










ORIGINAL ARTICLE

Medium-term effects of COVID-19 pandemic on epilepsy: A follow-up study

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Abstract

Objective: To analyze the medium-term impact of the COVID-19 pandemic on epilepsy patients, focusing on psychological effects and seizure control.

Methods: Prospective follow-up study to evaluate the medium-term effects of the COVID-19 pandemic on a cohort of epilepsy patients from a tertiary hospital previously surveyed during the first peak of the pandemic. Between July 1, 2020, and August 30, 2020, the patients answered an online 19-item questionnaire, HADS, and PSIQ scales. Short- and medium-term effects of the pandemic confinement and the perception of telemedicine were compared.

Results: 153 patients completed the questionnaire, mean \pm SD age, 47.6 ± 19.3 years; 49.7% women. Depression was reported by 43 patients, significantly more prevalent than in the short-term analysis (29.2% vs. 19.7%; $p = .038$). Anxiety (38.1% vs. 36.1%; $p = 0.749$) and insomnia (28.9% vs. 30.9%, $p = .761$) remained highly prevalent. Seventeen patients reported an increase in seizure frequency (11.1% vs. 9.1%, $p = .515$). The three factors independently associated with an increase in seizure frequency in the medium term were drug-resistant epilepsy (odds ratio [OR] = 8.2, 95% CI 2.06–32.52), depression (OR = 6.46, 95% CI 1.80–23.11), and a reduction in income (OR = 5.47, 95% CI 1.51–19.88). A higher proportion of patients found telemedicine unsatisfactory (11.2% vs. 2.4%), and a lower percentage (44.8% vs. 56.8%) found it very satisfactory ($p = .005$).

Conclusions: Depression rates increased significantly after the first wave. Depression, drug-resistant epilepsy, and a reduction in family income were independent risk factors for an increased seizure frequency. Perception of telemedicine worsened, indicating need for re-adaptation.

KEYWORDS

COVID-19, depression, epilepsy, pandemic, SARS-CoV-2, Seizures, telehealth

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused more than 2 million deaths worldwide since the first cases were reported in December 2019.^{1,2} This pandemic has presented the medical community and society with unprecedented challenges.

To control the spread of the COVID-19 pandemic in Spain, the government imposed a nationwide lockdown that lasted from March 13, 2020, to June 20, 2020. After this period, restrictions were gradually eased, giving way to a "new normal" characterized by curtailment of a wide range of everyday activities and new social distancing measures.³ In August 2020, the cumulative 7-day incidence of COVID-19 in Spain was 78.2 cases per 100,000 inhabitants, with nearly 400,000 total cases and 30,000 deaths.⁴ The healthcare system was striving to adapt to the new situation, while preparing for a probable second wave.

The collapse of the emergency services in March and April 2020 had a major effect on urgent medical conditions such as heart attacks and stroke, causing treatment delays and increased morbidity and mortality rates.⁵ Once a certain normalcy had been restored, studies on the medical and psychological effects of lockdown on patients with chronic illnesses began to emerge.^{6,7}

The medical community has made enormous efforts to enable and promote the use of telemedicine as a safe way of monitoring patients with stable illness,⁸ including those with chronic epilepsy, for whom an array of suitable new technologies exists.^{9,10} Although telemedicine still has a long way to go, it will certainly provide an essential alternative to traditional in-person visits for some time, and efforts must be made to ensure continued quality of care. Tertiary hospitals in Spain have adapted care protocols and procedures in many areas and prioritized the use of remote monitoring for patients with chronic disease.¹¹

Spanish studies of the impact of the pandemic and lockdown measures in the setting of epilepsy have mainly identified collateral effects,^{12,13} although one recent study described a higher incidence of COVID-19 in patients with epilepsy than in those without, probably because of the higher proportion of dependent and institutionalized patients in this population.¹⁴ A previous cross-sectional survey-based study by our group analyzing the short-term effects of the COVID-19 pandemic on epilepsy patients from a tertiary hospital in Barcelona, Spain, showed emerging lockdown-related symptoms such as anxiety and depression in addition to sleep disturbances and reduced family income.¹⁵ Almost 10% of the patients reported an increase in seizure frequency, found to be independently associated with tumor-related epilepsy, drug-resistant epilepsy, insomnia, and reduced income. The general perception of telemedicine among the patients surveyed was positive.

In this follow-up study, we analyzed the medium-term effects of the COVID-19 pandemic in the same cohort of patients,¹⁵ with a focus on the psychological impact of the pandemic and lockdown and their possible association with seizure control. We also re-evaluated

perceptions of telemedicine, which has since been incorporated into routine practice at our epilepsy unit.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

In a previous study, we evaluated the short-term effects of the COVID-19 pandemic in a cross-sectional survey of all patients from the epilepsy unit at Hospital Vall d'Hebron in Barcelona, Spain, who had received a telephone consultation during the first month of lockdown (March 16, 2020, to April 17, 2020). Their in-person appointment had been canceled following the Spanish Government's declaration of a national state of emergency on March 14.¹⁶ The full details of the study are described elsewhere.¹⁵ In brief, patients aged 17 years or older with a definitive diagnosis of epilepsy according to the International League Against Epilepsy (ILAE) criteria¹⁷ were consecutively included. Patients consulting for neurological symptoms other than seizure and patients/caregivers unable to answer the questionnaire were excluded. All epilepsies were classified according to the current ILAE classification.¹⁸ Information on antiepileptic drug (AED) treatment, mean baseline seizure frequency, and drug resistance was obtained from medical records. A note was also made of modified Rankin scale score, intellectual disability, dysphagia, and demographic data, including current living and employment situation. All the consultations were performed by an epileptologist by telephone. The patients or their caregivers were then administered a 19-item telephone survey by a neurologist.

The follow-up study to assess the medium-term effects of the pandemic on the same cohort of patients was performed between July 1, 2020, and August 30, 2020. Patients who had died were excluded from the analysis and cause of death recorded. Those who could not be contacted, were unwilling to participate, or did not complete the follow-up survey were also excluded. A link to access the online survey was sent by email following telephone contact with a neurologist to obtain consent. When contact by email was not possible (because of personal limitations or Internet access problems), the survey was administered directly to the patient or caregiver by telephone by a neurologist.

2.2 | Description of online survey

The online survey consisted of three questionnaires: the 19-item questionnaire used in the first study, the Hospital Anxiety and Depression Scale (HADS), and the Pittsburgh Sleep Quality Index (PSQI). They were intended to be completed by the patient or, in the case of patients with intellectual disability, dementia, or any another condition that prevented them from answering the questions, their caregiver.

The 19 items in the questionnaire were divided into five sections: (a) effects of patient/caregiver isolation or quarantine; (b) effects of

government-imposed lockdown on seizure frequency, AED treatment, emergency consultations, delays in epilepsy-related tests, anxiety and depression symptoms, and sleep disturbances; (c) socioeconomic effects (reduced income for patient/main caregiver as a result of the lockdown); (d) perception of telephone consultations during the pandemic; and (e) symptoms compatible with COVID-19. An increase in seizure frequency was defined as an increase of 50% or more in the number of seizures reported by the patient compared to baseline (information obtained from medical record) or the occurrence of unprovoked seizures in previously seizure-free patients.

The HADS is a validated 14-item self-administered scale for detecting states of depression and anxiety.¹⁹ It distinguishes between emotional and somatic illness, and there is evidence that scores are not affected by the presence of bodily illness. It has an anxiety subscale (HADS-A) and a depression subscale (HADS-D), both containing seven items rated on a four-point Likert-type scale, that also provide valid measures of severity. A HADS score of 0–7 is considered to be normal; scores of 8–10 indicate borderline cases, while those of 11–21 indicate pathological cases. In this last category, a score of 11–14 indicates moderate illness while one of 14 or higher indicates severe illness.

The PSQI²⁰ is a 19-item self-administered questionnaire that assesses sleep quality and disturbances over a 1-month interval. These 19 items, each rated on a four-point Likert-like scale, generate seven scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The scores are added to produce a global score. A global score of 5 or higher provides a sensitive and specific measure of poor sleep quality relative to clinical and laboratory measures.

2.3 | Statistical analysis

The statistical analyses were performed in the IBM SPSS Statistics software program version 22.0. Descriptive and frequency statistical analyses were obtained. Categorical variables were reported as frequencies (percentages) and continuous variables as mean \pm standard deviation or median and interquartile range, as appropriate. McNemar–Bowker's test for paired data was used to compare questionnaire responses from the first and second studies, while the Mann-Whitney U test was used to compare self-reported depression, anxiety, and insomnia with HADS/PSQI scores. Associations between the study variables and increased seizure frequency were assessed using Pearson's chi-square test for categorical variables or the Fisher exact test (for expected frequencies <5).

Variables with a p -value <.1 in the univariate analysis were entered into a forward stepwise multiple logistic regression model as independent variables to identify factors independently associated with an increase in seizure frequency. Odds ratios (ORs) and 95% confidence intervals (CIs) are shown in the final model. A bar chart was created to show the probability of an increase in seizure frequency according to the cumulative number of independently

associated factors. P -values <.05 were considered statistically significant.

3 | RESULTS

We analyzed data for 153 of the 255 epilepsy patients who participated in the initial study on the short-term effects of the COVID-19 pandemic.¹⁵ The details of the selection process are summarized in Figure 1. The mean age of the patients was 47.6 ± 19.3 years, and 49.7% ($n = 76$) were women. The most common type of epilepsy was focal epilepsy ($n = 134$; 87.6%), and the most common focal subtype was temporal lobe epilepsy ($n = 58$; 37.9%). Etiology was unknown in 40 patients (26.1%). Thirty-one patients (20.3%) had an intellectual disability, and 43 (28.1%) had dependency for activities of daily living. Thirty-two patients (20.9%) had drug-resistant epilepsy. The survey was answered by the patient in 93 cases (60.8%) and by a family member or caregiver in 69 (39.2%). The demographic and clinical characteristics are shown in Table 1.

3.1 | Medium-term impact of COVID-19 lockdown and social distancing

No significant differences in seizure control were observed on comparing the short- and medium-term effects of the COVID-19 pandemic on our cohort of patients with epilepsy. In the second study, conducted in July and August 2020, 17 patients (11.1%) reported an increase in seizure frequency, 125 (81.6%) reported no change, and five (3.3%) reported a decrease. Six patients (3.6%) did not know. The short- and medium-term effects are compared in Table 2.

Demand for emergency services increased following the easing of restrictions (11.1% vs. 3.3%; $p = .008$). Eight patients (5.3%) visited an emergency department because of seizures in the summer and three (2%) considered doing so but did not because they were afraid of becoming infected with SARS-CoV-2. Three (2%) called the emergency phone line and were told to stay at home, and another three (2%) tried to call but could not get through because the lines were overwhelmed.

No significant differences in the number of patients reporting delays in epilepsy-related tests were observed between the first and second study (14 vs. 15). Four of the 15 patient who reported delays during the new normal also reported an increase in seizure frequency. Just four patients (2.6% vs. 2% in the first study) reported difficulties obtaining their AEDs from the pharmacy, and in all cases, the reason was that their prescription had expired.

Forty-three patients (29.3%) reported feeling depressed in the questionnaire administered in July/August; this rate was significantly higher than the rate of 19.7% observed during lockdown ($p = .038$). Self-reported feelings of depression were significantly associated with HADS-D score ($p = <.001$); 17 patients (12.9%) had pathological scores on the HADS-D, while 15 (11.4%) had borderline scores. No significant changes in self-reported anxiety were

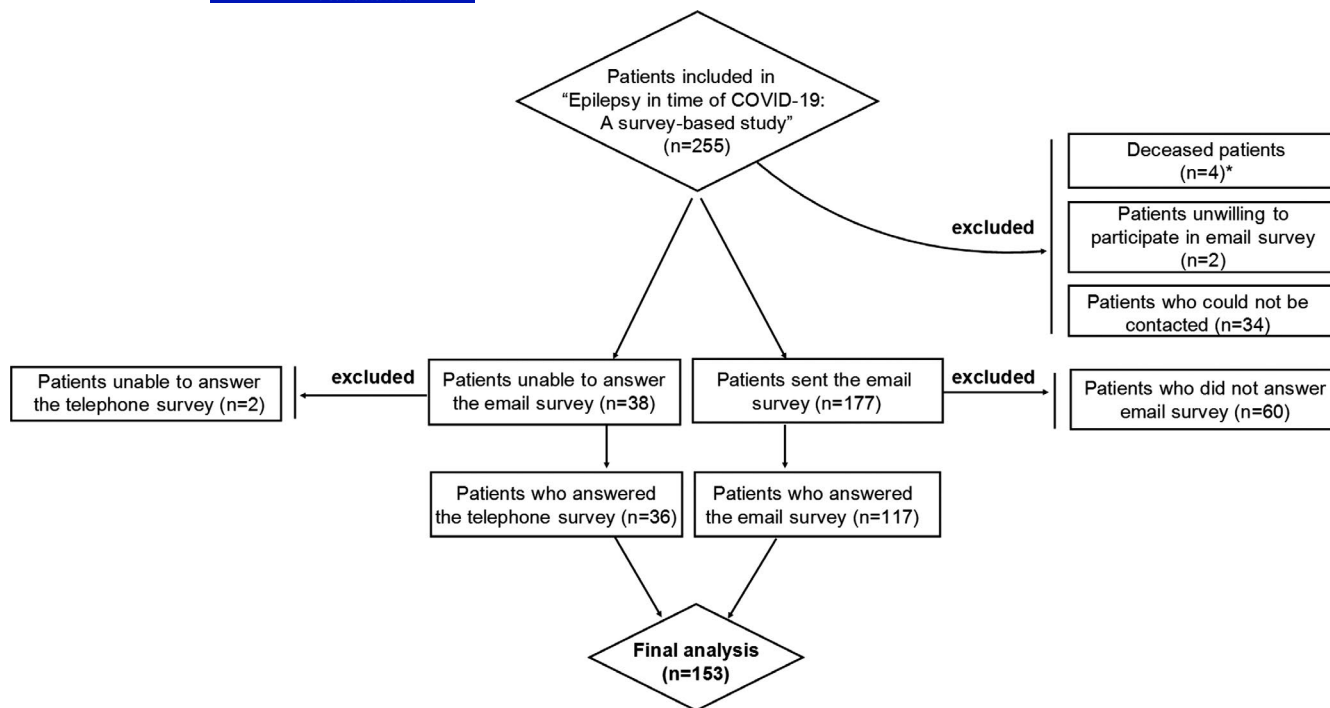


FIGURE 1 Flow chart of patient selection process. The causes of death in the four patients who died were severe acute coronavirus 2 pneumonia in two cases (see details elsewhere¹⁵), glioblastoma, and aspiration pneumonia

observed between the two studies (38.1% vs. 36.1%; $p = 0.75$). Self-reported anxiety was also significantly associated with HADS-A score ($p = <.001$). In this case, 25 patients (19.4%) had pathological scores and 17 (13.4%) had borderline scores. No differences were observed in self-reported sleep disturbances, with 30.9% of patients reporting insomnia in the second study compared with 28.9% in the first study ($p = .761$). In addition, 15 patients (9.8%) stated that they were sleeping more hours than usual. The PSQI score, which was also significantly associated with self-reported insomnia ($p = <.001$), indicated poor sleep quality in 66 patients (55%). Sleep efficiency was less than 85% in 48 patients (40%) (Figure 2).

The proportion of patients reporting that their main fear was COVID-19 (38.8% vs. 45.5%; $p = .268$) or epilepsy (16.5% vs. 14.9%; $p = .824$) remained unchanged, as did the proportion of patients reporting a reduction in family income (26.9% vs. 28.3%; $p = .845$).

Several changes were observed in the factors associated with an increase in seizure frequency. In the univariate analysis, the strongest predictor of an increase in the medium term was depression, assessed using both the 19-item questionnaire ($p = .001$) and the HADS-D ($p = .002$). No significant associations were observed for tumor-related epilepsy or fear of epilepsy ($p = .157$). Anxiety, evaluated with the 19-item questionnaire ($p = .008$) and the HADS-A ($p = .006$), drug-resistant epilepsy ($p = .010$), reduced income ($p = .002$), delayed performance of epilepsy-related tests ($p = .034$), and self-reported insomnia ($p = .004$), all maintained their association with an increased frequency of seizures (Table 3).

In the multivariate analysis, drug-resistant epilepsy (OR = 8.2, 95% CI 2.06–32.52, $p = .003$), depression (OR = 6.46, 95% CI 1.80–23.11, $p = .004$), and reduced income (OR = 5.47, 95% CI 1.51–19.88,

$p = .010$) were all independently associated with an increased seizure frequency. The combinations of these factors also provided a cumulative probability estimate of increased frequency (Figure 3).

3.2 | Perceptions of telemedicine

Perceptions of telemedicine worsened significantly between the first and follow-up study ($p = .005$), with a higher proportion of patients stating that they were dissatisfied (11.2% vs. 2.4%) or quite satisfied (44% vs. 40.8%) with remote visits, and a lower proportion (44.8% vs. 56.8%) stating that they were very satisfied. Their opinions regarding the usefulness of telemedicine in the near future remained unchanged ($p = .105$), with 40.8% (vs. 37.4%) stating they would prefer face-to-face visits, 36.7% (vs. 41.5%) stating that they found it convenient and would like to use it, and 22.4% (vs. 21.1%) stating that they had no preference between remote and face-to-face encounters (Table 2).

3.3 | COVID-19 in epilepsy patients

Eight patients (5.2%) without a confirmatory diagnostic test reported symptoms compatible with mild COVID-19 in the follow-up study. There was just one patient (0.63%) with a mild infection and fever as the main symptom who had a positive RT-PCR result from a nasopharyngeal specimen. The patient did not develop pneumonia or require hospitalization and reported no changes in seizure frequency or AED use during the illness.

TABLE 1 Demographic and clinical characteristics of the patients included in the study

Age, years, mean \pm SD (range)]	47.6 \pm 19.3 (17–77)
Sex, n (%)	
Male	77 (50.3)
Female	76 (49.7)
Type of epilepsy, n (%)	
Focal	134 (87.6)
Generalized	18 (11.8)
Unclassifiable	1 (0.7)
Subtype of focal epilepsy, n (%)	
Temporal	58 (37.9)
Frontal	34 (22.2)
Parietal	5 (3.3)
Posterior quadrant	6 (3.9)
Unknown	32 (20.9)
Etiology, n (%)	
Unknown	40 (26.1)
Genetic ^a	23 (15)
Vascular	20 (13.1)
Tumor	19 (12.4)
Perinatal anoxia	11 (7.2)
Infectious disease	9 (5.9)
Mesial temporal sclerosis	7 (4.6)
Post-traumatic	6 (3.9)
Malformations of cortical development	5 (3.3)
Inflammatory/Autoimmune	3 (2)
Post-anoxic encephalopathy	3 (2)
Toxic/Metabolic	2 (1.3)
Other	5 (3.3)
Intellectual disability, n (%)	31 (20.3)
Dysphagia, n (%)	10 (6.5%)
mRS, n (%)	
0	15 (9.8)
1	55 (35.9)
2	43 (28.1)
3	26 (17.1)
4	14 (9.2)
5	0
Dependence for ADLs, n (%)	43 (28.1)
Number of AEDs, n (%)	
0	4 (2.6)
1	81 (52.9)
2	43 (28.1)
3	17 (11.1)
4	8 (5.2)
Drug-resistant epilepsy, n (%)	32 (20.9)

TABLE 1 (Continued)

Usual place of residence, n (%)	
Own house	97 (63.4)
Parents' or caregiver's house	54 (35.3)
Nursing home	1 (0.7)
Other	1 (0.7)
Current activity, n (%)	
Unable to work	54 (35.5)
Employed	43 (28.1)
Retired	29 (19)
Unemployed	9 (5.9)
Student	12 (7.8)
Homemaker	6 (3.9)
Person responding to the survey, n (%)	
Patient	93 (60.8)
Family member/caregiver	60 (39.2)

Abbreviations: ADLs, activities of daily living; AEDs, antiepileptic drugs; mRS, modified Rankin scale; SD, standard deviation.

^aGenetic generalized epilepsy (formerly known as idiopathic generalized epilepsy) was considered to be of genetic etiology.

4 | DISCUSSION

We have described the medium-term effects of the COVID-19 pandemic on epilepsy patients in Spain and highlighted the psychological consequences of lockdown and social distancing measures, particularly evident in the rise in depression rates and persistence of anxiety and insomnia. Approximately 10% of patients reported an increase in seizure frequency; this rate is similar to that reported during lockdown, despite the decline in infection rates and easing of social restrictions at the time of data compilation.³

The sample was drawn from the “Epilepsy in time of COVID-19” cohort,¹⁵ a real-life cohort from an epilepsy unit at a tertiary hospital comprising a wide range of patients, including those with intellectual disability and/or dependency for activities of daily living. The percentage of patients with drug-resistant epilepsy was similar to that expected for the general epilepsy population.²¹ The online survey was designed by a trained epileptologist, and to minimize variations, the follow-up telephone interviews were conducted by the same epileptologists who took part in the first wave of the study. In this second study, self-reported psychiatric comorbidities (depression, anxiety, and sleep disturbances) were compared with scores on the HADS and PSIQ, which have both been validated in patients with epilepsy.^{22,23}

The main finding of this follow-up study of the medium-term effects of the COVID-19 pandemic on patients with epilepsy was a significant increase in depression rates. Almost a third of the patients reported feeling depressed, and 24.3% had borderline or pathologic scores on the HADS-D. This represents a 33% increase in self-reported depression compared with the first survey, which had already detected a rise in emerging psychiatric symptoms such as anxiety and depression during the first month of lockdown. While

(Continues)

TABLE 2 Comparison of short-term¹⁵ (Second column) and medium-term (Third column) responses to the 19-item questionnaire on the effects of the coronavirus disease 2019 pandemic on epilepsy patients. In the first column, the results of the initial analysis with the complete sample of patients are shown

	Short-term analysis ¹⁵ (first wave) (March 16, 2020, to April 17, 2020)		Medium-term analysis (new normal) (July 1, 2020, to August 30, 2020) (n = 153)	p-value
	*Patients included in the initial study (n = 255)	Patients included in the follow-up study (n = 153)		
Seizure frequency, n (%)				
Increased	25 (9.8)	14 (9.1)	17 (11.1)	.515
No change	219 (85.9)	134 (87.3)	125 (81.6)	
Decreased	11 (4.3)	5 (3.6)	5 (3.26)	
Do not know	0	0	6 (3.9)	
Emergency consultation^a n (%)	11 (4.4)	5 (3.3)	17 (11.1)	.008
Delays in epilepsy-related tests ^b n (%)	28 (11)	14 (9.2)	15 (9.8)	>.99
Difficulties obtaining medication, n (%)	7 (2.7)	3 (2)	4 (2.6)	>.99
Self-reported depression on 19-item questionnaire, n (%)	53 (21.2)	29 (19.7)	43 (29.3)	.038
Self-reported anxiety on 19-item questionnaire, n (%)	99 (39.6)	53 (36.1)	56 (38.1)	.749
Self-reported insomnia on 19-item questionnaire, n (%)	72 (28.7)	47 (30.9)	44 (28.9)	.761
Fear of COVID-19, n (%)	90 (41.3)	55 (45.5)	47 (38.8)	.268
Fear of epilepsy, n (%)	37 (17)	18 (14.9)	20 (16.5)	.824
Reduction in family income, n (%)	73 (29.1)	41 (28.3)	39 (26.9)	.845
Perception of telemedicine, n (%)				
Very satisfied	124 (56.1)	71 (56.8)	56 (44.8)	.005
Quite satisfied	90 (40.7)	51 (40.8)	55 (44)	
Not satisfied	7 (3.2)	3 (2.4)	14 (11.2)	
Interest in using telemedicine in the future, n (%)				.105
Yes	97 (39.6)	61 (41.5)	54 (36.7)	
Indifferent	55 (22.4)	31 (21.1)	33 (22.4)	
No	93 (38)	55 (37.4)	60 (40.8)	

Statistically significant differences are highlighted in bold.

^aIncludes emergency room visits and emergency telephone consultations.

^bIncludes routine EEG, MRI, and video-EEG monitoring.

these symptoms have also been detected in the general population,²⁴ their increase has been particularly noticeable in patients with chronic illness. In Italy, 35% of epilepsy patients surveyed during the peak of the first wave of the pandemic reported depressive symptoms,²⁵ while a multicountry online survey conducted around the same time found that 39.8% of patients with epilepsy had pathological HADS-D scores.²⁶ In Spain, a study conducted between May and June 2020 detected feelings of sadness and depression in 35% of epilepsy patients.²⁷ Pathological levels of stress and anxiety were reported in the first wave of the pandemic in up to 60% of the epilepsy population, and self-reported levels remained high (40%) during follow-up.²⁵⁻²⁷ The anxiety and depression rates

detected in our study are lower than those reported elsewhere, possibly because of differences in the questionnaires used, the profile of patients surveyed (the other studies, for example, did not include patients with intellectual disability), or the timing of the studies. Our detection of a significant increase in depression rates among epilepsy patients during the new normal restrictions highlights the risk of both medium- and long-term psychological consequences.

The impact of recently acquired depression is reflected in the seizure control data. Although the increase in seizure frequency with respect to baseline remained stable during follow-up, we detected changes in the factors associated with poor control, with depression becoming the main risk factor. Psychiatric comorbidities

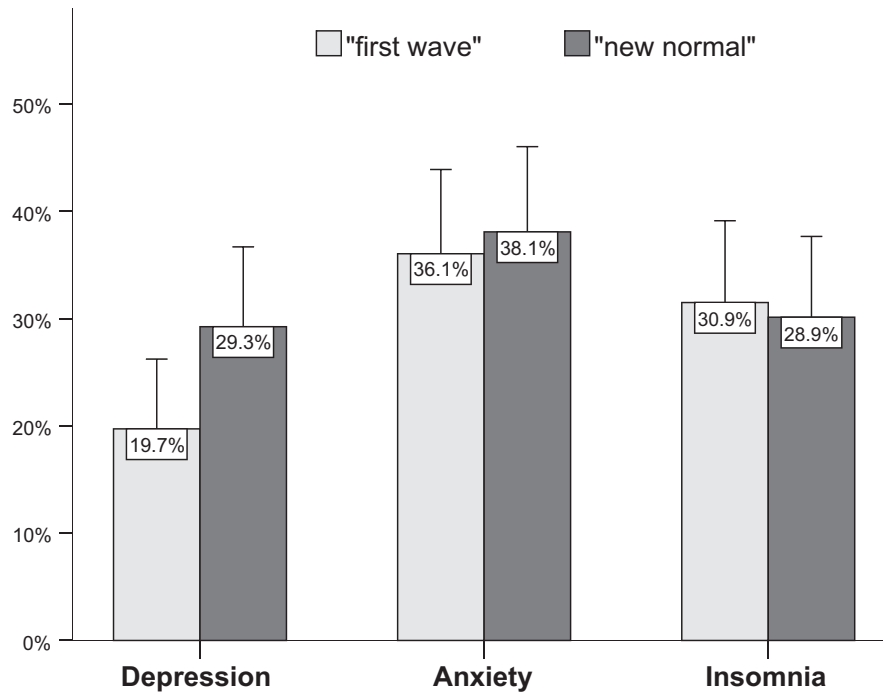


FIGURE 2 Comparison between self-reported depression (19.7% vs 29.3%), anxiety (36.1% vs 38.1%), and insomnia (30.9% vs 28.9%) rates during lockdown (March 16, 2020-April 17, 2020) and during the new normal (July 1, 2020-August 31, 2020). The increase in the prevalence of depression was statistically significant ($p = .038$)

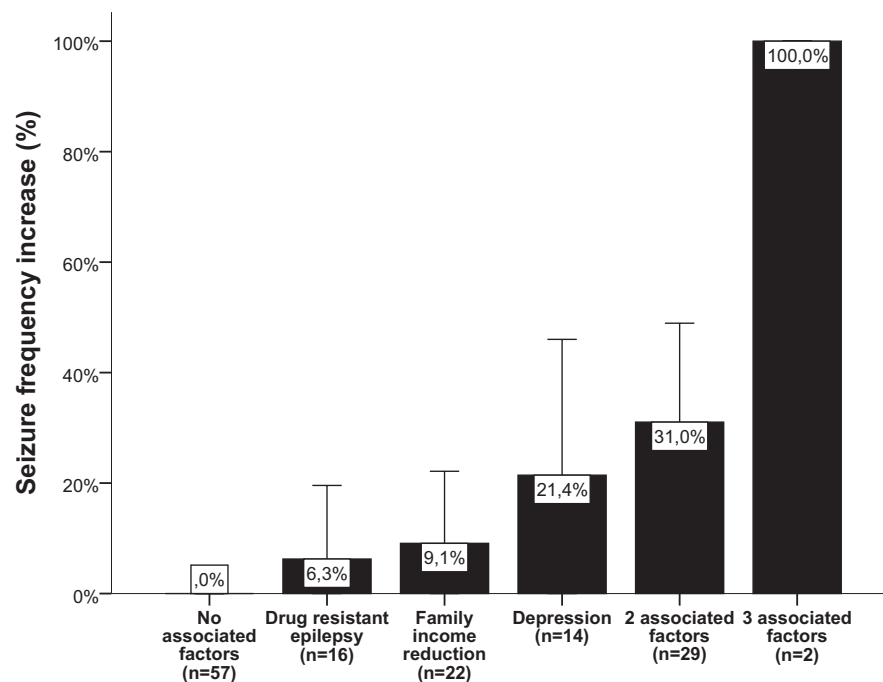


FIGURE 3 Probability of increased seizure frequency according to the cumulative association of three risk factors (drug-resistant epilepsy, income reduction, and self-reported depression). Error bars show the 95% confidence intervals

are known to have an important role in seizure control, even in non-pandemic times.^{28,29} A recent Spanish study identified lockdown-related emotional distress as the main risk factor for worsening seizure control in patients with epilepsy.²⁷ Insomnia remained highly

prevalent in our follow-up study, supporting previous findings showing worsening of sleep disturbances among epilepsy patients during the first peak of the pandemic and an association with seizure control.^{27,30}

TABLE 3 Clinical factors associated with seizure control during and after lockdown in the first wave of the coronavirus disease 2019 pandemic

	Increased seizure frequency					
	First wave (March 16, 2020, to April 17, 2020) (n = 255)			New normal (July 1 to August 30) (n = 147)		
	No (n = 230)	Yes (n = 25)	P-value	No (n = 130)	Yes (n = 17)	p-value
Depression						
19-item questionnaire, n (%)	46 (20.4)	7 (28)	0.381	28 (22.6)	11 (64.2)	0.001
HADS-D, n (%) ^a	-	-	-	9 (8.1)	6 (40)	0.002
Anxiety						
19-item questionnaire, n (%)	84 (37.3)	15 (60)	0.028	40 (32.3)	11 (64.7)	0.008
HADS-A, n (%) ^a	-	-	-	15 (13.9)	7 (46.7)	0.006
Insomnia						
19-item questionnaire, n (%)	58 (25.7)	14 (56)	0.001	31 (23.8)	10 (58.8)	0.004
PSQI, n (%) ^a	-	-	-	52 (51.5)	9 (14.8)	0.140
Drug-resistant epilepsy, n (%)	44 (19.1)	12 (48)	0.001	23 (17.7)	8 (47.1)	0.010
Reduction in family income, n (%)	61 (26.9)	12 (50)	0.018	28 (21.7)	10 (58.8)	0.002
Delays in epilepsy-related tests, n (%)	18 (7.8)	10 (30)	<.001	8 (6.2)	4 (23.5)	0.029
Tumor etiology, n (%)	21 (9.1)	8 (32)	0.011	15 (11.5)	4 (23.5)	0.157
Fear of epilepsy, n (%)	28 (14.4)	9 (39.1)	0.002	14 (12.5)	4 (26.7)	0.140

Abbreviations: HADS, Hospital Anxiety and Depression Scale; PSQI, Pittsburgh Sleep Quality Index.

^aThe HADS and PSQI were not evaluated in the first study.

The socioeconomic effects of the pandemic have also had a significant effect on psychological distress and mental health,³¹ being the socioeconomic status a known determinant of psychological distress and health outcomes among epilepsy patients.^{32,33} In our cohort, 27% of patients were still affected by a reduction in income several months after the easing of restrictions, and this factor was the second strongest predictor of an increase in seizure frequency.

Our findings also show a major shift in perceptions of telemedicine, with the proportion of patients reporting dissatisfaction with remote visits increasing from 2% during lockdown to around 11% in the summer. In a survey conducted during the first peak of the pandemic, 88% of Spanish epileptologists reported dealing with their patients by telephone and stated that it was difficult to handle complex issues via this channel.¹¹ In a US study of telehealth perceptions during the pandemic,³⁴ 66% of epilepsy patients reported being very satisfied with teleconsultations. In our study, the proportion of patients reporting high satisfaction levels fell from 57% during lockdown to 45% in the summer. In the US study, 66% of patients were optimistic about the future role of telemedicine, compared with just 41.5% and 36.7% of patients in the first and second waves of our survey. The more favorable opinions observed in the United States may partly be due to the younger age of the patients and the fact that the survey was conducted at a time when the pandemic had not yet affected the whole country.³⁵ The positive perceptions of telemedicine observed in our population in the first study may

be biased by the fact that the survey was conducted by telephone. Nevertheless, the significant change observed over the months should lead to reflection that several adjustments need to be made to adapt telemedicine to daily practice and strengthen patients' confidence in this valuable tool. On a more optimistic note, 67% of the patients surveyed in the United States suggested the possibility of a hybrid model combining telehealth, with telephone or video consultations, and traditional visits; this option was also spontaneously proposed by our patients and could be a good direction to pursue.

We also detected an increase in emergency consultations (from 3.3% in March/April to 11% in July/August). Some of these visits may correspond to visits that patients postponed during the early days of the pandemic because of fear of becoming infected with SARS-CoV-2 at the hospital. The proportion of patients reporting delays in testing remained similar, at around 10%, indicating that there was still a backlog to clear. Delays in the performance of epilepsy-related tests were associated with an increase in seizure frequency, and we believe that this relationship may be bidirectional, since a higher proportion of tests are ordered for patients with drug-resistant epilepsy. Nevertheless, a sooner performance of these tests could have provided important information and therefore allow treatment adjustment and a more accurate assessment in these patients.

Our study has several limitations. The pre-pandemic baseline scores for anxiety and depression were not collected in our sample, even though prior studies performed in our population area portrayed

lower rates of psychiatric pathologies before the COVID-19 pandemic.²⁹ Besides psychological comorbidities and sleep disturbances were measured using validated tests, changes in seizure frequency were based on self-reported data. Our findings may also be affected by selection bias as just 50% of the patients from the initial study completed the follow-up survey. This low response rate was partly related to technical difficulties encountered with the online questionnaire (such as difficulties to access it or receiving it). We think that the introduction of telemedicine in our day to day will require a progressive learning process in our population, both in patients and in healthcare professionals. This study has provided new evidence on the medium-term effects of the COVID-19 pandemic on patients with epilepsy, and effects we believe are likely to endure beyond the pandemic. Further longitudinal and multicenter studies of larger international populations are needed to confirm our observations and clarify uncertainties surrounding the future consequences of the COVID-19 pandemic.

5 | CONCLUSIONS

We detected a significant increase in the proportion of epilepsy patients experiencing depressive symptoms after the first peak of the COVID-19 pandemic. The main risk factors for an increase in seizure frequency were depression, reduced income, and drug-resistant epilepsy. Anxiety and insomnia rates remained high, and perceptions of telemedicine worsened significantly. The full consequences of the COVID-19 pandemic and social distancing measures have yet to be determined in the setting of epilepsy, although as our results suggest, they are likely to be lasting and will call for adjustments to daily practice.

6 | ETHICAL PUBLICATION STATEMENT

We confirm that we have read the journal's position on issues concerning ethical publication and that this report is consistent with these guidelines.

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CONFLICT OF INTEREST

E. Fonseca has received research funding and speakers' fees from UCB Pharma, Esteve laboratorios, Eisai Inc, and Sanofi Genzyme. L. Abreira has received research funding and speakers' fees from UCB Pharma, BIAL Pharmaceutical, EISAI Inc., Sanofi Genzyme, and Esteve laboratorios. E. Santamarina has received research funding and speakers' fees from UCB Pharma, BIAL Pharmaceutical, EISAI Inc. Arvelle, and Esteve laboratorios. I. Seijo-Raposo has received research funding from UCB Pharma, Neuraxpharm, and GW pharmaceuticals. M. Toledo has received research funding and speakers' fees from UCB Pharma, BIAL Pharmaceutical, EISAI Inc., Sanofi, Arvelle, and Esteve laboratorios. S. Lallana, M. Quintana,

JL. Restrepo and J. Álvarez-Sabín have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

After publication, anonymized data supporting the findings of this study will be available from the corresponding author upon reasonable request from any qualified investigator.

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