Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.9321-22
Intern Med 61: 2287-2293, 2022
http://internmed.jp

【 ORIGINAL ARTICLE 】

Seizure Control in Patients with Epilepsy during the COVID-19 Pandemic: A Systematic Review and Meta-analysis

Naoto Kuroda[1,2], Prasannakumar Kanubhai Gajera[3], Hongxuyang Yu[4] and Takafumi Kubota[5]

Abstract:

Objective To investigate seizure control in patients with epilepsy during the coronavirus disease 2019 (COVID-19) pandemic.

Method A systematic review and meta-analysis was conducted, and the MEDLINE, EMBASE, CENTRAL, and ClinicalTrials.gov databases were comprehensively searched for relevant studies. Studies that reported seizure control in patients with epilepsy during the COVID-19 pandemic were included. Pooled proportions with 95% confidence intervals (CIs) of patients with epilepsy who experienced seizure worsening during the COVID-19 pandemic were assessed using a random-effects model. The quality of the assessment for each study, heterogeneity between the studies, and publication bias were also evaluated. Subgroup analyses were performed, excluding studies with reports of seizures worsening from caregivers.

Results A total of 24 studies with 6,492 patients/caregivers were included in the meta-analysis. The pooled proportion of seizure worsening was 18.5% (95% CI: 13.9-23.6; I^2=96%; p<0.01). The pooled proportion of seizure worsening in the subgroup analysis was 18.9% (95% CI: 13.5-25.0; I^2=96%; p<0.01).

Conclusion Although the heterogeneity was high, our results showed a relatively high incidence of seizure worsening during the COVID-19 pandemic. During the COVID-19 pandemic, physicians should be aware of the likelihood of worsening seizures in patients with epilepsy.

Key words: epilepsy, COVID-19, seizure, novel coronavirus disease

(Intern Med 61: 2287-2293, 2022)
(DOI: 10.2169/internalmedicine.9321-22)

Introduction

Coronavirus disease 2019 (COVID-19) is a novel infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This disease represents one of the most significant pandemics in human history (1).

Epilepsy, a disease characterized by the spontaneous recurrence of unprovoked seizures, is one of the most common chronic neurological conditions. The prevalence of this pathology is reported to be 0.7-1.0%, with a particularly high incidence among elderly individuals and children (2).

It is important to consider the relationship between epilepsy and COVID-19, and we have discussed this in a previous study (3). In a previous review, we summarized articles that reported seizure worsening during the COVID-19 pandemic. However, the proportion of changes in seizure control varied across studies. In addition, a comprehensive and quantitative analysis of the findings of these studies has not been conducted.

Therefore, to clarify the proportion of patients who experienced seizure worsening during the COVID-19 crisis, we systematically and quantitatively investigated seizure control in patients with epilepsy during the COVID-19 pandemic.

[1]Department of Pediatrics, Wayne State University, USA, [2]Department of Epileptology, Tohoku University Graduate School of Medicine, Japan, [3]Department of Neurology, Reading Hospital, Tower Health, USA, [4]Department of Neurology, West Virginia University, USA and [5]Department of Neurology, Tohoku University Graduate School of Medicine, Japan
Received: January 1, 2022; Accepted: April 11, 2022; Advance Publication by J-STAGE: May 31, 2022
Correspondence to Dr. Naoto Kuroda, naoto.kuroda@wayne.edu

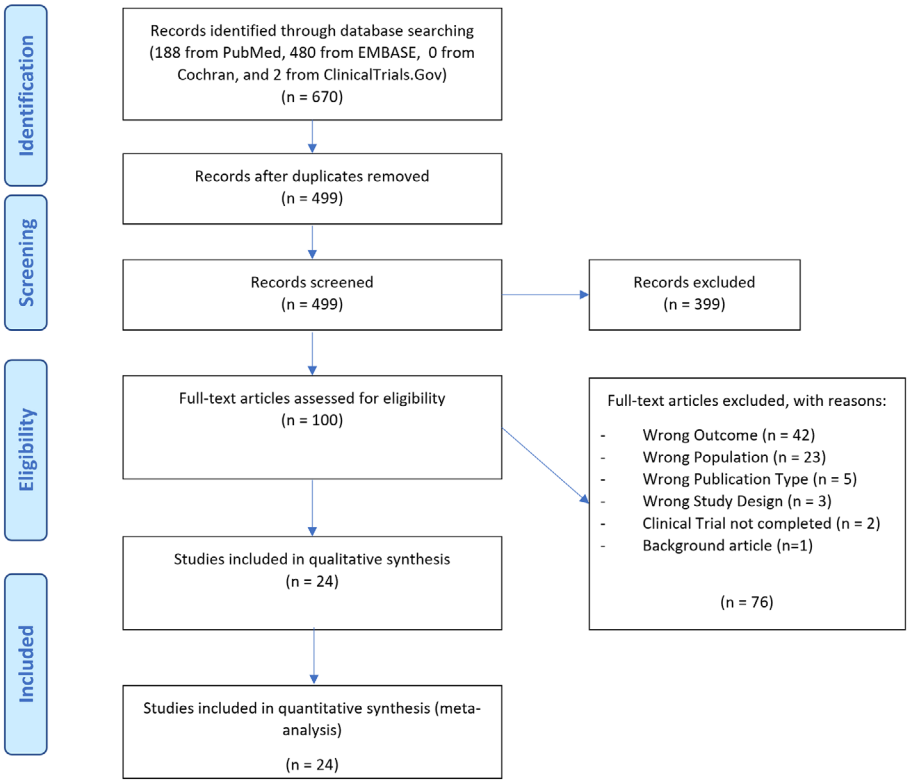

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram of this study.

Materials and Methods

Searching strategy

This study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (4). This review protocol has not been registered previously. The following databases were searched systematically up to February 13, 2021: MEDLINE (accessed from PubMed), EMBASE, CENTRAL (accessed from the Cochrane library), and ClinicalTrials.gov. In PubMed, the following key words were searched: ["Epilepsy" (MeSH Terms) OR "Epilepsy" (Title/Abstract) OR "seizure disorder" (Title/Abstract)] AND ["COVID-19"(MeSH Terms) OR "SARS-CoV-2" (MeSH Terms) OR "COVID-19" (Title/Abstract) OR "2019 ncov infection" (Title/Abstract) OR "SARS-CoV-2" (Title/Abstract) OR "2019 novel coronavirus" (Title/Abstract)]. In the EMBASE database, the following key words were searched: ("Epilepsy"/exp OR Epilepsy:ti,ab OR "seizure disorder":ti,ab) AND ("COVID-19"/exp OR "SARS-CoV-2"/exp OR COVID-19:ti,ab OR "2019 ncov infection":ti,ab OR SARS-CoV-2:ti,ab OR "2019 novel coronavirus":ti,ab). The following keywords were searched in the Cochrane library: [(mh Epilepsy) OR Epilepsy:ti,ab OR "seizure disorder":ti,ab] AND [(mh COVID-19) OR (mh SARS-CoV-2) OR COVID-19:ti,ab OR "2019 ncov infection":ti,ab OR SARS-CoV-2:ti,ab OR "2019 novel coronavirus":ti,ab]. We also used ClinicalTrials.gov to search for unpublished, ongoing, terminated, or completed studies to avoid publication bias. In ClinicalTrials.gov, the following keywords were searched: (Epilepsy OR Seizure disorder) AND (COVID-19 OR 2019-nCoV Infection OR SARS-CoV-2 OR 2019 Novel Coronavirus). We screened the reference lists of all relevant articles for additional data.

Inclusion and exclusion criteria

Studies were included based on the following criteria: 1) studies that reported data on changes in seizure frequency in patients with epilepsy during the COVID-19 pandemic; and 2) studies from which the incidence proportion of seizure worsening in patients with epilepsy during the COVID-19 pandemic could be calculated. We excluded studies with the following criteria: 1) studies that were not yet recruiting, were currently recruiting, or had been withdrawn according to Clinical.Trials.gov; 2) studies that reported on patients diagnosed with psychogenic non-epileptic seizures; 3) case reports; and 4) studies written in languages other than English.

We defined seizure worsening as increased seizures, new types of seizure, prolonged seizures, or seizures resistant to rescue medications. Studies with outcomes reported by patients, caregivers, or physicians were included. Any type of outcome measured by a questionnaire, survey, or the presence of consultation was accepted. We excluded studies that reported only the mean±standard deviation of seizure frequency because we could not calculate the incidence proportion.

Table 1. Summary of the Findings.

Reference	Country	Study design	Study period	Number of participants	Age (SD or IQR)	Female sex	Quality score	Definition of seizure worsening	Proportion of seizure worsening
(10)	Kuwait	QS	August 1 to August 10, 2020	151 PwE	31.11±11.69	64.9 %	2	SF	35/151
(11)	Spain	QS	April 7 to April 11, 2020	277 care givers of genetic epilepsy (38.60%) and non-genetic epilepsy (61.40%)	12.4	58.1 %	2	SF	39/277
(12)	Saudi Arabia	QS	Month of April 2020	156 PwE	Less than 20: 23 (14.7%), 20-40: 104 (66.7%), 40-60: 24 (15.4%), more than 60: 5 (3.2%)	62.2 %	3	SF	46/156
(13)	Iran	QS	March 27 to March 30, 2020	Phone call interviews of 100 PwE, random selected	32±13	47 %	2	SF	6/100
(14)	Italy	QS	April 11 to April 16, 2020	456 PwE	37.9±12.5	78 %	3	SF	82/456
(15)	Italy	QS	March 9 to April 30, 2020	189 PwE	Median 45 (33-57)	103 (54.5%)	3	SF	10/189
(16)	Spain	QS	N.D.	341 responded (out of 627)		181 (58.0%)	1	SF	40/341
(17)	Spain	QS	March 16 to April 14, 2020	255 PwE	48.2±19.8	121 (47.5%)	2	SF	25/255
(18)	Turkey	QS	During the pandemic declared in the country	110 PwE	32 (18-65)	62 (56.4)	2	SF	7/110
(19)	China	QS	February 23 and March 5, 2020	362 PwE (response rate 63.51%)	10-19 years 112 (30.94%) 20-60 years 244 (67.40%) ≥60 years 6 (1.66%)	166 (45.86%)	2	SF	31/362
(20)	Italy	QS	April 11 to April 16, 2020	427 PwE+452 PwoE=879	38.6±11.8 years	327 (76.58%)	2	SF	67/427
(21)	USA	QS	March 27 to March 30, 2020	94 PwE	36 (19-88)	47 (50%)	3	SF	33/94
(22)	Europe, South America, and Canada	QS	July 26 and December 3, 2020	407 PwE (337 patients and 70 caretakers)	34.52±14.03	304 (74.7%)	2	SF	122/407
(23)	Italy	QS	N.D.	222 PwE (157 patients and 65 caregivers)	43.5 (18-84)	128 (57.7%)	2	SF	14/222
(24)	Lithuania	QS	March 16, 2020 to June 16, 2020	143 PwE (94 in person+49 online)	35.1±13.4	84 (58.7%)	2	SF	22/143
(25)	India	QS	October 5 to October 15, 2020	325 PwE out of 600 completed the survey	26.4±12.3 (1-70)	132 (40.6%)	3	SF	22/325
(26)	UK	QS	May and June 2020	71 young PwE+130 via care givers	20.76±3.48 & 8.88±5.15	61 (86%) & 64 (49%)	1	SF	62/201
(27)	USA	QS	March 1, 2020 and May 31, 2020	177 PwE (183 which were 27% of eligible subjects completed the survey - 6 did not answer the questions of seizure control)	47 (range: 21-79)	120 (67.8%)	2	SF	133/177
(28)	Iran	QS	N.D.	141 PwE & 759 PwoE	36.01±19.78 (including PwoE)	55.4% (including PwoE)	2	SF	32/141
(29)	Pakistan	QS	July 13 and July 24, 2020,	213 caregivers of pediatric patients with active epilepsy	1-5, 87 (40.8) 6-10, 83 (39.0) 11-15 39, (18.3) 16-20, 4 (1.9)	128 (60.1%)	3	SF	57/213
(30)	Spain	QS	May 17 and June 7, 2020	100 PwE	42.4±16.4	52 (52%)	2	SF	29/100
(31)	China	QS	February 1 to March 31, 2020 (model time)	118 PwE (78.7% completed the survey)	27 (21.3-36.8)	64 (54.2%)	3	SF	34/118
(32)	Rome	QS	May 8 to May 31, 2020	3,321 parents of PwE (response rate: 50%)	0-1 year: 72 (2.2), 2-5 years: 529 (15.9), 6-12 years: 1,394 (41.9), 13-18 years: 746 (22.5), >18 years: 580 (17.5)	1,580 (47.6%)	1	SF	184/1,387
(33)	Sri Lanka	QS	N.D.	140 caregivers of children with epilepsy	7.87 years (SD 4.0)	N.D.	3	SF	17/140

IQR: interquartile range, N.D.: not described, QS: questionnaire survey, PwE: people/patients with epilepsy, PwoE: people without epilepsy, SD: standard deviation, SF: self-reported or reported by caregivers

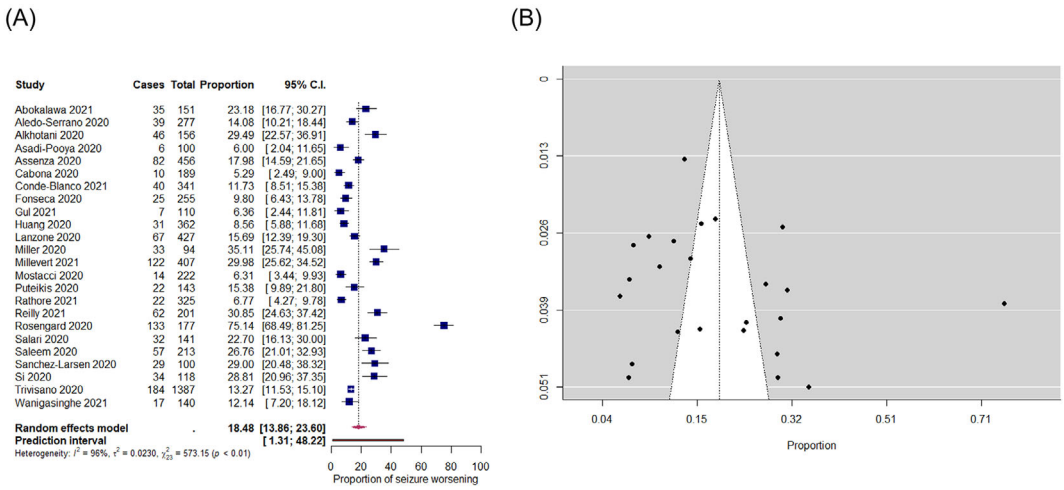

Figure 2. Results of the meta-analysis for seizure worsening in patients with epilepsy during the COVID-19 pandemic. (A) A random-effects meta-analysis of the pooled proportion and forest plot of the meta-analysis; (B) Funnel plot of the meta-analysis. COVID-19: coronavirus disease 2019, CI: confidence interval

To assess the quality of the included articles, we scored the level of risk of bias using the risk of bias instrument for cross-sectional surveys of attitudes and practices contributed by the CLARITY group at McMaster University (5). Any disagreements or discrepancies between the reviewers regarding outcomes were resolved through discussion.

Data extraction and outcome measurements

Two reviewers (PG and HY) independently screened the titles and abstracts and evaluated the full texts of the selected articles. The risk of bias was independently assessed. Any disagreements were resolved by a third reviewer (TK). The following variables were extracted: author, publication year, the country in which the study was conducted, study period, participants, study design, age, proportion of females, definition of seizure worsening, and proportion of seizure worsening. We also extracted independent risk factors for seizure worsening identified by the multivariate analysis and their odds ratios (ORs).

Statistical analyses

In this systematic review and meta-analysis, we used a single-arm analysis. For categorical variables, percentages, means, and standard deviations were calculated. We used random-effects models with the DerSimonian-Laird estimator to consider the variance between and among the studies. We calculated the pooled proportions using the variance-stabilized Freeman-Tukey double arcsine transformation. Confidence intervals (CIs) for individual studies were computed using the Wilson score CI method, with adjusting for continuity. The I^2 statistic and Cochran Q test were used to indicate heterogeneity between the studies. For the I^2 statistic, $0\% \leq I^2 < 25\%$, $25\% \leq I^2 < 50\%$, $50\% \leq I^2 < 75\%$, and $\geq 75\%$ were considered very low, low, moderate, and high heterogeneity, respectively (6). For the Cochran Q test, $p<0.10$ was considered as severe heterogeneity (7, 8). Publication bias was assessed using a funnel plot and Egger's test, which is a quantitative analysis of asymmetry in the funnel plot. For Egger's test, $p<0.10$ was considered to indicate significant publication bias (8, 9). We did not assess publication bias for outcomes reported in fewer than 10 studies. We conducted statistical analyses using the R software program (version 3.6.2; R Development Core Team 2019), with meta version 4.15-0 and metaphor version 2.4-0.

Subgroup analyses

Subgroup analyses were conducted to investigate potential explanatory variables of heterogeneity, excluding studies that included reports from caregivers of patients with epilepsy.

Results

Summary of reviewed articles

The selection process is illustrated in Fig. 1. A total of 670 studies were retrieved (188 studies from MEDLINE, 480 studies from EMBASE, 0 studies from CENTRAL, and 2 studies from ClinicalTrials.gov) up to February 13, 2021. After removing duplicates and screening the titles and abstracts, 100 studies were identified. The full-text screening of these studies led to the exclusion of 76 studies that did not meet the inclusion criteria. A total of 24 studies with 6,492 patients/caregivers fulfilled the eligibility criteria for inclusion in the meta-analysis (10-33). Table 1 summarizes the findings of the included studies. The mean score for the quality of 24 studies based on the questionnaire survey was 2.2 out of 5 (Table 1, Supplementary material 1).

The pooled proportion of seizure worsening was 18.5% (95% CI: 13.9-23.6); I^2=96%; p<0.01) (Fig. 2). Publication bias was examined using a funnel plot and Egger's test (Fig. 2). There was no significant publication bias (p=0.29). We have summarized the reported independent risk factors

Table 2. Reported Independent Risk Factors Identified by the Multivariate Analysis and Their ORs.

Reference	Factor	OR	95% CI
(10)	Full-time job	0.61	0.15-2.47
	Part-time job	0.33	0.05-2.13
	Student	0.56	0.15-2.05
	Not working/retired	1.78	1.25-2.54
	VNS	2.54	0.47-13.68
	Less than 3 months (time of the last seizure before the pandemic)	0.22	0.10-0.50
	More than 3 months (time of the last seizure before the pandemic)	0	-
	Less than 3 months (last medical review before the pandemic)	0.96	0.34-2.72
	Three months or earlier (last medical review before the pandemic)	0	-
	Shortage of ASMs	0.17	0.22-1.34
	No depression	3.13	0.81-12.02
	Mild depression	0.97	0.24-4.00
	Moderate depression	1.33	0.31-5.67
	Severe depression	0.93	0.27-3.18
	Extremely severe depression	0	-
	Impaired sleep during the pandemic	2.89	1.25-6.7
	No feeling of stress	2.8	0.9-8.7
	A mild feeling of stress	1.75	0.55-5.61
	A moderate feeling of stress	1.01	0.72-1.81
	A severe feeling of stress	1.66	1.20-2.27
	Extremely feeling of stress	0	-
	Concern about shortage of medications	3.87	1.37-9.09
	Concern to get COVID-19 infection	3.08	1.23-7.73
	Concern about seizure worsening	1.19	0.41-2.41
(14)	Number of ASM	1.58	1.12-2.2
	PSQI	1.2	1.1-1.3
(17)	Tumor-related etiology	7.36	2.17-24.96
	Drug-resistant epilepsy	3.26	1.09-9.74
	Insomnia	3.65	1.21-10.95
(18)	Seizure frequency	0.958	0.198-4.619
	Number of ASM	8.941	1.905-41.961
	Duration of illness	1.046	0.97-1.128
	Lack of access to medication	25.75	0.095-6986
(19)	Exposure history to COVID-19	3.953	1.713-9.122
	Uncontrolled seizure after ASM therapy	4.656	1.268-17.092
	Two or more seizures per month before the outbreak	2.245	1.275-3.952
	Increased drug regimen during the outbreak	9.49	0.712-126.529
	Reduction/withdrawal/replacement/skipping of ASMs	5.417	1.848-15.886
	Moderate-to-critical worries about the adverse effect of the outbreak on overall seizure-related issues	2.539	1.053-6.124
(23)	Reported psychiatric condition and/or medication	12.59	4.06-38.99
	Sleep disorders	8.41	2.31-30.70
	Problems with limited access to healthcare	4.71	1.34-16.56
	Experiencing at least one seizure after 2/23	4.51	1.51-13.47
(24)	Baseline seizure frequency	1.51	1.04-2.20
	Reported physical health (before lockdown)	0.63	0.414-0.959
	Reported physical health (during lockdown)	0.98	0.749-1.647
	Reported mental health (before lockdown)	1.11	0.749-1.647
	Reported mental health (during lockdown)	0.926	0.647-1.326
	Reported stress during lockdown	1.18	0.888-1.578
	Ease of appropriate ASM use	0.586	0.401-0.856
	GAD-7	1.014	0.922-1.151
(30)	Experiencing higher stress/anxiety	5.78	1.57-21.18
	Having a prior higher seizure frequency	12.14	2.6-56.74

ASM: antiseizure medication, CI: confidence interval, COVID-19: coronavirus disease 2019, GAD-7: General Anxiety Disorder-7, OR: odds ratio, PSQI: Pittsburgh Sleep Quality Index, VNS: vagus nerve stimulation

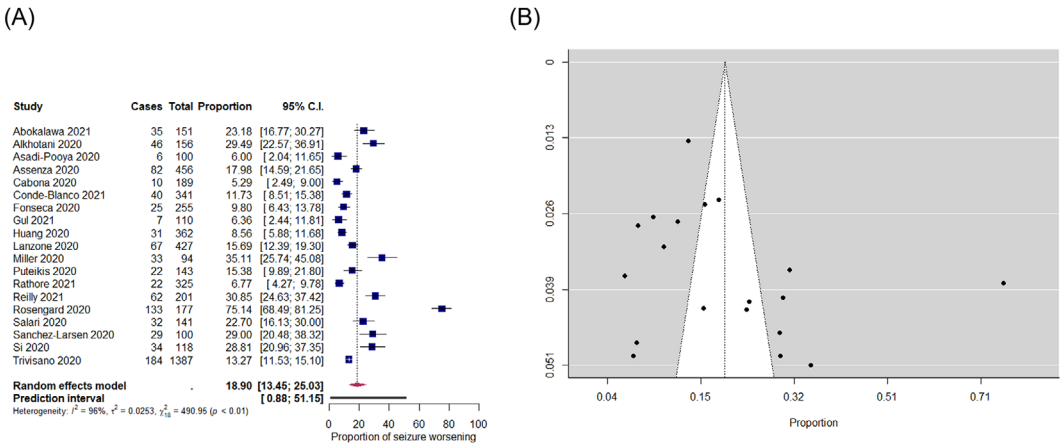

Figure 3. **Results of the subgroup meta-analysis excluding studies that included a report from caregivers of patients with epilepsy. (A) A random-effects meta-analysis of the pooled proportion and forest plot of the meta-analysis; (B) Funnel plot of the meta-analysis. CI: confidence interval**

for seizure worsening and their ORs in Table 2.

Results of the subgroup analysis

Subgroup analysis for each outcome with the removal of studies that included reports from caregivers of patients with epilepsy still had high heterogeneity (I^2=96%, p<0.01) (Fig. 3), with a pooled response proportion of 18.9% (95% CI: 13.5-25.0) (Fig. 3). Publication bias was examined using a funnel plot and Egger's test (Fig. 3). There was no significant publication bias (p=0.21).

Discussion

This systematic review and meta-analysis including 24 studies showed that the incidence of seizure worsening during the COVID-19 pandemic was 18.5%. The possible causes of worsening seizure control included infection with SARS-CoV-2, stress due to limited social activity, lifestyle changes, and a lack of necessary medical intervention due to limited access to medical facilities. As shown in Table 2, stress due to limited social activities, lifestyle changes, and the lack of necessary medical intervention due to limited access to medical facilities are reported as risk factors for seizure worsening. Among these risk factors, limited access to medical facilities can be improved by promoting telemedicine (34). Wearable device/smartphone applications for monitoring or prescription of rescue doses of antiseizure medications for patients with these risk factors might also be helpful. In addition, Table 2 shows that people taking multiple antiseizure medications or those with poor seizure control are more likely to be vulnerable to the impact of the COVID-19 pandemic than others. This is probably because patients with severe epilepsy are more vulnerable to stress during the COVID-19 pandemic than others (35).

A previous study reported that 28 of 227 cases (12.3%) experienced seizure worsening during the SARS outbreak, which is an infectious disease that spread in 2003 (36). In addition, 49 patients (21.6%) did not receive antiseizure medications due to loss of contact with medical care providers (36). Of note, the proportion of people with increased seizures due to COVID-19 was higher than that of people with increased seizures due to the SARS outbreak (SARS: 12.3% vs. COVID-19: 18.5%). This suggests that COVID-19 not only has a larger area of prevalence than SARS but also a greater impact on each person, such as patients with epilepsy. In addition, the prolonged duration of the pandemic, unlike SARS in 2003, may have contributed to the increase in seizures.

As a limitation, the heterogeneity in the meta-analysis was very high (I^2=96%). We performed subgroup analyses after excluding studies that included reporting by caregivers. This is because seizure worsening reported by caregivers may include the fact that home confinement during lockdown resulted in caregivers conducting observations more carefully (detection bias). However, even in the subgroup analysis by participants or validity of the measurement, the heterogeneity did not improve. These results indicate that the incidence of seizure worsening may vary greatly by study geography, such as the country or region where the study was conducted, the study period, and the condition of the disease, such as the severity of epilepsy or the presence of complications.

Conclusion

We investigated seizure worsening in patients with epilepsy during the COVID-19 pandemic by performing a systematic review and meta-analysis. Although the heterogeneity was high, our results showed a relatively high incidence of seizure worsening. During the COVID-19 pandemic, physicians need to be aware of the worsening of seizures in patients with epilepsy.

The authors state that they have no Conflict of Interest (COI).

Financial Support

This work was supported by Internal Regulations on Tohoku University Advanced Graduate School Pioneering Research Support Project for PhD Students (grant number J210002127).

References

1. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med **382**: 1708-1720, 2020.
2. Fiest KM, Sauro KM, Wiebe S, et al. Prevalence and incidence of epilepsy: a systematic review and meta-analysis of international studies. Neurology **88**: 296-303, 2017.
3. Kuroda N. Epilepsy and COVID-19: updated evidence and narrative review. Epilepsy Behav **116**: 107785, 2021.
4. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemol **62**: e1-e34, 2009.
5. Distiller SR. Risk of bias instrument for cross-sectional survey of attitudes and practices [Internet]. 2021 [cited 2021 Jun 5]. Available from: https://www.evidencepartners.com/resources/methodological-resources / risk-of-bias-instrument-for-cross-sectional-surveys-of-attitudes-and-practices-distillersr
6. Sedgwick P. Meta-analyses: what is heterogeneity? BMJ **350**: h1435, 2015.
7. Lau J, Ioannidis JPA, Schmid CH. Quantitative synthesis in systematic reviews. Ann Intern Med **127**: 8206, 1997.
8. Haidich A. Meta-analysis in medical research. Hippokratia **14**: 2937, 2010.
9. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Br Med J **315**: 62934, 1997.
10. Abokalawa F, Ahmad SF, Al-Hashel J, Hassan AM, Arabi M. The effects of coronavirus disease 2019 (COVID-19) pandemic on people with epilepsy (PwE): an online survey-based study. Acta Neurol Belg **8**: 1-8, 2021.
11. Aledo-Serrano Á, Mingorance A, Jiménez-Huete A, et al. Genetic epilepsies and COVID-19 pandemic: Lessons from the caregiver perspective. Epilepsia **61**: 1312-1314, 2020.
12. Alkhotani A, Siddiqui MI, Almuntashri F, Baothman R. The effect of COVID-19 pandemic on seizure control and self-reported stress on patient with epilepsy. Epilepsy Behav **112**: 107323, 2020.
13. Asadi-Pooya AA, Farazdaghi M, Bazrafshan M. Impacts of the COVID-19 pandemic on Iranian patients with epilepsy. Acta Neurol Scand **142**: 392-395, 2020.
14. Assenza G, Lanzone J, Brigo F, et al. Epilepsy care in the time of COVID-19 pandemic in Italy: risk factors for seizure worsening. Front Neurol **11**: 737, 2020.
15. Cabona C, Deleo F, Marinelli L, et al. Epilepsy course during COVID-19 pandemic in three Italian epilepsy centers. Epilepsy Behav **112**: 107375, 2020.
16. Conde Blanco E, Manzanares I, Centeno M, et al. Epilepsy and lockdown: a survey of patients normally attending a Spanish centre. Acta Neurol Scand **143**: 206-209, 2021.
17. Fonseca E, Quintana M, Lallana S, et al. Epilepsy in time of COVID-19: a survey-based study. Acta Neurol Scand **142**: 545-554, 2020.
18. Gul ZB, Atakli HD. Effect of the COVID-19 pandemic on drug compliance and stigmatization in patients with epilepsy. Epilepsy Behav **114**: 107610, 2021.
19. Huang S, Wu C, Jia Y, et al. COVID-19 outbreak: the impact of stress on seizures in patients with epilepsy. Epilepsia **61**: 1884-1893, 2020.
20. Lanzone J, Cenci C, Tombini M, et al. Glimpsing the impact of COVID19 lock-down on people with epilepsy: a text mining approach. Front Neurol **11**: 870, 2020.
21. Miller WR, Von Gaudecker J, Tanner A, Buelow JM. Epilepsy self-management during a pandemic: experiences of people with epilepsy. Epilepsy Behav **111**: 107238, 2020.
22. Millevert C, Van Hees S, Siewe Fodjo JN, et al. Impact of COVID-19 on the lives and psychosocial well-being of persons with epilepsy during the third trimester of the pandemic: results from an international, online survey. Epilepsy Behav **116**: 107800, 2021.
23. Mostacci B, Licchetta L, Cacciavillani C, et al. The impact of the COVID-19 pandemic on people with epilepsy. An Italian survey and a global perspective. Front Neurol **11**: 613719, 2020.
24. Puteikis K, Jasionis A, Mameniškienė R. Recalling the COVID-19 lockdown: insights from patients with epilepsy. Epilepsy Behav **115**: 107573, 2021.
25. Rathore C, Baheti N, Bansal AR, et al. Impact of COVID-19 pandemic on epilepsy practice in India: a tripartite survey. Seizure **86**: 60-67, 2021.
26. Reilly C, Muggeridge A, Cross JH. The perceived impact of COVID-19 and associated restrictions on young people with epilepsy in the UK: young people and caregiver survey. Seizure **85**: 111-114, 2021.
27. Rosengard JL, Donato J, Ferastraoaru V, et al. Seizure control, stress, and access to care during the COVID-19 pandemic in New York City: the patient perspective. Epilepsia **62**: 41-50, 2021.
28. Salari M, Etemadifar M, Gharagozli K, Etemad K, Ashrafi F, Ashourizadeh H. Incidence of anxiety in epilepsy during coronavirus disease (COVID-19) pandemic. Epilepsy Behav **112**: 107442, 2020.
29. Saleem T, Sheikh N, Abbasi MH, Javed I, Khawar MB. COVID-19 containment and its unrestrained impact on epilepsy management in resource-limited areas of Pakistan. Epilepsy Behav **112**: 107476, 2020.
30. Sanchez-Larsen A, Gonzalez-Villar E, Díaz-Maroto I, et al. Influence of the COVID-19 outbreak in people with epilepsy: analysis of a Spanish population (EPICOVID registry). Epilepsy Behav **112**: 107396, 2020.
31. Si Y, Sun L, Sun H, Niu Y, Mo Q. Epilepsy management during epidemic: a preliminary observation from western China. Epilepsy Behav **113**: 107528, 2020.
32. Trivisano M, Specchio N, Pietrafusa N, et al. Impact of COVID-19 pandemic on pediatric patients with epilepsy - the caregiver perspective. Epilepsy Behav **113**: 107527, 2020.
33. Wanigasinghe J, Jayawickrama A, Hewawitharana G, et al. Experience during COVID-19 lockdown and self-managing strategies among caregivers of children with epilepsy: a study from low middle income country. Seizure **84**: 112-115, 2021.
34. Kuroda N. Decision making on telemedicine for patients with epilepsy during the coronavirus disease 2019 (COVID-19) crisis. Front Neurol **11**: 722, 2020.
35. Kuroda N. Mental health considerations for patients with epilepsy during COVID-19 crisis. Epilepsy Behav **111**: 107198, 2020.
36. Lai SL, Hsu MT, Chen SS. The impact of SARS on epilepsy: the experience of drug withdrawal in epileptic patients. Seizure **14**: 557-561, 2005.