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Effect of COVID-19 on seizures and patient behavior in people with epilepsy

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A COVID-19 hatása a rohamokra és a viselkedésre epilepsziás betegeknél

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Background and purpose – To evaluate the long-term effects of the COVID-19 pandemic on seizure frequency and levels of mental distress in individuals with epilepsy and identify potential risk factors associated with increased seizure frequency.

Methods – This is a cross-sectional study conducted in Türkiye in May 2021 by phone. Information on epilepsy syndromes, antiseizure medications, average seizure frequency, and drug resistance was obtained from medical records. A questionnaire was completed that included demographic and clinical characteristics and Kessler Psychological Distress Scale 10 (K-10). From people with epilepsy (PWE), seizure control in the month before the pandemic and perceived stress, sleep changes, changes in adaptation during this period, and whether there were changes in seizure control after the pandemic were questioned.

Results – A total of 227 patients were included, and the K-10 score of 81.9% (186/227) of PWE was found to be ≥ 30 . An increase in seizure frequency was detected in 34 (15%) patients. The factors affecting the increase in seizure frequency were analyzed using logistic regression analysis. In the univariate model hesitate to go to the emergency room despite having seizures during the pandemic (OR= 8.325; 95% CI: [2.943 - 23.551], $p < 0.001$) was evaluated as the parameter with the highest risk of increased seizure frequency. In multivariate analyses (enter model) only polytherapy (OR= 2.945; 95% CI: [1.152 - 7.532], $p = 0.024$) was detected as the parameter with increased seizure frequency.

Conclusion – One year after the declaration of the pandemic, we found that stress was still common, the frequency of seizures

Háttér és cél – A COVID-19 világjárvány-nak a rohamok gyakoriságára és a mentális distressz szintjére gyakorolt hosszú távú hatásainak értékelése epilepsziás személyeknél, valamint a rohamgyakoriság növekedésével összefüggő lehetséges kockázati tényezők azonosítása.

Módszerek – Ez egy keresztmetszeti vizsgálat, amit 2021 májusában, Törökországban végeztünk, telefonon. Az epilepsziás szindrómákra, a rohamellenes gyógyszerekre, az átlagos rohamgyakoriságra és a gyógyszer-rezisztenciára vonatkozó információt az orvosi feljegyzésekből szereztük be. A betegek kérdőívet töltöttek ki, ami demográfiai és klinikai jellemzőket, valamint a 10 kérdéses Kessler Pszichológiai Distressz Skálát (K-10) tartalmazta. Az epilepsziás személyeknél rákérdeztünk a rohamkontrollra a világjárványt megelőző hónapban és az észlelt stresszre, az alvás és az alkalmazkodás változásaira ebben az időszakban, valamint arra, hogy a világjárványt követően történt-e változás a rohamkontrollban.

Eredmények – Összesen 227 beteget vontunk be, akik 81,9%-ának (186/227) K-10-pontszáma ≥ 30 volt. A rohamgyakoriság növekedését 34 (15%) beteg észlelte. A rohamgyakoriság növekedését befolyásoló tényezőket logisztikus regresszióanalízissel elemeztük. Az egyváltozós modellben a hezitálás, hogy a világjárvány idején fellépő rohamok ellenére elmenjenek-e a sürgősségi osztályra (OR = 8,325; 95%-os CI: [2,943–23,551], $p < 0,001$) volt a rohamgyakoriság növekedésének legnagyobb kockázatával járó paraméter. A többváltozós elemzések (enter modell) szerint csak a politerápia (OR = 2,945; 95%-os CI: [1,152–7,532], $p = 0,024$) volt a rohamok gyakoriságának növekedésével járó paraméter.

increased. In multivariate analyses, only polytherapy was detected as the parameter with increased seizure frequency.

Keywords: COVID-19, epilepsy, Kessler-10 scale, stress, pandemic

Következtetés – Egy évvel a világijárvány meghirdetése után azt találtuk, hogy a stressz még mindig gyakori, a rohamok gyakorisága nőtt. A többváltozós elemzések csak a politerápiát mutatták ki mint a rohamok gyakoriságának növekedésével járó paramétert.

Kulcsszavak: COVID-19, epilepszia, Kessler-10 skála, stressz, világijárvány

In December 2019, a new coronavirus was reported in Wuhan, China¹. The virus was named SARS-CoV2 and the disease was designated as coronavirus 2019 (COVID-19). Then, it was declared a global pandemic by the World Health Organization (WHO) on March 11th, 2020². The pandemic has forced governments to put pressure on people, including isolation measures, to contain the spread of infection. Quarantine measures were introduced at various times around the world to prevent the spread of the virus. These measures created new social, economic, and health problems. The coronavirus crisis, quarantine, and isolation leading to feelings of loneliness, boredom, anger, and fear have affected the mental health of the population³.

Epilepsy is a chronic neurological condition characterized by a tendency to generate recurrent seizures, necessitating long-term and consistent medication treatment⁴. Both physical and psychological factors have the potential to trigger seizures. These factors include missing antiseizure medication (ASM) (40.98%), emotional stress (31.35%), sleep deprivation (19.75%), fatigue (15.30%), missing meals (9.13%), smoking (6.41%), and fever (6.41%)⁴. Additionally, inflammation is an important factor in the pathophysiology of seizure occurrence and epileptogenesis. It has been shown in an animal study that inflammatory mediators occurring due to systemic reasons can trigger seizures⁵. *Butler et al.* reported that although inflammation at the seizure focus had been detectable during a seizure-free period, it had increased significantly after a seizure⁶.

This study aimed to evaluate the long-term effects of the COVID-19 pandemic on seizure frequency and levels of mental distress in people with epilepsy (PWE). Also, to identify potential risk factors associated with increased seizure frequency and develop medical care strategies for PWE.

Methods

Subjects

This cross-sectional study included patients followed for at least 1 year in the epilepsy outpatient clinic of Kutahya Health Sciences University. Patients aged 18 years and older who were diagnosed with definitive epilepsy according to the International League Against Epilepsy (ILAE) criteria⁷ were included in the study. The presence of non-epileptic psychogenic seizures, paroxysmal neurological symptoms of unclear or non-epileptic nature, and patients with acute symptomatic seizures were excluded from the study. The included variables were as follows: demographic and basic clinical features such as age, sex, living situation, employment status, epilepsy type, epilepsy duration, treatment, the presence of additional disease, and psychiatric drug use.

Between May 1st and May 31st, 2021, patients were contacted by telephone. All included patients gave verbal consent to participate. Information on epilepsy syndromes, antiseizure medications, average seizure frequency, and drug resistance was obtained from medical records. A questionnaire was completed that included demographic and clinical characteristics and the Kessler Psychological Distress Scale 10 (K-10). From PWE, seizure control in the month before the pandemic and perceived stress, sleep changes, changes in adaptation during this period, and whether there were changes in seizure control after the pandemic were questioned.

The study protocol was approved by the local ethics committee (Kutahya Health Sciences University 2021/04-25.1) and local institutional approvals were also obtained. The study was conducted in accordance with the Declaration of Helsinki and the International Council for Harmonisation Guidelines for Good Clinical Practice.

Questionnaires

K-10 is one of the few relatively brief screening instruments with 10 questions. It was developed to assess psychological distress, including depressive disorders and anxiety, another common psychological disorder⁸. Response options are based on a five-point Likert scale ranging from 1 (never) to 5 (always). A minimum of 10 points and a maximum of 50 points are assigned. The K-10 total was grouped into the following levels of psychological distress: low (K-10 = 10-15), moderate (K-10 = 16-21), high (K-10 = 22-30), and very high (K-10 = 31-50)⁹. We used the validated Turkish-language version of the K-10¹⁰. The participants were dichotomized according to whether they had very high levels of psychological distress.

Statistical analysis

The Statistical Package for the Social Sciences (IBM SPSS Statistics, New York, USA) 25.0 software was used for statistical evaluations. Descriptive statistics were evaluated using numbers, percentages, mean, standard deviation (SD), and median (minimum-maximum). In the comparison of two independent groups, the Mann-Whitney U test was used for continuous variables that did not meet the parametric assumptions, and the Chi-square test (two or more groups) was used for categorical variables. We used a two-sided Mann-Whitney U test. As a result of the Chi-square test, the Bonferroni-corrected Z test was used for ratio comparisons. Statistically significant variables were analyzed using a multivariate logistic regression model to detect independently associated factors of increased seizure frequency. The multivariate model contained variables that were associated with $p < 0.05$ in univariate analyses and $p \leq 0.05$ was accepted as the limit of significance.

Results

A total of 227 patients were included, 55.90% ($n = 127$) were female. The average age of the patients was 34.97 ± 14.22 (range, 18-80) years, and the average epilepsy duration was 15.43 ± 11.81 (range, 1-57) years. The K-10 score of 81.9% (186/227) of PWE was found as ≥ 30 . Demographic data and clinical features of epilepsy were compared between the groups with and without high levels of psychological distress (**Table 1**). 95 (41.9%) patients had additional diseases. The diseases and number of patients are shown in **Figure 1**. The highest rate was found to be thyroid disease with 69.5%. A statistically significant difference was found between the groups in terms of sex, education, and increase in seizure frequency ($p=0.009$, $p=0.005$, and $p=0.002$, respectively) (**Table 1**). We observed no differences between the

groups regarding age, marital status, living situation, living place, working status, smoking, and resistant epilepsy ($p=0.053$, $p=0.999$, $p=0.709$, $p=0.636$, $p=0.064$, $p=0.511$, and $p=0.261$, respectively) (**Table 1**).

Table 2 shows the relationship between increasing seizure frequency and various demographic and clinical characteristics. It was revealed that there had been an increase in the frequency of seizures during the pandemic in the patient group aged 41-60 years, in patients receiving polytherapy, and in patients with resistant epilepsy ($p=0.042$, $p=0.001$, and $p=0.005$, respectively). In addition, we found that the change in sleep pattern had been another reason for the increase in seizure frequency ($p=0.03$). Increased stress during pandemic and the K-10 scale score was also significantly associated with an increase in seizure frequency ($p=0.043$ and $p=0.002$, respectively). It was found that the frequency of seizures had been associated with an increase in the frequency of seizures because the patients avoided presenting to the outpatient clinic ($p=0.001$) and the emergency department ($p<0.001$) despite having seizures.

The factors affecting the increase in seizure frequency were analyzed using logistic regression analysis (**Table 3**). In the univariate model hesitate to go to the emergency room despite having seizures during the pandemic (OR= 8.325; 95% CI: [2.943 – 23.551], $p<0.001$) was evaluated as the parameter with the highest risk of increased seizure frequency. In multivariate analyses (enter model) only polytherapy (OR= 2.945; 95% CI: [1.152 – 7.532], $p=0.024$) was detected as the parameter with increased seizure frequency.

Discussion

This research was conducted 1 year after the WHO declared COVID-19 a pandemic. Due to the pandemic, quarantine practices at different times and intervals were enforced while restrictions on work and public services (especially health care delivery) continued. Our finding of 81.9% PWE with a K-10 score ≥ 30 in our study was the highest among those reported so far in previous PWE studies. We saw the self-reported increase in stress as 36.1%. Cross et al. reported severe psychological distress in 57.1% of PWE¹¹, and in 13.1% of PWE in another study in which the evaluation was performed according to the K-6 scale¹². Fonseca et al. reported anxiety rates of 26.7% and depression at 8.6%³. An increase in self-reported stress was detected in a total of 59.4% of patients during this period, and no scale was used in the study². In the study conducted by Abokalawa et al., 5 months after the declaration of the pandemic, depression was reported in 66.2%, anxiety in 72.2%, and increased stress in 75.5% of PWE¹³. These differences can be explained by the fact that the studies were conducted at different times and in different geographies after the onset of the pandemic. In

Table 1. Demographic and clinical features among the groups according to K-10 scores

	Total		K-10 score < 30 (n=41)	K-10 score ≥30 (n=186)	test statistic	p
	n (%)	Mean±SD	Med (min-max) / Mean Rank	Med (min-max) / Mean Rank		
Age (year)		35 ± 14.2	39 (19 – 69) / 131.9	30 (18 – 80) / 110.0	3078.0	0.053*
Sex						
Female	127 (55.9)		31 (24.4) ^a	96 (75.6) ^b		0.009†
Male	100 (44.1)		10 (10.0) ^a	90 (90.0) ^b		
Marital status						
Married	120 (52.9)		22 (18.3)	98 (81.7)		0.999†
Single	107 (47.1)		19 (17.8)	88 (82.2)		
Living situation						
With family	214 (94.3)		38 (17.8)	176 (82.2)		0.709†
Alone	13 (5.7)		3 (23.1)	10 (76.9)		
Living place						
City center	191 (84.1)		36 (18.8)	155 (81.2)		0.636†
Village	36 (15.9)		5 (13.9)	31 (86.1)		
Education						
Illiterate	11 (4.8)		1 (9.1) ^a	10 (90.9) ^a		0.005†
Middle school	93 (41.0)		27 (29.0) ^a	66 (71.0) ^b		
High school	73 (32.2)		7 (9.6) ^a	66 (90.4) ^b		
University and above	50 (22.0)		6 (12.0) ^a	44 (88.0) ^a		
Working status						
Working	59 (26.0)		5 (8.5)	54 (91.5)		0.064†
Not working	95 (41.9)		25(26.3)	70 (73.7)		
Cannot work	19 (8.4)		3 (15.8)	16 (84.2)		
Retired	21 (9.3)		4 (19.0)	17 (81.0)		
Student	33 (14.5)		4 (12.1)	29 (87.9)		
Smoking						
No	165 (72.7)		32 (19.4)	133 (80.6)		0.511†
Yes	62 (27.3)		9 (14.5)	53 (85.5)		
Resistant epilepsy						
No	188 (82.8)		31 (16.5)	157 (83.5)		0.261†
Yes	39 (17.2)		10(25.6)	29 (74.4)		
Increase in seizure frequency						
No	193 (85.0)		28 (14.5) ^a	165 (85.5) ^b		0.002†
Yes	34 (15.0)		13 (38.2) ^a	21 (61.8) ^b		

*Mann-Whitney U test, †Chi-square test, ^{a, b} There is no statistically significant difference between groups with the same letters for each line, SD: standard deviation, Med: median, min: minimum, max: maximum, BMI: body mass index, K-10 score: Kessler-10 score

the literature, studies examining the relationship between COVID-19 and stress seizures noted that causality could be misinterpreted¹⁴. Our study had the longest interval among studies conducted after the declaration of the

pandemic^{2, 3, 11–13}. With this long interval, we concluded that we made an examination in a period when people were spiritually exhausted, and therefore we found a very high level of distress at a rate of 81.9%. Also, we found a

36.1% increase in self-reported stress by the patients during the pandemic period. For this reason, we thought that using objective tests while evaluating the mental state also contributed to the result. We concluded that it would be more accurate to conduct objective tests with the correct aim of obtaining psychiatric support for patients.

We found a very high level of psychological distress in males. People with negative economic conditions are more vulnerable to mental health problems¹⁵. We thought that with the prolongation of the pandemic, the problem of finding a job and economic concerns might cause

stress in men. Several studies have reported that education is a factor associated with mental health status and problems during the COVID-19 pandemic¹⁵⁻¹⁷. Similarly, in our study, we detected a higher rate of stress in our patient group who were secondary school or high school graduates. Resistant epilepsy was not significant in our study, unlike in the literature¹².

An increase in seizure frequency was detected in 34 (15%) patients. There are studies in the literature showing that the frequency of seizures is between 8.56 and 29.5%^{2, 3, 13, 18-20}. In a meta-analysis including 24 studies,

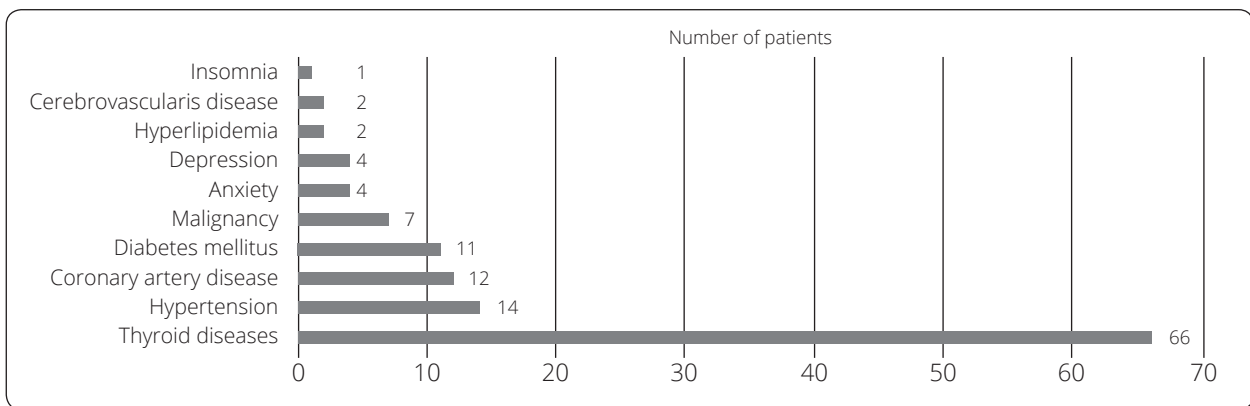


Figure 1. Diseases and number of patients

Table 2. Demographic and clinical features among the groups according to the increase in seizure frequency

	Total	Increase in seizure frequency		Likelihood ratio	p
		No	Yes		
	n (%)	n (%)	n (%)		
Age (year)					
<21	33 (14.5)	28 (14.5) ^a	5 (14.7) ^a	7.633	0.042
21-40	125 (55.1)	112 (58) ^a	13 (38.2) ^b		
41-60	57 (25.1)	42 (21.8) ^a	15 (44.1) ^b		
>60	12 (5.3)	11 (5.7) ^a	1 (2.9) ^a		
Sex					
Female	127 (55.9)	108 (56)	19 (55.9)	0.000	0.999
Male	100 (44.1)	85 (44)	15 (44.1)		
Marital status					
Married	120 (52.9)	97 (50.3)	23 (67.6)	3.588	0.092
Single	107 (47.1)	96 (49.7)	11 (32.4)		
Living situation					
With family	214 (94.3)	183 (94.8)	31 (91.2)	0.632	0.419
Alone	13 (5.7)	10 (5.2)	3 (8.8)		
Living place					
City center	191 (84.1)	159 (82.4)	32 (94.1)	3.638	0.141
Village	36 (15.9)	34 (17.6)	2 (5.9)		

Continuation of Table 2.

	Total	Increase in seizure frequency		Likelihood ratio	p
		No	Yes		
	n (%)	n (%)	n (%)		
Education					
Illiterate	11 (4.8)	10 (5.2)	1 (2.9)	6.276	0.131
Middle school	93 (41)	74 (38.3)	19 (55.9)		
High school	73 (32.2)	62 (32.1)	11 (32.4)		
University and above	50 (22)	47 (24.4)	3 (8.8)		
Working status					
Working	59 (26)	52 (26.9)	7 (20.6)	9.420	0.083
Not working	95 (41.9)	74 (38.3)	21 (61.8)		
Cannot work	19 (8.4)	17 (8.8)	2 (5.9)		
Retired	21 (9.3)	18 (9.3)	3 (8.8)		
Student	33 (14.5)	32 (16.6)	1 (2.9)		
Smoking					
No	165 (72.7)	140 (72.5)	25 (73.5)	0.014	0.999
Yes	62 (27.3)	53 (27.5)	9 (26.5)		
Epilepsy duration					
0-5 year	58 (25.6)	52 (26.9)	6 (17.6)	1.523	0.485
6-10 year	38 (16.7)	31 (16.1)	7 (20.6)		
>11 year	131 (57.7)	110 (57.0)	21 (61.8)		
Seizure type					
Focal Onset	61 (26.9)	48 (24.9)	13 (38.2)	3.021	0.237
Generalized Onset	164 (72.2)	143 (74.1)	21 (61.8)		
Unknown Onset	2 (0.9)	2 (1)	0 (0)		
Epilepsy Etiology					
Unknown	5 (2.2)	5 (2.6)	0 (0)	5.965	0.582
Structural	84 (37)	73 (37.8)	11 (32.4)		
Genetic	128 (56.4)	105 (54.4)	23 (67.6)		
Infectious	6 (2.6)	6 (3.1)	0 (0)		
Metabolic	2 (0.9)	2 (1)	0 (0)		
Immune	2 (0.9)	2 (1)	0 (0)		
Treatment type					
Monotherapy	142 (62.6)	130 (67.4) ^a	12 (35.3) ^b	12.268	0.001
Polytherapy	85 (37.4)	63 (32.6) ^a	22 (64.7) ^b		
Resistant Epilepsy					
No	188 (82.8)	166 (86) ^a	22 (64.7) ^b	7.875	0.005
Yes	39 (17.2)	27 (14) ^a	12 (35.3) ^b		
Comorbid disease					
No	132 (58.1)	113 (58.5)	19 (55.9)	0.084	0.919
Yes	95 (41.9)	80 (41.5)	15 (44.1)		
Change in sleep pattern					
No	165 (72.7)	146 (75.6) ^a	19 (55.9) ^b	5.267	0.030
Yes	62 (27.3)	47 (24.4) ^a	15 (44.1) ^b		

Continuation of Table 2.

	Total	Increase in seizure frequency		Likelihood ratio	p
		No	Yes		
	n (%)	n (%)	n (%)		
Increased stress during the pandemic					
No	145 (63.9)	129 (66.8)	16 (47.1)	4.726	0.043
Yes	82 (36.1)	64 (33.2)	18 (52.9)		
Kessler 10 scale					
K-10 score <30	41 (18.1)	28 (14.5)a	13 (38.2)b	9.370	0.002
K-10 score ≥30	186 (81.9)	165 (85.5)a	21 (61.8)b		
Avoided follow-up during the pandemic					
No	161 (70.9)	137 (71.0)	24 (70.6)	0.002	0.999
Yes	66 (29.1)	56 (29.0)	10 (29.4)		
Avoided EEG during the pandemic					
No	182 (80.2)	154 (79.8)	28 (82.4)	0.122	0.911
Yes	45 (19.8)	39 (20.2)	6 (17.6)		
Avoided MRG during the pandemic					
No	182 (80.2)	154 (79.8)	28 (82.4)	0.122	0.911
Yes	45 (19.8)	39 (20.2)	6 (17.6)		
Did you hesitate to visit the outpatient clinic despite having seizures during the pandemic?					
No	206 (90.7)	181 (93.8) ^a	25 (73.5) ^b	10.769	0.001
Yes	21 (9.3)	12 (6.2) ^a	9 (26.5) ^b		
Did you hesitate to go to the emergency department despite having seizures during the pandemic?					
No	210 (92.5)	185 (95.9) ^a	25 (73.5) ^b	14.919	<0.001
Yes	17 (7.5)	8 (4.1) ^a	9 (26.5) ^b		
COVID-19 infection					
No	182 (80.2)	159 (82.4)	23 (67.6)	3.569	0.079
Yes	45 (19.8)	34 (17.6)	11 (32.4)		

Chi-square test, ^{a, b} There was no statistically significant difference between groups with the same letters for each line

it was shown that the incidence of increased seizures during the COVID-19 pandemic had been 18.5%²¹. Similar results were obtained in our study. Although there were differences in the design and timing of the studies, we found significant differences in seizure frequency and mental status. This indicates that it is important for physicians to focus on both seizure control and mental health. *Alkhotani* et al. demonstrated that an increase in seizure frequency was significantly associated with various factors, including higher baseline seizure frequency, polytherapy, non-adherence to medication regimens, increased stress, and changes in sleep patterns². *Huang* et al. indicated differences between groups with and without seizure increase, including factors such as age, living in Wuhan, exposure to COVID-19, concerns about the pandemic's negative effects on seizures, pre-pandemic seizure frequency, uncontrolled epilepsy, and medication

regimen changes¹⁸. *Assenza* et al. found that the increase in seizure frequency and severity during the pandemic was related to the number of anti-epileptic drugs used and sleep quality²². Risk factors for increased seizure frequency include tumor-related and drug-resistant epilepsy, the presence of insomnia, and decreased economic income³.

Limited social activities, lifestyle changes, lack of necessary medical intervention due to restricted access to medical facilities, multiple drug use, and poor seizure control are reported as risk factors for worsening seizures²¹. In our study, differences were observed between groups with and without increased seizures in terms of age range (21-60 years), polytherapy, drug-resistant epilepsy, changes in sleep patterns, increased stress during the pandemic, and higher K-10 scores, similar to the literature. Furthermore, avoidance of seeking medical care at

Table 3. Variables of increased seizure frequency using logistic regression analysis

	Multivariate		Univariate	
	OR (%95 CI)	p	OR (%95 CI)	p
Resistant epilepsy	1.671 (0.607 – 4.602)	0.320	3.354 (1.488 – 7.557)	<i>0.004</i>
Polytherapy	2.945 (1.152 – 7.532)	<i>0.024</i>	3.783 (1.76 – 8.13)	<i>0.001</i>
Change of anti-seizure medication dose	2.099 (0.883 – 4.986)	0.093	2.295 (1.06 – 4.971)	<i>0.035</i>
Increase stress during the pandemic	1.407 (0.585 – 3.387)	0.446	2.268 (1.085 – 4.739)	<i>0.029</i>
Change in sleep pattern	2.432 (0.99 – 5.975)	0.053	2.452 (1.155 – 5.205)	<i>0.019</i>
Hesitate to visit the outpatient clinic despite having seizures during the pandemic	1.757 (0.175 – 17.627)	0.632	5.43 (2.079 – 14.183)	<i>0.001</i>
Hesitate to go to the emergency room despite having seizures during the pandemic	2.786 (0.247 – 31.417)	0.407	8.325 (2.943 – 23.551)	<i>0.000</i>
Constant	0.039 (0 – 0)	0.000		

Cox & Snell R Square=0.135, Nagelkerke R Square=0.238, Accuracy=0.881. Bold indicates statistical significance
OR (%95 CI): odds ratio (95% confidence interval, CI)

outpatient/emergency departments despite experiencing seizures also showed differences between groups with and without seizure increase. Factors known to affect seizures, such as polytherapy, drug-resistant epilepsy, stress, and sleep changes, exhibited differences in our study.

Logistic regression analysis was used to examine the variables affecting the increase in seizure frequency. Among them, hesitate to go to the emergency room despite having seizures during the pandemic emerged as the parameter with the highest risk of increasing the frequency of seizures. Resistant epilepsy, polytherapy, change of anti-seizure medication dose, change in sleep pattern, hesitate to visit the outpatient clinic despite having seizures during the pandemic and increase in stress due to the COVID-19 pandemic were found to be significant in terms of an increase in seizure frequency in the model. It is known that seizures and stress affect each other mutually.

It was found that psychological stress among individuals had been common in the early stages of the COVID-19 pandemic and might be associated with sleep disturbance²³. Changes in sleep-wake rhythm and sleep quality have been described in cross-sectional studies conducted during the quarantine period^{2, 3, 13, 24, 25}. In our study, it was found that there had been a change in sleep pattern at a rate of 27.3%, similar to the literature (11.3–71.2%)^{2, 3, 25}.

The COVID-19 pandemic had significantly disrupted the healthcare services provided to PWE. Outpatient visits had been delayed, and essential epilepsy-related tests like electroencephalogram (EEG) and magnetic resonance imaging (MRI) studies had been canceled due to the overwhelming strain on the healthcare system and disruptions in medical supply chains^{3, 26}. This had resulted in challenges in responding to emergencies promptly.

Moreover, PWE are experiencing more isolation, anxiety, and stress compared to the general population; these factors have been linked to an increase in the frequency of seizures^{26, 27}. Our research indicates that the avoidance of presenting to the emergency/outpatient clinic despite having seizures was higher in the group with increased seizures. With the continuation of the pandemic, we concluded that although administrators produced solutions for the purchase of drugs and the opening of isolated examination rooms, the service was not interrupted, but it was not enough for patients. The pandemic had led to a decline in the quality of life, a higher prevalence of depression, and increased difficulties in accessing essential healthcare services. The pervasive sense of fear and uncertainty during the pandemic had only exacerbated these challenges for PWE²⁸.

Forty-six patients (20.3%) were admitted to the hospital with suspicion of COVID-19. PCR was positive in 41 (18.1%) patients. A total of 7 patients were treated in hospital, 1 patient in Intensive Care Unit. The seizure frequency increased in 8 (17.4%) patients during infection. Of the 8 patients with increased seizure frequency, 3 (37.5%) had mild, 1 (12.5%) had moderate, and 4 (50.0%) had severe mental distress symptoms. In addition, one patient, whose seizure frequency increased during the infection period, also reported an increase in seizure frequency during the pandemic period.

34 of our patients reported an increase in seizure frequency. In the study by *Elger et al.*, in which they showed that patients noticed less than 50% of their seizures²⁹, the importance of different measurements such as video EEG, mobile EEG, and the history given by people living together was mentioned. We think that only obtaining information from patients led to these results.

Our study has some limitations. We cannot rule out the possibility of sample bias because the participants were contacted by phone. We had to evaluate the changes in seizure frequency according to patient statements. We could not exclude psychiatric illness or medication use. In addition, because there was no control group and no evaluations were made before the pandemic, the findings cannot be completely attributed to the pandemic.

Conclusion

One year after the declaration of the pandemic, we found that stress was still common, and the frequency of seizures increased. Resistant epilepsy, polytherapy, change of anti-seizure medication dose, change in sleep pattern, hesitate to visit the outpatient clinic despite having sei-

zures during the pandemic and increase in stress due to the COVID-19 pandemic were found to be significant in terms of an increase in seizure frequency in the univariate analyses. In multivariate analyses only polytherapy was detected as the parameter with increased seizure frequency. It is known that seizures and stress affect each other mutually. When there are important public health problems such as pandemics, we should be careful to evaluate the patients' seizures, evaluate their mental state, and not ignore their medical needs. Knowing that there is a multifaceted interaction between epilepsy, stress, and sleep, we conclude that we should approach them holistically.

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