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# Effect of the COVID-19 Pandemic on Seizure Control Status in Patients with Epilepsy

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## What's Known

- During the COVID-19 pandemic, people with epilepsy have perceived more psychological distress than healthy individuals, and cases with new-onset focal seizures, serial seizures, and status epilepticus have been reported in the literature.

## What's New

- Overall, the COVID-19 pandemic has not been a major precipitating factor and has not affected the seizure control status of patients with epilepsy.
- In treated epilepsy, a fluctuating course with periods of seizure freedom followed by relapses is part of its natural history.

## Abstract

**Background:** Previous studies have shown that patients with epilepsy (PWE) perceived significant disruption in the quality and provision of care due to the coronavirus disease 2019 (COVID-19) pandemic. The present study aimed to investigate the effect of this pandemic on seizure control status and changes in seizure frequency in PWE.

**Methods:** A consecutive sample of adult PWE registered in the database of Shiraz Epilepsy Center (Shiraz, Iran) was included in the study. In July 2021, phone interviews were conducted with all selected patients. Information such as age, sex, last seizure, seizure type, and frequency during the 12 months before the study, and history of COVID-19 contraction was extracted. The seizure control status of the patients in 2019 (pre-pandemic) was compared with that during the COVID-19 pandemic. Data were analyzed using SPSS software with the Fisher's exact test and Pearson's Chi squared test.  $P < 0.05$  was considered statistically significant.

**Results:** A total of 158 patients were included in the study, out of which 62 (39.2%) patients had a stable seizure control status, 47 (29.7%) had fewer seizures, and 50 (31.6%) had more seizures. Breakthrough seizures were reported by 32 (34.4%) patients. Seizure frequency increased in 18 (27.7%) and decreased in 46 (70.7%) patients.

**Conclusion:** Overall, the COVID-19 pandemic has not been a major precipitating factor nor has it affected the seizure control status of PWE. In treated epilepsy, a fluctuating course with periods of seizure freedom followed by relapses is part of its natural history.

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**Keywords** • Coronavirus • Epilepsy • Seizures

## Introduction

Epileptic seizures often occur spontaneously without any apparent cause or trigger, but many patients believe that seizures are precipitated by external or internal stimuli. Some of these precipitating factors have been well defined, including sleep deprivation, premature awakening, and photic stimulation.<sup>1</sup>

The world has recently experienced a pandemic of the novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>2</sup> The virus has a high transmission potential; therefore, the implementation of social distancing measures has been advocated worldwide to control its outbreak. Iran reported its first confirmed cases

of SARS-CoV-2 infection on 19 February 2020, and the first wave of the COVID-19 pandemic occurred in March-April 2020.<sup>3</sup> In response to the pandemic, a lockdown was initiated, and the government canceled all public events, closed schools, universities, shopping centers, holy shrines, and banned all festivities. Soon after, a ban on intercity travel was introduced following an increase in the number of newly infected cases.<sup>3</sup>

The outbreak of COVID-19 has created a lot of stress and anxiety among people and has disrupted many businesses, including the provision of health care services.<sup>4-6</sup> During the COVID-19 pandemic, patients with epilepsy (PWE) have experienced more psychological distress than healthy individuals, and cases of new-onset focal seizures, serial seizures, and status epilepticus have been reported in the literature.<sup>4</sup> Previous studies indicated that PWE perceived significant disruption in the quality and provision of health care services (31%-95%), increased stress and social isolation, and increased seizure frequency (6%-35%) during the COVID-19 pandemic.<sup>7-11</sup> However, the reported effect on seizure frequency in previous studies were based on patients' perceptions and binary (yes/no) surveys. Hence, the present study aimed to investigate the effect of the COVID-19 pandemic on seizure control status and changes in seizure frequency in PWE. We also investigated the occurrence of breakthrough seizures in PWE with well-controlled epilepsy. We hypothesized that the COVID-19 pandemic has been a major precipitating factor and has negatively affected the seizure control status of PWE.

## Patients and Methods

A consecutive sample of 200 adult PWE with focal epilepsy or idiopathic generalized epilepsy (IGE) was included in the study based on the duration of follow-up and in a retrograde fashion. These patients were registered in the database of Shiraz Epilepsy Center (Shiraz, Iran). The inclusion criterion was at least three years of follow-up at the center. Exclusion criteria were patients with impaired awareness, myoclonic seizures, focal seizures without impaired awareness, not willing to participate, and those with incomplete files. Out of the selected adult PWE, a total of 100 patients with no seizures in 2019 were arbitrarily selected to investigate breakthrough seizures during the pandemic. In addition, 100 patients with at least two seizures in 2019 were recruited to investigate changes in seizure frequency during

the pandemic. However, we could not evaluate all the patients due to the limited workforce. Eventually, 158 patients were included in the study, out of which 93 belonged to the seizure-free and 65 to the not seizure-free category. Written informed consent was obtained from all the participants. The study was approved by the Institutional Review Board of Shiraz University of Medical Sciences, Shiraz, Iran (IR.SUMS.REC.1400.608).

## Data Collection

The data registered at the epilepsy center database included age (at seizure onset, diagnosis, and follow-up), sex, seizure type, frequency, and final diagnosis. Due to the confidentiality regulations of Shiraz University of Medical Sciences, patients' data may not be shared.

Phone interviews with all 158 patients were conducted in July 2021, and the following information was extracted: age, sex, last seizure, seizure type, and frequency during the 12 months prior to the start of the study (from July 10<sup>th</sup>, 2020 to July 9<sup>th</sup>, 2021), and history of COVID-19 contraction. The interview guide is presented in table 1.

## Statistical Analysis

Data were analyzed using SPSS software, version 25.0 (IBM Corp., Armonk, N.Y., USA). Based on the normality criterion, continuous variables were expressed as mean±SD or median/interquartile range (IQR). Categorical variables were expressed as numbers and percentages. Fisher's exact test and Pearson's Chi squared test were used for statistical analyses. P values (2-sided) less than 0.05 were considered statistically significant.

## Results

During the study period, a total of 3,737 patients registered at Shiraz Epilepsy Center, of which 158 patients out of the eligible 200 individuals were included in the study. The inclusion rate was determined at 79% due to missing data in 42 cases. Of these participants, 93 (58.9%) were seizure-free and 65 (41.1%) were not seizure-free in 2019 (pre-pandemic era). In terms of seizure control, 62 (39.2%) patients had a stable status (seizure-free=61, not seizure-free=1). The remaining patients had varying seizure control status, namely, 47 (29.7%) had fewer seizures, and 50 (31.6%) had more seizures. Figure 1 shows the effect of the COVID-19 pandemic on seizure control status in these patients (focal epilepsy vs. IGE).

**Table 1: The phone interview guide**

Interview guide	
1	How old are you? What is your sex?
2	When was your last seizure?
3	Have you had seizures with staring and impaired awareness (without significant stiffness and body movements) recently? How many times during the past year?
4	Have you recently had severe seizures with stiffness and body movements? How many times during the past year?
5	Have you contracted COVID-19? If yes, how severe was it? <ul style="list-style-type: none"> <li>• Without signs and symptoms</li> <li>• With mild symptoms</li> <li>• Were hospitalized</li> </ul>
6	Have your seizures become more frequent after contracting COVID-19?

**Seizure-free patients (before the pandemic)**

**Focal** Focal epilepsy (63 patients)

- 44 patients remained seizure-free (69.8%)
- 19 patients had breakthrough seizures (30.2%)

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**IGE** Idiopathic generalized epilepsy (30 patients)

- 17 patients remained seizure-free (56.7%)
- 13 patients had breakthrough seizures (43.3%)

• The difference between focal epilepsy and IGE is not significant (Fisher’s exact test: P=0.247; df: 1).

**Not seizure-free patients (before the pandemic)**

**Focal** Focal epilepsy (49 patients)

- 13 patients became seizure-free (28.6%)
- 17 patients had increased seizure frequency (34.7%)
- 18 patients had decreased seizure frequency (36.7%)
- 1 patient had no change in seizure frequency (2%)

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**IGE** Idiopathic generalized epilepsy (16 patients)

- 11 patients became seizure-free (68.8%)
- 1 patient had increased seizure frequency (6.3%)
- 4 patients had decreased seizure frequency (25%)

• The difference between focal epilepsy and IGE is significant (Pearson’s Chi square: P=0.007; df: 2).

**Figure 1:** Effect of the COVID-19 pandemic on seizure control status in patients with epilepsy. Thirty-two patients had breakthrough seizures, and 24 patients became seizure-free. df: Degree of freedom

**Seizure-free Patients**

The seizure-free category included 56 (60.2%) female and 37 (39.8%) male patients. The mean age of these patients was 33±11 years (range: 18-69 years), and their mean follow-up duration was 7.8 years (median: 9, IQR: 6, range: 3-13 years). Focal epilepsy was diagnosed in 63 (67.7%) patients, and IGE was diagnosed in 30 (32.3%) patients. Breakthrough seizures with

impaired awareness were reported by 32 (34.4%) patients during the study period. The frequency of seizures during this period was 16 (IQR: 26; range: 1-52), where three patients had only one seizure, and 11 patients had 30 or more seizures. As stated by seizure-free patients, 8 (8.6%) contracted COVID-19 during the pandemic, but symptoms were mild, and hospitalization was not required. Breakthrough seizures and seizure-free periods were reported by three and five patients, respectively (Fisher’s exact test: P>0.99, df: 1).

**Not Seizure-free Patients**

The not seizure-free category included 32 (49.2%) female and 33 (50.8%) male patients. The mean age of these patients was 33±11 years (range: 18-61 years), and their mean follow-up duration was 7.8 years (median: 9, IQR: 1, range: 3-10 years). Focal epilepsy was diagnosed in 49 (75.4%) patients, and IGE was diagnosed in 16 (24.6%) patients. The mean number of seizures before the COVID-19 pandemic was 55 per year (median: 18, IQR: 46, range: 2-730 seizures). Whereas the mean number of seizures during the pandemic was 16 per year (median: 4, IQR: 30, range: 0-90 seizures). Seizure frequency status during the pandemic compared to pre-pandemic increased in 18 (27.7%) patients (negative change), unchanged in 1 (1.5%) patient, and decreased in 46 (70.7%) patients (positive change). The number of patients who became seizure-free during the previous 12 months, was 24 (36.9%). The mean change in seizure frequency was -39 per year (median: -9; range: -640 to -40; IQR: 53).

As stated by not seizure-free patients, 2 (3.1%) contracted COVID-19 during the pandemic but did not require hospitalization, as the symptoms were mild. Neither patient reported an increase in seizure frequency after contracting COVID-19.

**Discussion**

In the present study, we observed that PWE have experienced different seizure control

status scenarios during the COVID-19 pandemic compared to the pre-pandemic era. In approximately 40% of the patients, seizure control status remained stable, whereas 30% reported a positive change and 30% a negative change. In a previous study of 456 PWE, worsened and improved seizure control status was reported in 67 and 61 patients, respectively.<sup>10</sup> Since the authors did not specify details of their findings, it was not possible to draw a comparison with our results. In another study of 189 patients with a short follow-up period of two months, 16 patients reported a change in seizure frequency (an increase in eight patients and a decrease in eight other patients).<sup>12</sup> In general, 6% to 35% of PWE perceived an increase in seizure frequency since the start of the pandemic.<sup>7-11, 13, 14</sup> A systematic review found a causal relationship between psychological stress and seizure worsening (during the COVID-19 pandemic) without considering temporality.<sup>15</sup>

A study in 2012 investigated the patterns of treatment response in newly diagnosed epilepsy in 1,098 patients.<sup>16</sup> The seizure outcomes were categorized into four patterns, namely (A) early and sustained seizure freedom, (B) delayed but sustained seizure freedom, (C) fluctuating between periods of seizure freedom and relapse, and (D) seizure freedom never attained. The outcome pattern A was observed in 37%, B in 22%, C in 16%, and D in 25% of the patients.<sup>16</sup> In another study of 159 patients, who were seizure-free for the first five years after resection epilepsy surgery, 32 (20%) patients had at least one recurrent seizure during follow-up.<sup>17</sup> Therefore, it is very common for treated epilepsy to fluctuate between periods of seizure freedom and relapse. As a result, reported findings in previous studies about seizure worsening during the COVID-19 pandemic, including our previous study,<sup>7-11, 13, 14</sup> should not be attributed to the pandemic period nor to SARS-CoV-2 infection. It is simply part of the natural history of treated epilepsy to observe improvement or deterioration in seizure control status over time, at least in many patients. Similar to our results, two other studies<sup>10, 12</sup> reported an equal number of patients with seizure worsening and improvement during the COVID-19 pandemic. Clearly, a severe illness due to COVID-19 may precipitate seizures in PWE and even in healthy individuals.<sup>4</sup> Seizures in patients with SARS-CoV-2 infection may occur due to a variety of reasons, including fever, neurotropism, hypoxia, multiorgan failure, and so on.<sup>18</sup> However, seizures are a rare presenting symptom of COVID-19.<sup>19</sup> It is noteworthy that PWE is no more prone to

contracting COVID-19 than other individuals, and COVID-19 in PWE is not associated with a more severe illness or a poorer prognosis.<sup>20, 21</sup> In the current study, despite the low sample size, we did not observe any indication of worsening seizure control status in PWE due to COVID-19 contraction.

Finally, it is important to highlight that restructuring of health care services to cope with the COVID-19 pandemic resulted in the closure of epilepsy/neurology clinics and epilepsy monitoring units in many countries.<sup>22</sup> Recently, international organizations (e.g., the International League Against Epilepsy and the International Federation of Clinical Neurophysiology) have called for the continued functioning of Epilepsy Monitoring Units (EMUs) during emergency situations, such as the COVID-19 pandemic. Long-term video-EEG monitoring is an essential diagnostic service. It is also requested that access to video-EEG monitoring of the patients in the EMUs must be given high priority.<sup>22</sup> Similarly, epilepsy/neurology clinics should be considered essential and should continue to serve the patients, at least in the form of virtual communication.

The main limitations of the study were the low sample size and a single-center study design. Besides, our patients did not routinely keep a seizure journal (diary), and the stated seizure frequency was based on their recollections.

## Conclusion

Overall, the COVID-19 pandemic has not been a major precipitating factor affecting seizure control status in PWE. In many patients, it is the natural history of treated epilepsy to fluctuate between periods of seizure freedom and relapse.

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## Authors' Contribution

A.A.A, S.A.N and M.F: Substantial contributions to the conception/design, acquisition, analysis, and interpretation of the data, drafting and revising the manuscript for important intellectual content as well as final approval for its publication. The authors accept accountability for all aspects of the work and ensure that questions related to the accuracy or integrity of any part of the work are duly investigated and resolved.

**Conflict of Interest:** None declared.

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