

## FULL-LENGTH ORIGINAL RESEARCH

# Severe psychological distress among patients with epilepsy during the COVID-19 outbreak in southwest China

Xiaoting Hao<sup>1</sup>  | Dong Zhou<sup>1</sup>  | Zhe Li<sup>2</sup> | Guojun Zeng<sup>3</sup> | Nanya Hao<sup>1</sup> | Enzhi Li<sup>1,4</sup> | Wenjing Li<sup>4,5</sup> | Aiping Deng<sup>4,5</sup> | Mintao Lin<sup>6</sup> | Bo Yan<sup>1</sup> 

<sup>1</sup>Department of Neurology, West China Hospital, Sichuan University, Sichuan Province, Chengdu, China

<sup>2</sup>Mental Health Center, West China Hospital, Sichuan University, Sichuan Province, Chengdu, China

<sup>3</sup>Department of Vascular Surgery, West China Hospital, Sichuan University, Sichuan Province, Chengdu, China

<sup>4</sup>West China School of Nursing, Sichuan University, Sichuan Province, Chengdu, China

<sup>5</sup>Outpatient Department, West China Hospital, Sichuan University, Sichuan Province, Chengdu, China

<sup>6</sup>West China School of Medicine, Sichuan University, Sichuan Province, Chengdu, China

## Correspondence

Bo Yan, Department of Neurology, West China Hospital, Sichuan University, Chengdu 610000, Sichuan Province, China. Email: yanbo\_huaxi@126.com

## Funding information

National Key R&D Program of China, Grant/Award Number: 2017YFC0907705; The National Key R&D Program of China, Grant/Award Number: 2017YFC0907702

## Abstract

**Objective:** To compare the severity of psychological distress between patients with epilepsy and healthy controls during the COVID-19 outbreak in southwest China, as well as identify potential risk factors of severe psychological distress among patients with epilepsy.

**Methods:** This cross-sectional case-control study examined a consecutive sample of patients older than 15 years treated at the epilepsy center of West China Hospital between February 1 and February 29, 2020. As controls, sex- and age-matched healthy visitors of inpatients (unrelated to the patients) were also enrolled during the same period. Data on demographics and attention paid to COVID-19 were collected by online questionnaire, data on epilepsy features were collected from electronic medical records, and psychological distress was evaluated using the 6-item Kessler Psychological Distress Scale (K-6). Potential risk factors of severe psychological distress were identified using multivariate logistic regression.

**Results:** The 252 patients and 252 controls in this study were similar along all demographic variables except family income. Patients with epilepsy showed significantly higher K-6 scores than healthy controls and spent significantly more time following the COVID-19 outbreak (both  $P < .001$ ). Univariate analyses associated both diagnosis of drug-resistant epilepsy and time spent paying attention to COVID-19 with severe psychological distress (defined as K-6 score  $>12$ ; both  $P \leq .001$ ). Multivariate logistic regression identified two independent predictors of severe psychological distress: time spent paying attention to COVID-19 (odds ratio [OR] = 1.172, 95% confidence interval [CI] = 1.073-1.280) and diagnosis of drug-resistant epilepsy (OR = 0.283, 95% CI = 0.128-0.623).

**Significance:** During public health outbreaks, clinicians and caregivers should focus not only on seizure control but also on mental health of patients with epilepsy, especially those with drug-resistant epilepsy. K-6 scores  $>12$  indicate severe psychological distress. This may mean, for example, encouraging patients to engage in other activities instead of excessively following media coverage of the outbreak.

**KEYWORDS**

COVID-19, drug-resistant epilepsy, epilepsy, outbreak, psychological distress, stress status

## 1 | INTRODUCTION

Epilepsy is a common chronic neurological disorder.<sup>1</sup> Approximately 5 million people are diagnosed with epilepsy worldwide, and more than one-quarter of people with epilepsy have a mental disorder.<sup>2-4</sup> Suicide is at least three times more prevalent among patients with epilepsy than in the general population,<sup>5</sup> and mental illness is the strongest predictor of suicide among patients with epilepsy.<sup>6</sup> Mental illness comorbidity in epilepsy reduces quality of life, increases health care costs, lowers medication compliance, and worsens side effects from antiepilepsy drugs (AEDs).<sup>4,7,8</sup> Early identification of mental illness in patients with epilepsy can improve their management and prognosis, and the ability to recognize such psychiatric comorbidity is recognized as a key competency by the American Academy of Neurology and the International League Against Epilepsy (ILAE).<sup>9,10</sup>

Since the first reported case of coronavirus disease 2019 (2019-nCoV) in Wuhan, China on December 8, 2019,<sup>11</sup> which is caused by a novel coronavirus, first named 2019-nCoV<sup>12</sup> and renamed COVID-19 or SARS-CoV-2, the outbreak has spread around the world.<sup>13</sup> The lack of effective treatment and ease of infection through contact and aerosols has created mass panic in China and other countries. This situation can be likened to other major public health emergencies, such as the global SARS outbreak in 2003 and the Fukushima Daiichi nuclear power plant accident in 2011. These situations can threaten the mental health of affected populations, based on a World Health Organization assessment.<sup>14</sup> One problem is the flood of disaster-related information that can create anxiety and panic in the public. Although scientifically framed information can help people understand the developing situation,<sup>15</sup> excessive attention to media reports about disasters can increase risk of mental illness.<sup>16</sup>

The present study compared the severity of psychological distress between patients with epilepsy and healthy controls during the COVID-19 outbreak in southwest China. It also explored risk factors for severe psychological distress among patients with epilepsy, which we hypothesized might include demographic features, epilepsy characteristics, and attention paid to media coverage of the COVID-19 outbreak.

## 2 | MATERIALS AND METHODS

This is a cross-sectional case-control study. The study was conducted from February 1 to February 29, 2020 and asked respondents about the previous 30 days, approximately 1 month into the COVID-19 outbreak. This survey-based study

### Key Points

- Psychological distress is highly prevalent among patients with epilepsy during public health emergencies
- During such emergencies, patients with drug-resistant epilepsy are at elevated risk of severe psychological distress
- Spending less time paying attention to media coverage of public health emergencies is associated with lower psychological distress among patients
- Patients with K-6 scores > 12 suffer severe psychological distress and should consult a psychiatrist during the public health emergency

was approved by the ethics committee of Sichuan University, and participants gave informed consent.

### 2.1 | Participants and definitions

We invited a consecutive sample of patients treated at the Epilepsy Center of West China Hospital to participate. To be eligible, patients had to be at least 15 years old by February 1, 2020, they had to have been diagnosed with epilepsy at least 1 year before, and they had to be followed up monthly by an epilepsy specialist. Patients were excluded if their epilepsy showed psychogenic nonepileptic onset; they self-reported seizures within 48 hours before completing the questionnaires (see below); they had a history of mental retardation, alcohol or drug abuse, or uncontrolled psychosis; they changed the type or dosage of prescribed AEDs within 1 month before completing the questionnaires; or they were unable to read or understand the questionnaires.

In parallel, we invited a control group of healthy visitors of patients who were unrelated to those patients. Controls were age- and sex-matched to patients with epilepsy.

Epilepsy was diagnosed according to the revised 2014 definition of the ILAE, which stipulates (1) two unprovoked seizures >24 hours apart or (2) one unprovoked seizure and at least 60% probability of another unprovoked seizure in the following 10 years.<sup>17</sup> Seizures were defined according to the most recent definition from the ILAE.<sup>18</sup> Type of epilepsy was classified as idiopathic generalized, focal, or unknown.<sup>18</sup> Drug response was evaluated based on level 1 and level 2 outcomes for each AED, as defined by the ILAE. Data on

etiology, seizure characteristics, and any undetermined level 1 outcomes were collected for patients whose level 2 outcomes were classified as seizure-free, undefined, or drug-resistant.<sup>19</sup> Based on drug response, patients were classified as having drug-resistant epilepsy or not.

## 2.2 | Survey instruments

Enrolled participants were sent online questionnaires via WeChat and were asked to fill them out before February 29, 2020.

### 2.2.1 | Questionnaire on demographics, clinical data, epidemiological contact history, and concern and attention to the COVID-19 outbreak

This questionnaire was custom-designed for this study to collect information about age, sex, education level, financial circumstances, and family members. Respondents were also asked about their level of concern over the COVID-19 outbreak (on a 5-point scale from “very unconcerned” to “very concerned”), and the time they spent each day receiving information about the outbreak. Data on medical history (including mental illness history, seizure and epilepsy type, and treatment history) were collected from electronic clinical records in the West China Hospital outpatient department. Respondents were asked to self-identify as unemployed, employed, or retired.

### 2.2.2 | Six-item Kessler Psychological Distress Scale

The 6-item Kessler Psychological Distress Scale (K-6) has been validated to assess nonspecific psychological distress during the past month, including symptoms of anxiety and depression,<sup>20,21</sup> and it has been used to screen for psychological distress.<sup>22–24</sup> The Mandarin version was validated in the World Mental Health Survey,<sup>25</sup> and it has been used to screen for severe psychological distress in China.<sup>22,26–28</sup> On this questionnaire, participants respond on a 5-point Likert scale, and responses are scored from 0 to 4. Individual scores are summed to obtain total scores of 0–24.<sup>20</sup> We defined severe psychological distress as a total score > 12.<sup>22</sup>

## 2.3 | Statistical analysis

Statistical analysis was performed using SPSS 25.0 (IBM). Categorical variables were reported as numbers

and percentages; continuous variables, as mean and standard deviation. Intergroup differences were assessed for significance using Student *t* test and chi-squared test. K-6 scores showed a skewed distribution, so they were compared between groups using the rank sum test. Multivariate logistic regression was used to explore factors independently associated with severe psychological distress in patients with epilepsy. The multivariate model contained variables that were associated with  $P < .1$  in univariate analysis.

## 3 | RESULTS

Of the 309 patients with epilepsy invited to participate, 20 (32%) were excluded because they were younger than 15 years, 14 (23%) because they refused to participate, and 23 (37%) because they changed AED type and/or dosage during the previous month. In the end, 252 patients with epilepsy were enrolled, together with the same number of healthy controls. Most patients (81%) had focal epilepsy, whereas 14% had generalized epilepsy; the temporal lobe was involved in 26 (10.3%) of patients. Epilepsy was drug-resistant in 93 (36.9%) patients.

Patients and controls showed no significant differences in marriage status, education level, or history of mental illness (Table 1). Patients reported significantly lower family income than controls.

### 3.1 | Attention and concern about the COVID-19 outbreak

Patients reported significantly greater concern about the outbreak than controls, and they spent significantly longer per day following media reports of the outbreak (Table 1). A similar number of controls and patients reported close contact with confirmed COVID-19 cases. Significantly fewer patients than controls reported living in communities containing confirmed cases.

### 3.2 | Psychological distress

Patients with epilepsy had significantly higher K-6 scores than healthy controls (Table 2), including for the items about feeling “nervous,” “hopeless,” “restless or fidgety,” “so depressed that nothing could cheer you up,” and “everything is an effort.” In contrast, the two groups scored similarly on the item about “feeling worthless.” The proportion of patients who scored >12 (13%), defined as severe psychological distress, was significantly greater than the corresponding proportion of controls (<2%).

**TABLE 1** Clinico-demographic characteristics of participants

Characteristic	Patients with epilepsy, n = 252	Healthy controls, n = 252	P
Male	120 (47.6)	120 (47.6)	1.0
Age, y	29.3 ± 11.6	29.4 ± 11.5	.982
Married	115 (45.6)	103 (40.9)	.323
Education level			
≤12 y	118 (46.8)	133 (52.8)	.212
>12 y	134 (53.2)	119 (47.2)	
Mental illness history	14 (5.6)	6 (2.4)	.108
Family monthly income in RMB <sup>a</sup>			
0-4999	116 (46.0)	87 (34.5)	.022
5000-9999	80 (31.7)	78 (31.0)	
10 000-14 999	35 (13.9)	49 (19.4)	
15 000-19 999	9 (3.6)	16 (6.3)	
≥20 000	12 (4.8)	22 (8.7)	
Seizures in previous 30 d			
None	164 (65.0)		
≤4	57 (22.6)		
>4	29 (3.6)		
Epilepsy type			
Generalized	35 (13.8)		
Focal	203 (80.6)		
Unclassified	14 (5.6)		
Temporal lobe epilepsy	26 (10.3)		
Drug-resistant epilepsy	93 (36.9)		
Total number of antiepilepsy drugs	2 (8, 0)		
History of epidemiological contact <sup>b</sup>	3 (1.2)	5 (2.0)	.724
COVID-19 cases in respondent's residential community	35 (13.9)	58 (23.0)	.008
Level of concern about COVID-19 outbreak			
Very concerned	100 (39.7)	68 (27.0)	.015
Concerned	85 (33.7)	94 (37.3)	
Average	54 (21.4)	79 (31.3)	
Relatively unconcerned	7 (2.8)	8 (3.2)	
Very unconcerned	6 (2.4)	3 (1.2)	
Time spent paying attention to outbreak, h/d	2.34 ± 3.165	1.45 ± 2.114	<.001

Note: Values are n (%), mean ± SD, or median (maximum, minimum).

Abbreviation: RMB, renminbi.

<sup>a</sup>1 RMB = 0.143 US dollars as of February 29, 2020.

<sup>b</sup>History of epidemiological contact means close contact with confirmed patients.

### 3.3 | Factors associated with severe psychological distress

Univariate analyses showed that of all variables examined as potential risk factors of K-6 score > 12, only diagnosis of drug-resistant epilepsy and time spent following media

reports of the COVID-19 outbreak were significantly associated with severe psychological distress (Table 3). Both associations remained significant in multivariate logistic regression, with respective odds ratios of 0.283 (95% confidence interval [CI] = 0.128-0.623) and 1.172 (95% CI = 1.073-1.280; Table 4).

K-6 item	Patients with epilepsy	Healthy controls	P
Nervous	1 (2, 1)	1 (1, 0)	<.001
Hopeless	0 (1, 0)	0 (0, 0)	<.001
Restless or fidgety	1 (2, 0)	1 (1, 0)	<.001
So depressed that nothing could cheer you up	1 (2, 0)	0 (1, 0)	<.001
Everything is an effort	1 (1, 0)	0 (1, 0)	<.001
Worthless	0 (1, 0)	0 (1, 0)	.126
Total score	5 (8.75, 2)	2 (5, 1)	<.001
Severe psychological distress	33 (13.1)	4 (1.6)	<.001

Note: Values are median (maximum, minimum) or n (%).

Abbreviation: K-6, 6-item Kessler Psychological Distress Scale.

**TABLE 3** Exploration of factors associated with severe psychological distress (K-6 score > 12) among patients with epilepsy

Factor	Odds ratio (95% CI)	P
Sex	0.786 (0.375-1.645)	.552
Mean age	0.987 (0.954-1.022)	.467
Marriage	1.341 (0.635-2.831)	.441
Education level	1.428 (0.685-2.978)	.342
Mental illness history	0.529 (0.139-2.005)	.349
Temporal lobe epilepsy	0.452 (0.167-1.226)	.119
Drug-resistant epilepsy	0.280 (0.130-0.600)	.001
Seizures in previous 30 d		
≤4	0.473 (0.170-1.315)	.151
> 4	0.719 (0.228-2.262)	.572
Multiple AEDs	0.514 (0.514-1.193)	.121
Seizure in previous 30 d	1.737 (0.828-3.646)	.144
COVID-19 cases in respondent's residential community	1.837 (0.729-4.627)	.197
Daily time spent on COVID-19 outbreak	1.172 (1.073-1.280)	<.001

Note: Reference conditions for odds ratio calculations: female, unmarried, <12 y of education, no mental illness history, non-temporal lobe epilepsy, non-drug-resistant epilepsy, no seizure, single AED, seizure-free in previous 30 d, no COVID-19 cases in respondent's residential community.

Abbreviations: AED, antiepilepsy drug; CI, confidence interval.

## 4 | DISCUSSION

This study describes the mental health status of patients with epilepsy in southwest China during the COVID-19 outbreak, compares it with the status of healthy controls from the same region, and explores risk factors for severe psychological distress. This is the first study, to our knowledge, that investigates factors that may influence mental health status of patients with epilepsy during a global public health emergency.

**TABLE 2** Scores of participants on the K-6

**TABLE 4** Multivariate logistic regression to identify independent predictors of severe psychological distress (6-item Kessler Psychological Distress Scale score ≥ 12) in patients with epilepsy

Predictor	OR	95% CI	P
Time spent daily on COVID-19 outbreak	1.172	1.073-1.280	.001
Drug-resistant epilepsy <sup>a</sup>	0.283	0.128-0.623	.002

Abbreviations: CI, confidence interval; OR, odds ratio.

<sup>a</sup>Reference conditions for OR calculations: non-drug-resistant epilepsy

### 4.1 | Significantly higher psychological distress in patients than controls during an international public health emergency

After excluding individuals with psychosis, we found a significantly higher level of psychological distress among patients with epilepsy than controls. Less than 2% of our control group reported severe psychological distress, defined as a K-6 score > 12, which is consistent with the 3% prevalence of mental health problems reported for healthy individuals in Japan in the absence of an international disaster.<sup>29</sup> More than 13% of our patients showed severe psychological distress during the COVID-19 outbreak, and this result supports the finding that patients with epilepsy are at high risk for mental disease.<sup>4,30-32</sup> Although only one of our patients had been diagnosed with COVID-19 at the time of the survey, patients' psychological distress level was similar to that of evacuees from the Fukushima Daiichi nuclear power plant accident in 2011.<sup>33</sup> Our results are consistent with previous work suggesting high prevalence of mental health problems among individuals with epilepsy.<sup>31</sup> Although a small proportion of patients reported living in communities with COVID-19 cases, their psychological distress was similar to that of evacuees from the Fukushima Daiichi nuclear power plant accident in Japan.<sup>29</sup>



## 4.2 | Factors related to severe psychological distress in patients with epilepsy during an international public health emergency

We found that a diagnosis of drug-resistant epilepsy and amount of time spent daily on media coverage of the COVID-19 outbreak were associated with severe psychological distress among patients with epilepsy during the outbreak. Our results contrast with meta-analyses suggesting no relationship between drug-resistant epilepsy and severe psychological distress<sup>3,34,35</sup> in the absence of an international public health emergency. This discrepancy may mean that individuals with drug-resistant epilepsy are particularly vulnerable to stress induced by such an emergency.

Another risk factor for severe psychological distress among our patients was time spent paying attention to the COVID-19 outbreak. The outbreak gripped China during the western New Year as well as the traditional Chinese Spring Festival, which was extended for disease control. The government banned all celebrations and closed businesses and sources of public entertainment. At the same time, media reports on the internet, television, and newspapers continuously provided outbreak information.<sup>15</sup> It is not surprising that this situation should contribute to greater psychological distress among patients with epilepsy. A previous study of university undergraduates found that excessive dependence on information obtained from smartphones can significantly increase risk of mental illness.<sup>36</sup> Likely the same was true among our patients. Our results suggest that encouraging patients with epilepsy to cultivate hobbies and providing them with online learning opportunities may help protect them from severe psychological distress during public health emergencies.

None of the other clinicodemographic variables in our study showed a significant association with risk of severe psychological distress, including sex and mental illness history, similar to previous work.<sup>37</sup> Seizure frequency also did not relate to the increased risk in our study. Although results from the general public suggested that stress would increase the risk of epileptogenesis, especially in childhood,<sup>38</sup> the relationship between seizure onset of patients with epilepsy and stress was evaluated through different methods. The different results may come from potential confounders between stress and mental status,<sup>39</sup> such as bad habits under pressure, and patients' use of a stress reduction method if they feel stress triggers their seizures.<sup>40</sup> Whether our patients received multi- or monotherapy also did not influence this risk, consistent with the reported lack of association between multi- or monotherapy and prevalence of depression or anxiety among patients with epilepsy.<sup>3</sup> Temporal lobe epilepsy was not a risk factor for severe psychological distress in our study, in contrast to previous work<sup>41</sup>; this difference may reflect that our patients, but not those in the previous study, were exposed to

an international public health emergency. Future study should examine under what conditions temporal lobe epilepsy is associated with mental disorders.

## 4.3 | Limitations of the study

Because the epidemic was widespread, we did not analyze potential relationships of psychological distress with distance from the epicenter of the epidemic. Such a relationship has been shown for earthquake survivors.<sup>29</sup> We found that a significantly higher proportion of controls than patients reported living in communities with COVID-19 cases, yet their psychological stress was lower. Future work should examine the potential influence of "closeness to outbreak" on psychological distress. Psychological distress and time spent daily paying attention to the outbreak were based on self-report, which may increase risk of bias. Our results should be verified and extended in larger patient samples.

## 5 | CONCLUSIONS

During public health outbreaks, health care professionals should focus not only on seizure control but also on the mental health of patients with epilepsy, especially those with drug-resistant disease. They should advise patients not to pay too much time on media coverage of the outbreak, such as by distracting themselves with other activities. Patients with K-6 scores > 12 should be regarded as suffering from severe psychological distress and should consult a psychiatrist.

## ACKNOWLEDGMENTS

This work was funded by the National Key R&D Program of China (2017YFC0907702 and 2017YFC0907705).

## CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## ORCID

Xiaoting Hao  <https://orcid.org/0000-0002-0372-1634>

Dong Zhou  <https://orcid.org/0000-0001-5096-7023>

Bo Yan  <https://orcid.org/0000-0001-5767-2535>

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**How to cite this article:** Hao X, Zhou D, Li Z, et al. Severe psychological distress among patients with epilepsy during the COVID-19 outbreak in southwest China. *Epilepsia*. 2020;61:1166–1173. <https://doi.org/10.1111/epi.16544>