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# Interaction between COVID-19 and epilepsy during the omicron surge: A cross-sectional survey conducted in China tertiary hospital



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ARTICLE INFO	ABSTRACT		
Keywords: Epilepsy COVID-19 Omicron virus SARS-CoV-2 Seizures	<i>Objective</i> : It is unclear whether patients with epilepsy are more susceptible to SARS-CoV-2 infection, whether they experience more severe manifestations of COVID-19, and whether seizures worsen after SARS-CoV-2 infection. Our study aims to explore these points and provide comprehensive and practical guidance for patients with epilepsy. <i>Methods</i> : We designed a questionnaire to collect variables from epilepsy patients. We used the Chi-square test, Fisher's exact test, or Mann-Whitney <i>U</i> test to analyze differences between the two groups. Multiple logistic regressions were employed to determine the risk factors for relevant outcome variables. <i>Results</i> : We identified a total of 181 patients, with 74% (n = 134) reporting COVID-19. The patients' educational level was found to be a risk factor for COVID-19 (OR = 0.33, 95% CI 0.14–0.80, P = 0.013). When comparing seizure frequency changes between epilepsy patients with and without COVID-19, no statistically significant difference was observed (P > 0.05). However, an increase in seizure frequency was significantly associated with higher levels of anxiety (P < 0.001) and depression (P < 0.005). <i>Conclusion:</i> The risk of COVID-19 infection may be increased in patients with epilepsy. COVID-19 infection does not seem to worsen seizures in epilepsy patients. Patients with epilepsy rarely develop more severe clinical manifestations of COVID-19 after SARS-CoV-2 infection. During the COVID-19 pandemic, patients with epilepsy who also suffer from anxiety and depression may experience an increase in the frequency of their seizures.		

# Introduction

Coronavirus disease 2019 (COVID-19) was first reported in Wuhan City, Hubei Province, China, in December 2019. In January 2020, the World Health Organization identified it as an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. As of February 2023, there have been over 675 million confirmed cases and >6.87 million deaths reported worldwide [2]. Since the outbreak of COVID-19, 21 different SARS-CoV-2 virus variants have been identified. The Omicron variant, named B.1.1.529, is a new highly mutated virus type and was designated as a variant of concern by the World Health Organization on November 26, 2021 [3]. Since its first discovery in Africa in November 2021, the variant has rapidly spread worldwide [4] and has been dominant since May 25, 2022. There is evidence suggesting that this variant increases the risk of reinfection [5]. Following the relaxation of epidemic control measures in China at the end of December 2022, the number of COVID-19 infections with the Omicron variant as the primary strain has surged. Up to one-fifth of people infected with COVID-19 may experience symptoms of nervous system damage, including loss of smell and taste, muscle weakness and pain, tingling in the hands and feet, dizziness, delirium, ischemic and bleeding strokes, and epilepsy [6]. Moreover, 90% of people infected with COVID-19 have reported abnormal electroencephalograms [7].

Epilepsy is one of the most common chronic diseases of the nervous system, characterized by frequent spontaneous and recurrent unprovoked seizures, affecting approximately 70 million people worldwide [8]. Studies have suggested that patients with chronic diseases may be at a higher risk of COVID-19 infection and experience a more severe disease course after infection. Patients with epilepsy may be more susceptible to COVID-19 infection and have a more severe disease course due to their physical and psychiatric comorbidities [9].

The impact of the COVID-19 epidemic on patients with epilepsy is

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undeniable. Several studies have shown that in many cases, severe psychological problems, limited access to epilepsy care, and difficulties in obtaining anti-seizure medications can worsen seizures in patients with epilepsy during the COVID-19 epidemic [10–13]. However, there is limited data on the prevalence of COVID-19 infection in patients with epilepsy and its impact on epilepsy [10,14]. In a nationwide multicenter study involving 2,751 patients with epilepsy, Sanchez-Larsen et al. reported moderate prevalence of COVID-19 in this population. One out of every five patients required medical attention, and 4.6% died due to COVID-19. Older age, dyslipidemia, institutionalization, and intellectual disability were significant risk factors associated with severe COVID-19. However, seizure control remained stable during COVID-19 and throughout long-term follow-up in the majority of patients with epilepsy who contracted the infection [15]. Only a few studies have systematically evaluated COVID-19 infection in patients with epilepsy [16,17]. In a cross-sectional observational study involving 1,537 patients, 21 (1.3%) had active epilepsy, and a control group was used to compare the cumulative incidence and case-fatality rate (CFR). The cumulative incidence of COVID-19 was higher in patients with active epilepsy (1.2%) compared to controls (0.5%). Epilepsy was associated with fatality during hospitalization, and hypertension was associated with fatality in patients with epilepsy [16]. These studies suggest that patients with epilepsy are at higher risk of COVID-19 and that patients with active epilepsy have a higher mortality rate compared to other hospitalized patients with severe COVID-19.

Our research aims to further investigate the interaction between epilepsy and COVID-19, analyze SARS-CoV-2 infection in patients with epilepsy and its risk factors, and describe the clinical manifestations of patients with epilepsy after SARS-CoV-2 infection and its impact on epilepsy. This will provide comprehensive and effective guidance and support for patients with epilepsy.

#### Materials and methods

## Study design

This study was conducted at the Outpatient Department of Neurology, Qilu Hospital, Shandong University, from February to March 2023. The study focused on patients with epilepsy in Shandong Province, China. To avoid inquiring about patients' previous COVID-19 infection history, we only collected information on infections occurring within a month after the implementation of the epidemic unblocking policy in China for patients with epilepsy. Patients were recruited based on the following criteria: 1. Patients diagnosed with epilepsy according to the standards proposed by the International League Against Epilepsies (ILAE) in 2017; 2. Age range of 0–65 years old; 3. The patient or their guardian has provided informed consent and is willing to participate in the study. Exclusion criteria included: 1. Patients with a doubtful diagnosis of epilepsy; 2. Inability to participate in the survey; 3. Loss to follow-up or withdrawal from the study. Patients who met the criteria completed a survey consisting of four parts: (1) Demographic information, (2) Presence/Absence of prior COVID-19 infection, (3) Symptoms/severity of COVID-19 infection, and (4) Psychosocial sequelae of COVID-19 infection. Written consent was obtained from the patients and/or their legal guardians. The survey was conducted under the guidance of well-trained medical staff. The questionnaire collected data on participants' age, gender, age at seizure onset, cause of epilepsy, type of epilepsy (classified according to the ILAE 2017 guidelines) and its treatment, seizure frequency, comorbidities, intellectual disability, and vaccine status. COVID-19-related information included main symptoms, duration of symptoms, medication status, and the effect of COVID-19 on epilepsy control. Changes in seizure frequency were defined as a number of seizures in the month following the infection greater or lower than that occurred in the month before, even by a single additional episode. Patients who tested positive for anti-SARS-CoV-2 IgM/IgG antibodies in nasopharyngeal swabs or serum by RT- PCR were diagnosed with COVID-19. Probable COVID-19 cases were diagnosed based on specific criteria defined by the World Health Organization (WHO). Due to the highly infectious Omicron variant, some patients rejected COVID-19 diagnosis methods despite the implementation of restrictions. In our study, epilepsy patients with COVID-19, including confirmed and suspected cases, were reclassified.

#### Statistical analysis

The collected variables were analyzed as follows: Qualitative variables were expressed as percentages, and quantitative variables were expressed as mean  $\pm$  standard deviation (SD) or median-quartile range (IQR) depending on their distribution. All epilepsy patients were grouped based on whether they had a first-time SARS-CoV-2 infection. The differences between the two groups were analyzed using the Chi-square test, Fisher's exact test, or Mann-Whitney *U* test, as appropriate. Multiple logistic regressions were performed to determine the risk factors for SARS-CoV-2 infection in epilepsy patients. The clinical manifestations of COVID-19 in SARS-CoV-2 infected epilepsy patients were described. Additionally, all epilepsy patients were grouped based on changes in seizure frequency, and the differences in psychology-related variables between the two groups were analyzed. Significance was set at p < 0.05, and the data were analyzed using SPSS 26.0.

## Results

# Baseline information

A total of 181 patients who met the inclusion criteria were included in the analysis. Among them, 51.9% (n = 94) were male and 48.1% (n = 94)87) were female. The median age was 28 years (Q1: 20, Q3: 37), and the median number of people with epilepsy living together was 3 (Q1: 3, Q3: 4). The median age at seizure onset in epilepsy patients was 18 years (Q1: 14, Q3: 31). The cause of seizure was unknown in 110 patients (60.8%), while it was known in 71 patients (39.2%). Generalized seizures were the most common seizure type among epilepsy patients (n = 122, 67.4%). The majority of patients were treated with one or two antiseizure medications, with 40.3% (n = 73) using a single drug and 35.4% (n = 64) using two drugs. The most commonly used drugs were oxcarbazepine and levetiracetam. 75.7% (n = 137) of patients had a low seizure frequency, defined as less than once a year. Epilepsy surgery was performed in 7.2% (n = 13) of patients. Intellectual disability was present in 13.8% (n = 25) of patients. Furthermore, 16.0% (n = 29) of patients had at least one other disease. Table 1 presents the demographic and clinical characteristics of epilepsy patients.

# SARS-CoV-2 infection in patients with epilepsy

Among the 181 patients with epilepsy included in the study, 74.0% (n = 134) had COVID-19, while 26.0% (n = 47) did not. There were no significant differences between the two groups in terms of sex, age, number of anti-seizure medications used, type and frequency of previous seizures, and vaccination against COVID-19. However, significant differences were observed in educational level and etiology of epilepsy between the two groups (P < 0.05). When comparing epilepsy patients with and without COVID-19, those with COVID-19 were more likely to have unknown causes for their epilepsy. However, after conducting a more detailed analysis, no significant correlation was found between the etiology of epilepsy patients with higher education levels had a lower risk of contracting COVID-19, and this difference was statistically significant (OR = 0.33, 95% CI 0.14–0.80, P = 0.013 < 0.05).

# SARS-CoV-2 infection and the severity of epilepsy

Comparing the changes in seizure frequency among epilepsy patients

#### Table 1

Comparison of demographic and epilepsy characteristics, disability and comorbidities between patients with and without COVID-19. \*P < 0.05.

Variable	All subjects N = 181	Patients without COVID-19 N = 47 (26.0%)	Patients with COVID-19 N = 134 (74.0%)	P-value Patients with COVID-19 vs. patients without COVID-19
Sex (male), n (%)	94	24(51.1%)	70(52.2%)	0.890
Age (<18), n (%)	(51.9%) 19 (10.5%)	5(10.6%)	14(10.4%)	1.000
Adult (≥18), n (%)	(10.5%) 162 (89.5%)	42(89.4%)	120(89.6%)	
Education, n (%)	63 (34.8%)	16(34.0%)	47(35.1%)	
<high school<="" td=""><td>46 (25.4%)</td><td>18(38.3%)</td><td>28(20.9%)</td><td>0.039*</td></high>	46 (25.4%)	18(38.3%)	28(20.9%)	0.039*
High school or Equivalent Higher professional or university	72 (39.8%)	13(27.7%)	59(44.0%)	
Number of people living together, median [IQR]	3[3–4]	4[3-4]	3[3–4]	0.611
Age at onset, median [IQR]	18 [14–31]	18[13–30]	19[14–31]	0.404
Type of epilepsy, n (%) Focal	22	7(14.9%)	15(11.2%)	0.684
Conoralizad	(12.2%)	22(60 10/)	00(67 204)	
University	(67.4%)	9(17.00/)	20(21.6%)	
UIIKIIOWII	37 (20.4%)	8(17.0%)	29(21.0%)	
Etiology, n (%)				
Genetic	5(2.76%)	0(0.0%)	5(3.7%)	
Infection Structure1	15(8.3%)	7(14.9%)	8(6.0%)	0.024*
Unknown	51(28.2)	18(38.3%)	33(24.0%) 99(6E 704)	
	(60.8%)	22(40.8%)	88(03.7%)	
Number of AEDs, n (%)	-	10(00.00/)	FF(11 00()	
1	73 (40.3%)	18(38.3%)	55(41.0%)	
2	64 (35.4%)	16(34.0%)	48(35.8%)	0.116
3	25 (13.8%)	4(8.5%)	21(15.7%)	
≥4	19 (10.5%)	9(19.1%)	10(7.5%)	
Epileptic frequency, n (	%)			
High	21 (11.6%)	7(14.9%)	14(10.4%)	0.177
Moderate	23 (12.7%)	9(19.1%)	106(79.1%)	
Low	137 (75.7%)	31(66.0%)	14(10.4%)	
Epilepsy surgery, n (%)	13(7.2%)	4(8.5%)	9(6.7%)	0.744
Intellectual disability, n (%)	25 (13.8%)	7(14.9%)	18(13.4%)	0.803
Comorbidities, n (%)	29 (16.0%)	6(12.8%)	23(17.2%)	0.479
COVID-19 vaccination, n (%)	119 (65.7%)	30(63.8%)	89(66.4%)	0.748
Epileptic seizures during the COVID- 19 epidemic No	153 (84.5%)	41(87.2%)	112(83.6%)	0.551
change in seizures	28 (15.5%)	6(12.8%)	22(16.4%)	

with and without COVID-19, the results did not show a significant difference (P > 0.05). Out of the 47 epilepsy patients without COVID-19, 6 (12.8%) experienced changes in their seizure frequency, with 4 of them actually experiencing an increase in seizure frequency, suggesting that the pandemic and its associated stressors may have had a negative impact on their condition. It is worth noting that seizure frequency can be influenced by a wide range of factors, including stress, sleep patterns, medication adherence, and more. Among the 134 epilepsy patients with COVID-19, 22 (16.4%) also had a change in seizure frequency, with 14 of them experiencing an increase in seizure frequency. However, there could be alternative explanations for their increased seizures aside from COVID-19. Out of these patients, 5 experienced stress and anxiety, 5 reported a decrease in sleep quality, 2 had reduced anti-seizure medication intake, 1 had hypocalcemia, and 1 had no discernible cause.

#### Clinical manifestations of epilepsy patients infected with SARS-CoV-2

Among the 134 epilepsy patients with COVID-19, the most common clinical symptoms were fever (91.0%), cough (67.2%), sore throat (56.0%), headache (45.5%), fatigue (41.0%), and myalgia (36.6%). The median duration of fever was 3 days (Q1: 2, Q3: 3). None of the patients with epilepsy had fever-related seizures. Based on the severity grading of clinical manifestations of COVID-19, 2 (1.5%) were positive and asymptomatic, 123 (91.8%) were mild (mainly manifested as upper respiratory tract infection, such as dry throat, sore throat, cough, fever, etc.), 9 (6.7%) were moderate (persistent high fever for > 3 days and/or cough, shortness of breath, etc., characteristic "white lung" pneumonia was seen on imaging), and no severe cases (shortness of breath, respiratory rate  $\geq$  30 times, or (and) resting oxygen saturation  $\leq$  93%; or (and) PaO2/O2<300mHg; Progressive aggravation of clinical symptoms and critical type (respiratory failure, shock, organ failure)) were reported. Out of the 9 patients presenting as moderate cases, 4 had other comorbidities (1 patient had a history of allergic disease, 3 had anxiety or depression, and 1 had meningioma). The median duration of COVID-19 clinical symptoms was 7 days (Q1: 5, Q3: 7). The clinical presentation data of epilepsy patients with COVID-19 are shown in Table 2.

## Mental status of patients with epilepsy during the SARS-CoV-2 epidemic

According to the GAD-7 scale, 49 out of the 181 epilepsy patients had mild anxiety, 12 had moderate anxiety, 13 had severe anxiety, and the remaining 107 did not have anxiety. In the analysis of the NIDD-E scale, it was found that 29 patients with epilepsy were likely to have depression, while the remaining 152 patients were not depressed. The group of epilepsy patients was divided into two categories: those who experienced a change in seizure frequency during the COVID-19 epidemic and those who did not. Surprisingly, 15.5% of the patients experienced a

Table 2

Epilepsy characteristics and clinical symptoms in patients with COVID-19.

Variables	Total (n = 134)
Symptoms, n (%)	
Fever	122 (91.0%)
Cough	90 (67.2%)
Sore throat	75(56.0%)
Headache	61(45.5%)
Fatigue	55(41.0%)
Muscle pain	49(36.6%)
Fever time days, median [IQR]	3[2,3]
Symptom severity grading, n (%)	
Asymptomatic	2(1.5%)
Mild	123(91.8%)
Moderate	9(6.7%)
Duration of COVID-19	7[5-7]
Symptoms, median [IQR]	
Changes of seizure frequency during infection, n (%)	
Increase	14(10.4%)
Reduce	8(6.0%)
No change	112(83.6%)
Fever-related seizures during infection, n (%)	0(0.0%)
Medication alteration during infection, n (%)	
None	108(80.6%)
Increase	22(16.4%)
Reduction/withdrawal	4(3.0%)

change in their seizure frequency, and the majority of these patients saw an increase in seizure frequency. This increase in seizure frequency was found to be significantly associated with higher levels of anxiety (P < 0.001) and depression (P < 0.005). Detailed data are presented in Table 3.

# Discussion

The United States Centers for Disease Control and Prevention (CDC) has indicated that some neurological disorders, such as epilepsy, may be risk factors for COVID-19, partly due to their higher likelihood of having other physical comorbidities [18]. A cross-sectional study in Spain showed higher cumulative COVID-19 morbidity and mortality in patients with active epilepsy compared to the population without epilepsy [16]. A study in Korea demonstrated that the presence of epilepsy was associated with an increased susceptibility to SARS-CoV-2 infection but not with infection-related mortality [19]. Information from studies in countries like China, Italy, and the United States also failed to demonstrate that patients with epilepsy are more susceptible to SARS-CoV-2 infection and rarely develop more severe COVID-19 clinical manifestations after infection. However, our study reported that the majority (74%) of 181 patients with epilepsy who met the inclusion criteria reported COVID-19, which was significantly higher than the incidence of COVID-19 in the healthy Chinese population during the same period. This suggests that patients with epilepsy may be at an increased risk of COVID-19 infection. However, it is important to exercise caution when interpreting the results of our study on epilepsy patients with COVID-19, as it also included patients with suspected COVID-19 and was conducted retrospectively.

Furthermore, the clinical manifestations of patients with epilepsy infected with SARS-CoV-2 were similar to those of healthy individuals. The most common symptoms were fever, cough, sore throat, etc., with a median duration of 7 days. Most patients exhibited mild COVID-19 symptoms, which is consistent with the conclusions of relevant studies conducted thus far, indicating that patients with epilepsy infected with SARS-CoV-2 rarely experienced more severe clinical manifestations of COVID-19. Although some physical comorbidities associated with more severe COVID-19 clinical manifestations (e.g., cardiovascular and cerebrovascular diseases, chronic respiratory diseases, diabetes mellitus) were present in a certain proportion of our patients, all patients with COVID-19 and epilepsy had mild or moderate degrees of infection. This may be due to the fact that the median age of patients with epilepsy who participated in the study was 31 years, and young age has been associated with an asymptomatic or mild COVID-19 disease course. Another possibility is that after multiple passages of SARS-CoV-2, the virulence of the Omicron variant, which is the predominant strain in China, has significantly weakened. Moreover, most of the epilepsy patients participating in the study had been vaccinated with at least one dose of vaccine, thereby significantly reducing the threat to their health and resulting in mild clinical manifestations after infection. However, due to

#### Table 3

Comparison of PWE without seizure change and PWE with seizure change in mental health. \*\*P < 0.01.

Variables	PWE without seizure change (n = 153)	PWE with seizure change (n = 28)	P value
GAD-7			
0–4 (No anxiety)	95(62.1%)	12(42.9%)	0.000**
5–9 (Mild anxiety)	45 (29.4%)	4(14.3%)	
10–14 (Moderate anxiety)	5(3.3%)	7(25.0%)	
$\geq$ 15 (Severe anxiety)	8(5.2%)	5(17.9%)	
NDDI-E			
$\leq$ 12 (No depression)	134(87.6%)	18(64.3%)	0.004**
>12 (May have	19(12.4%)	10(35.7%)	
depression)			

the small sample size of our study, a larger sample is needed to further elucidate the incidence of COVID-19 in patients with epilepsy and the association of epilepsy with the severity of COVID-19 symptoms.

Our study demonstrates that the higher the level of education among patients with epilepsy, the lower their risk of COVID-19. This association may be related to the fact that individuals with higher education levels tend to have better health knowledge, health behaviors, and access to medical resources, making them less likely to be infected with COVID-19.

Our findings suggest that seizures in patients with epilepsy may not be exacerbated by COVID-19. We found that 10.4% (n = 14) of epilepsy patients with COVID-19 experienced worsening seizures; however, their increased seizures could be attributed to other factors such as reduction in anti-seizure medication, anxiety, or depression during infection. A study conducted in Sweden, which included 12,221,801 SARS-CoV-2 infected individuals, showed that SARS-CoV-2 infection was not associated with an increased risk of epilepsy at the overall population level, and the virus-induced epileptogenic effect may be minimal [20]. Nonetheless, there have been several case reports of patients developing new-onset epilepsy after SARS-CoV-2 infection [21–24].

We also observed that only 8.5% (n = 4) of epilepsy patients without COVID-19 experienced increased seizures, which was lower than the proportion of epilepsy patients with COVID-19. However, we caution that this result should be interpreted with care due to the relatively small sample size and the lack of sufficient research data to support an association between COVID-19 and increased seizures. Additionally, 6% (n = 8) of epilepsy patients with COVID-19 appeared to have experienced a recovery from epilepsy, most of whom were taking COVID-19 drugs during the infection and had been prescribed new anti-seizure medications based on this treatment. The most commonly added new drug was levetiracetam. It is crucial to consider the possible interactions between anti-seizure medications and COVID-19 drugs and take into account the potential drug interaction when guiding epilepsy patients with COVID-19 in adding new anti-seizure medications. The Italian League against Epilepsy provides a table detailing some interactions between these two types of drugs (https://www.lice.it/pdf/Antiepileptic drugs interacti ons in COVID-19.pdf). For more up-to-date information, refer to this website (https://www.covid19-druginteractions.org/). Among the drugs examined, levetiracetam is particularly interesting because it has minimal interactions with COVID-19 drugs. This may make it more suitable as a newly added anti-seizure medication to provide seizure relief during SARS-CoV-2 infection.

It is well known that high fever can increase the risk of seizures in the general population, especially in people with epilepsy. Our study revealed that 91% (n = 122) of 134 epilepsy patients with COVID-19 developed febrile symptoms, but no fever-related exacerbation of epilepsy was reported. Lu et al. found that despite the presence of potential factors known to trigger acute symptomatic seizures, such as high fever due to encephalitis, no new seizures or status epilepticus were observed in COVID-19 patients without a previous history of epilepsy [25]. The International League Against Epilepsy (ILAE) states that fever caused by SARS-CoV-2 infection may pose a risk of exacerbating seizures in certain types of epileptic syndromes, such as Dravet syndrome or other types of seizures that may be induced by fever. However, no cases of increased seizures in these patient populations have been reported.

Anxiety and depression are common comorbidities in patients with epilepsy [26]. In this study, the frequency of depression and anxiety among all patients with epilepsy was 16.0% and 41.0%, respectively. The patients experienced significant psychological problems during the infection, which aligns with the results of a previous survey on the psychological status of patients with epilepsy during the SARS-CoV-2 epidemic [27]. Our research demonstrates that patients with epilepsy faced numerous challenges due to external factors during the COVID-19 epidemic. Disruptions in their daily routines and limited access to medical care caused significant stress and anxiety, which can trigger seizure activity. Additionally, quarantine measures and social isolation

led to feelings of loneliness, and the lack of support and social interaction can exacerbate depressive symptoms that are commonly observed among patients with epilepsy. Despite these challenges, our study did not find any evidence to suggest that COVID-19 itself contributes to an increase in seizure activity among patients with epilepsy. However, it is important to continue monitoring the situation and ensure that patients receive the care and support they need to manage their condition during these difficult times. China's National Health Council has released guidelines to promote psychological crisis intervention for patients during the COVID-19 outbreak. The Chinese government has made efforts to raise public awareness of prevention and protection by providing daily monitoring and accurate updates on active cases of COVID-19 on websites and social media. Moreover, an increasing number of psychologists and psychiatrists are using the internet and social media platforms such as WeChat, Weibo, TikTok, etc., to share strategies for dealing with psychological stress [28,29].

# Limitations

Our research has several limitations. Firstly, it is important to note that the sample size used in our study was relatively small, and all the patients were from Shandong Province, China. Due to variations in the level of COVID-19 understanding and regional epidemic situations across different provinces, some of our conclusions may not be generalizable. It is necessary to conduct similar studies with larger sample sizes in the future. Secondly, we included epilepsy patients with suspected COVID-19 in the group of patients with COVID-19. It is important to consider that these patients may have had influenza or other viral illnesses concurrently, which could affect the accuracy of our findings. Thirdly, since the participants of this survey were patients from a tertiary epilepsy clinic, there may have been an overrepresentation of patients with a longer disease duration, higher seizure frequency, combined medication, and comorbidities. Lastly, the subjects answered many questions retrospectively, which could affect the accuracy of the data due to misdescriptions of past episodes.

# Conclusion

Our study suggests that patients with epilepsy may have an increased risk of contracting COVID-19, and there is a negative association between the educational level of patients with epilepsy and COVID-19. However, patients with epilepsy may not experience aggravated seizures due to COVID-19. Further studies with larger sample sizes are needed to confirm these findings. Additionally, during the COVID-19 epidemic, patients with epilepsy who also suffer from anxiety and depression may experience an increase in the frequency of their seizures.

# **Ethical approval**

The study was approved by the Medical Ethics Committee of Qilu Hospital of Shandong University, and written informed consent was obtained from all patients.

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## **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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