19 or not were captured in the sociodemographic data form that was developed by the authors in line with the data from previous studies in the relevant literature.

Headache Impact Test-6

The HIT-6 is considered to be a more subjective tool, as it reflects patients' own evaluation of headache severity on their quality of life. The HIT-6 is a self-report survey designed by Bayliss et al. to assess the impact of headache on quality of life19. The Turkish validity and reliability study of the scale was performed by Yalınay Dikmen et al 20. The test consists of six items on the frequency of headache and the consequences of the pain. The total score ranges between 36 and 78, wherein the higher scores indicate that the individual's quality of life is adversely affected. Total scores of ≥60 based on the four subdomains are indicative of pain that has a severe impact on quality of life. Internal consistency analyzed via Cronbach's α values for visit 1 and visit 2 HIT-6 scores in all patients were 0.753 (acceptable) and 0.864 (excellent), respectively 20. A reliability coefficient

calculated for a psychological test of 0.70 or higher was reported to be adequate for the reliability of the scale scores

Coronavirus Anxiety Scale Short Form

The CAS-SF was developed by Lee to investigate anxiety associated with coronavirus21. The Turkish validity and reliability study of the scale was performed by Biçer et al22. The total score of the 5-item Likert-type scale ranges between 0 and 20. Scores of ≥9 are associated with coronavirus anxiety. As a result of the analysis, the Cronbach Alpha reliability coefficient of the scale with 5 items and one dimension was calculated as 0.832. Factor loadings on the items of the scale consisting of one factor and 5 items vary between 0.625 and 0.78422.

COVID-19 Disease Perception Scale

COVID-19 Disease Perception Scale is a Likert-type scale developed by Geniş et al. with the aim to investigate the perception of COVID-19 disease23. This 7-item scale consists of two subdomains as follows: dangerousness and contagiousness. The dangerousness subdomain aims to address the perceptions and beliefs with regard to the danger posed by the virus, whereas the contagiousness subdomain evaluates the perception with regard to the contagiousness of the virus. The total score, i.e., the sum of subdomain scores, is divided by the number of items of the relevant subdomain to give a value between 1 and 5. Higher subdomain scores indicate a higher perception in the relevant subdomain. The cronbach alpha internal reliability coefficients of the scales in present study ranged between 0.74 and 0.8823.

Statistical Analysis

The data obtained at the end of the data collection phase were transferred to a computer and analyzed. SPSS® 26.0 (SPSS Inc., Chicago, IL, USA) package program was used for statistical analysis. All baseline parameters were analyzed. Arithmetic mean, standard deviation, and minimum and maximum values were used to summarize numerical data. Frequency distributions and percentages were used to summarize categorical data. Categorical variables are defined as percentages, and continuous variables are defined as mean±SD. Chi-square test was used to compare categorical data (The relationship between patient/control and COVID-19 (+)/(-) groups with the presence of CAS and HIT). The relationship between the CDPS- C, CDPS- D, HIT-6, CAS-SF Scores of the patient/control, COVID-19 (+)/(-) groups was analyzed with the Independent-Samples T test. $p < 0.05$ was considered significant in all statistical analyses.

RESULTS

Among the 905 participants considered for the study, 36 were excluded owing to the presence of psychiatric conditions. As a result, 869 participants, with 408 (46.9%) patients with headache (Patient Group) and 461 (53.1%) healthy volunteers (Control Group), were included in the study. The number of female and male participants were 539 (62%) and 330 (38%), respectively. In the Patient Group, 259 (63.5%) participants were women and 149 (36.5%) were men. In the Control Group, 280 (60.7%) participants were women and 181 (39.3%) were men. The mean participant ages in the Patient and Control Groups were 39.97 ± 12.07 and 38.81 ± 10.04, respectively.

In the Patient Group, 182 (20.9%) participants had migraine, 180 (20.7%) Tension-type headache (TTH), 12 (1.4%) had trigeminal autonomic cephalalgia, and 34 (3.9%) had other types of headache. In the Patient Group, 93 (10.9%) participants had comorbid physical conditions, while 305 (35.6%) participants did not. In the Control Group, the number of participants with and without comorbid physical conditions was 100 (11.7%) and 359 (41.9%), respectively. The number of participants in the Patient Group with and without COVID-19 was 179 (45%) and 219 (55%), respectively. However, in the Control

Group, 143 (31.1%) participants had COVID-19, while 317 (68.9%) participants did not. Sociodemographic data and selected clinical characteristics of the participants are given in Table 1.

Table I: Demographic characteristics of both groups

	Patients*	**Controls**	**Totals**
Age (Years)	39.97 ± 12.07	38.81 ± 10.04	39.35 ± 11.04
Gender n, (%)			
Female	259 (29.8)	280 (32.2)	539 (62)
Male	149 (17.1)	181 (20.8)	330 (38)
Total	408 (46.9)	461 (53.1)	869 (100)
COVID-19 (+)** n, (%)	179 (20.9)	143 (16.7)	322 (37.5)
Comorbidity n, (%)			
Yes	93 (10.9)	100 (11.7)	193 (22.5)
No	305 (35.6)	359 (41.9)	664 (77.5)
Education Status n, (%)			
Primary	68 (8.0)	43 (5.0)	111 (13.0)
High	103 (12.0)	96 (11.2)	199 (23.3)
College or University	225 (26.3)	320 (37.4)	545 (63.7)

** Has a the Primary Headaches history ** Test positive for COVID-19*

Certain clinical characteristics and scale scores of the Patient and Control groups were evaluated. There was a severe effect on the quality of life in 187 participants (45.8%) in the Patient Group and 73 participants (15.8%) in the Control Group. A statistically significant intergroup difference was found (p=0.001) in terms of whether there was a severe effect on the quality of life based on HIT-6 scores. The participants in the Patient Group had a higher rate of severe effects on quality of life than those in the Control Group. Coronavirus anxiety was observed in 59 (14.5%) participants in the Patient Group and 8 participants (1.7%) in the Control Group. There was a statistically significant intergroup difference (p=0.001) as indicated by a comparison in terms of the presence of coronavirus anxiety. The participants in the Patient Group had a higher rate of coronavirus anxiety than those in the Control Group. The mean HIT-6 scores in the Patient and Control Groups were 56.83±11.89 and 47.99±10.47, respectively. The mean CAS-SF scores in the Patient and Control Groups were 2.80±4.27 and 1.04±2.02, respectively. There was a statistically significant difference between the two groups (p=0.001 for both) as indicated by a comparison by the HIT and CAS-SF scores. The Patient Group had a higher mean HIT-6 and CAS-SF scores compared to the Control Group. There was no statistically significant difference between the two groups (p=0.519, p=0.178, respectively) upon a comparison by the dangerousness and contagiousness subdomains of the CDPS.

Participants were divided into two groups as patients, who underwent COVID-19 (COVID-19 positive) and who did not (COVID-19 negative) and some certain clinical characteristics and scale scores were taken into evaluation. A severe effect on the quality of life based on the HIT scores was observed in 101 participants (31.4%) in the COVID-19 Group with and 158 participants (29.5%) in the COVID-19 negatives. There was no statistically significant difference between the groups (p=0.560) upon a comparison of the two groups in terms of whether there was a severe effect on the quality of life based on the HIT-6 scores. There was anxiety associated with coronavirus in 44 (13.7%) participants in the positive group and in 22 (4.1%) participants in the negative group. There was a statistically significant difference the two groups (p=0.001) as suggested by a comparison of the groups by anxiety associated with coronavirus. The participants in the COVID-19 positive group had a higher rate of anxiety associated with coronavirus compared to the negative group. The mean HIT-6 score in the positive and negative groups was 53.85±9.58 and 51.77±11.99, respectively. The mean CAS-SF score in the COVID-19 positive and negative groups was 2.71±4.01 and 1.37±2.83, respectively. There was a statistically significant difference between the two groups (p=0.009, p=0.001, respectively) upon a comparison of the groups by HIT-6 and CAS-SF scores. The clinical characteristics and scale scores of the groups are given in Table 2.

Table II: Assessment of scales respect to headache and COVID-19 condition

	Patients*	Controls**	*p*	COVID-19 (+)	COVID-19 (-)	*p*
Severe Headache (HIT)						
Yes - n (%)	187 (% 45.8)	73 (% 15.8)	*0.001*	101 (% 31.4)	158 (% 29.5)	*0.560*
No - n (%)	221 (% 54.2)	388 (% 84.2)		221 (% 68.6)	378 (% 70.5)	
Coronavirus Anxiety						
Yes - n (%)	59 (% 14.5)	8 (% 1.7)	*0.001*	44 (% 13.7)	22 (% 4.1)	*0.001*
No - n (%)	349 (% 85.5)	453 (% 98.3)		278 (% 86.3)	514 (% 95.9)	
CDPS- D	3.76±1.05	3.85±0.89	*0.519*	3.91±0.91	3.79±0.91	*0.073*
CDPS- C	3.61±1.06	3.66±1.05	*0.178*	3.74±0.94	3.62±1.04	*0.090*
HIT-6 Score	56.83±11.89	47.99±10.47	*0.001*	53.85±9.58	51.77±11.99	*0.009*
CAS-SF Score	2.80±4.27	1.04±2.02	*0.001*	2.71±4.01	1.37±2.83	*0.001*

** Has a the Primary Headaches history **No the Primary Headaches history*
HIT: Headache Impact Test, CDPS- D: COVID-19 Disease Perception Scale – dangerousness, CDPS- C: COVID-19 Disease Perception Scale – contagiousness, CAS-SF: Coronavirus Anxiety Scale Short Form

DISCUSSION

Psychiatric factors may play an important role in the context of susceptibility, trigger, duration, and severity of headache[24]. It was reported that the incidence of psychiatric conditions, especially the anxiety disorders and depression, comorbid to primary headache was higher compared to the healthy population[25]. Jahangir et al. reported in their study that newly diagnosed treatment naïve patients with headache had a history of anxiety in addition to severe somatic symptoms[26]. One of the most important findings of the present study was that anxiety associated with coronavirus was at a higher rate in the Patient Group (14.5%) compared to the Control Group (1.7%) (p=0.001). Similarly, the mean CAS-SF score was higher in the Patient Group (2.80±4.27) compared to the Control Group (1.04±2.02) (p=0.001). In addition, migraine (20.9%) and TTH (20.7%) were the most common manifestations in the Patient Group. Consistent with the results of the present study, it was reported in the relevant studies on patients with headache suggested that the likelihood of anxiety disorder and depression was 2.2–4 times increased, especially in the individuals with migraine and chronic TTH compared to healthy controls[27]. It was reported that individuals with migraine experienced intense anxiety and were more likely to commit suicide[28]. It was suggested in a Turkish study that anxiety, depression, and stress levels were significantly elevated in people with migraine compared to healthy controls (p=0.030, p=0.030, p=0.02, respectively) and that stress and anxiety were associated with an exaggerated perception of bodily senses[29]. It was reported that the COVID-19 epidemic disrupted daily routines, reduced social communication among people, increased economic concerns, and gave a rise to worries about the future. This can lead to worsening of pre-existing mental disorders or the emergence of new mental disorders, particularly anxiety disorder and depression[15]. In the light of above, it can be suggested that anxiety and headache are closely associated neuropsychiatric symptoms.

Another important finding of the present study was that there was a higher rate of participants with severely deteriorated quality of life in the Patient Group (45.8%) compared to the Control Group (15.8%) (p=0.001). Furthermore, the mean HIT-6 score was higher in the Patient Group (56.83±11.89) compared to the Control Group (47.99±10.47) (p=0.001). This result suggested that a higher rate of participants in the Patient Group might have impaired functionality compared to the healthy controls. Given that there was a higher rate of anxiety associated with coronavirus in the Patient Group, such patients might be suggested to have more serious somatic symptoms, similar to the results of previous studies[26]. It was reported

that psychosomatic complaints increased (p=0.001) during the COVID-19 pandemic, and that perceived threat and intolerance to uncertainty might account for the foregoing increase[4]. Consistently, a study by Koc et al. performed during the second month of the pandemic, reported that among the 10 most prevalent symptoms in the participants headache ranked the first (60.1%), followed by any pain or discomfort (57.1%)[30].

Another important finding of the present was that there was no statistically significant difference in the dangerousness and contagiousness subdomains of the CDPS in the Patient Group (3.76±1.05, 3.61±1.06) and the Control Group (3.85 ± 0.89, 3.66 ± 1.05). Both groups had similar perceptions and beliefs about the COVID-19 disease. Although the contagiousness subdomain scores of both groups in the present study was similar to that reported in Koc et al., the participants of the present study had comparatively lower scores in the dangerousness subdomain[30]. This result suggested that during the prolonged pandemic period, the individuals' perception about the danger posed by COVID-19 weakened over time, and that various adaptation mechanisms might have been activated to facilitate adaptation to COVID-19, which was perceived as a threat during the early pandemic period3. This might also have resulted in lower CDPS scores in both groups, generally.

Another important finding of the present study was that there was a higher rate of anxiety associated with coronavirus in the COVID-19 positives (13.7%) compared to negatives (4.1%) (p=0.001). Similarly, the mean CAS-SF score was higher in the COVID-19 Group (2.71±4.01) than the healthy controls (1.37±2.83) (p=0.001). Consistent with the results of the present study, it was reported that anxiety disorder, depression, obsessive-compulsive disorder, post-traumatic stress disorder, and insomnia were highly prevalent in people with COVID-19, especially in women, and it was suggested that hypoxemia might be a predisposing factor for mental disorders[16].

The last important finding of the present study was that the mean HIT-6 score was higher in the COVID-19 positives group (53.85±9.58) compared to negatives group (51.77±11.99) (p=0.009). Consistently, it was reported in the relevant literature that headache was among the common neurological symptoms of COVID-19 infection[8].

This study has certain limitations. The present study was limited by the limited sample size and time. The authors did not have data on the anxiety levels of the participants prior to the pandemic. Scales were used for the assessment of mental status in the study; thus, it was not possible to discuss the diagnoses. Finally, another limitation is that psychiatric interviews were not held in order to minimize the contact with the participants due to the risk of contagion, hence scales were used for the purpose of investigation and the study focused on the level of symptoms.

CONCLUSION

In summary, the prominent result of the present study was that there was a higher rate of anxiety associated with coronavirus in patients with headache compared to healthy controls, and in patients, who underwent COVID-19 compared to those did not. Headache and anxiety are two closely associated neuropsychiatric symptoms in the COVID-19 pandemic. Further studies on larger samples are necessary for investigating the long term neuropsychiatric effects of COVID-19 in individuals.

Ethics Committee Approval: Present research was designed retrospective and case-control study. This study was conducted between August 10, 2021 and October 10, 2021 in Malatya Training and Research Hospital and Yeşilyurt State Hospital, located in the Eastern Anatolia region of Turkey. The study was

approved by the Ministry of Health and the local Ethics Committee (Decision No. 2021/46) and performed pursuant to the criteria stipulated in the Declaration of Helsinki.

Conflict of Interest: The authors declared no conflicts of interest.

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