



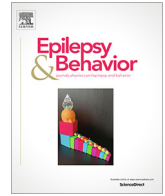
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COVID-19 and epilepsy: How are people with epilepsy in Brazil?

Laura Maria Guilhoto^{a,c,d,*}, Amanda Cristina Mosini^{a,b,c,1}, Maria Alice Susemihl^a,
Lécio Figueira Pinto^{a,e}

^a Associação Brasileira de Epilepsia, São Paulo, Brazil^b Departamento de Fisiologia, Escola Paulista de Medicina/Universidade Federal de São Paulo (EPM/Unifesp), São Paulo, Brazil^c Programa de Pós-Graduação em Neurociências e Neurologia da EPM/Unifesp, São Paulo, Brazil^d Hospital Universitário, University of São Paulo (USP), São Paulo, Brazil^e Divisão de Clínica Neurológica, HC-FMUSP, São Paulo, Brazil

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ABSTRACT

Purpose: During COVID-19 pandemic the global population is facing an important psychosocial distress. The aim of this study was to evaluate how people with epilepsy (PWE) in Brazil is dealing with the pandemic, in relation to seizure frequency, access to antiseizure medicines (ASM), medical follow-up, and well-being.

Methods: An online questionnaire survey among PWE (group 1) and caregivers (group 2) was applied in the social networks of the Brazilian Association of Epilepsy, the official Brazilian chapter of the International Bureau for Epilepsy. The questionnaire was composed of 46 generic questions in four areas, namely, demographics and baseline clinical data as well as epilepsy and quality-of-life impact by COVID-19 pandemic based on the domains of the abbreviated World Health Organization Quality of Life (WHOQOL-BREF) instrument.

Results: The questionnaire was answered by 464 participants including 380 (81.9%) PWE (78.7% female; age 34.3 yrs.; ± 9.76) and 84 (18.1%) caregivers (patients' age 14.1 yrs.; ± 10.30). During the COVID-19 pandemic, 36.8% of PWE and 36.4% of caregivers reported difficulties in accessing the epilepsy healthcare provider, and visits occurred normally only in 29.7% of PWE and in 34.5% of the caregivers group. Telehealth was not provided for 66.6% of group 1 and for 58.5% of group 2. Lack of availability of ASM was reported by 21.9% of PWE and 28.0% of caregivers in public dispensing units and by 19.2% and 17.8%, respectively, in private pharmacies. Increase in seizures during pandemic was mentioned by 26.3% and 27.9% of groups 1 and 2, respectively. Patients who had increase in seizure frequency had more frequently reported problems with treatment and in quality-of-life concepts. Fear of having a more severe COVID-19 presentation because of epilepsy was reported by 74.5% of PWE and by 89.8% of caregivers. Dissatisfaction with current health status was reported by 36.7% and 38.1% in groups 1 and 2, respectively, and that the support from others has decreased (56.1% and 66.1%, in groups 1 and 2) during the pandemic. The factors with higher Odds Ratio of increase in seizure frequency during pandemic were age >41 yrs., treatment in public healthcare system, drug-resistant epilepsy, adversities in getting ASM in public dispensing units, difficulties with prescription renewals, current financial problems and belief that epilepsy or ASM are risk factors for contracting COVID-19.

Conclusion: During COVID-19 pandemic in Brazil, PWE and caregivers reported increase in seizures in one-fourth of the patients and several difficulties, namely problems in accessing the healthcare system including ASM dispensation, telehealth, and fear of having a more severe COVID-19 because of epilepsy. There were also physical, psychological, and social concerns which affected quality-of-life-related aspects in this population. These facts may increase treatment gap in epilepsy in Brazil as well in other developing countries.

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* Corresponding author at: Universidade Federal de São Paulo, Rua Pedro de Toledo 650, andar térreo, sala 11, São Paulo, SP, Brazil

E-mail address: lauragui@gmail.com (L.M. Guilhoto).

¹ These authors contributed equally to this work.

1. Introduction

The new coronavirus disease (COVID-19) emerged in Wuhan, China in late 2019 and rapidly spread resulting in a world-class

pandemic [1] and it is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Infected patients may be asymptomatic or have clinical symptoms of varying severity, which may include neurological manifestations. Most severe cases require admission to the intensive care unit and are at higher risk of death [2]. The COVID-19 pandemic is a challenge for healthcare systems worldwide. A drastic restructuration of health systems was necessary, with the relocation of health professionals and supplies, and a consequent increase in costs. This had a drastic impact on the treatment of chronic diseases, including epilepsy [3].

Epilepsy is a chronic neurologic disorder that affects over 70 million people around the world [4]. It is characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition [5]. So far there is no scientific evidence that epilepsy is a risk factor for COVID-19 or that people with epilepsy (PWE) are at increased risk of death when infected [7–9]. However, those with comorbidities, such as hypertension, diabetes, cardiovascular, respiratory, and metabolic diseases will be at increased risk [4,6,10].

Regular follow-up is a cornerstone in the treatment of PWE to check for seizure control, adverse effects, optimize antiseizure therapy, prescription renewals, treat concomitant neuropsychiatric conditions, or associated comorbidities and provide psychological support for patients and their families [11]. With the uncontrolled viral transmission, most governments were forced to create and implement measures of social isolation, reduction in business hours and the containment of the circulation of people on public roads. These measures significantly impacted the lives of PWE and medical treatments, including postponing outpatient appointments, difficulties in obtaining prescription renewals or contacting doctors, cancellation of epilepsy-related tests, and less access to emergency departments due to saturation of health services and fear of infection [12]. An important alternative to repair the postponement of medical appointments and to improve doctor–patient communication is telemedicine [13]. Although the modality started more than 20 years ago it only recently became possible due to technological advance [14].

Epilepsy affects physical, behavioral, and mental functions and there are frequent comorbidities such as psychiatric disorders, like depression, psychoses, and anxiety, which affect 1 in 3 PWE [15]. During the pandemic, people have faced a higher level of stress. Daily updates on the number of cases and mortality, lack of information about the virus, false news, uncertainty about the future, and the need for social isolation resulted in increased psychological problems and sleep disorders, more intense in PWE [16,17]. Surveys carried out in several countries point out significant impact of the pandemic in this population [11,17]. The aim of this study was to assess how PWE in Brazil are being affected by the pandemic, with regard to seizure frequency, medical follow-up, prescriptions, access to medicines, and well-being.

2. Methods

An online questionnaire survey among PWE was applied between August 1st and October 10th, 2020 in Brazil. During the study period the country was in social isolation but not in full lockdown. The healthcare services were focused on COVID-19 interventions such as measures of physical distancing that were recommended by regional and local governments. After approval of the local Ethics Committee (CAAE 33078820.0.0000.8647), an anonymous questionnaire composed of 46 generic questions developed on Google Docs® was divulged in the social networks of the Brazilian Epilepsy Association, the official Brazilian chapter of the International Bureau for Epilepsy. All participants consented

virtually for inclusion, either PWE older than 18 years (group 1) or caregivers (group 2). The caregivers were asked to answer regarding the patient's situation. Although caregiver report of quality of life may be not accurate, we considered these answers as a valid exploratory information.

This questionnaire was composed of four areas, namely, demographics and baseline clinical data as well as epilepsy and quality-of-life impact by COVID-19 pandemic. All questions had one of multiple choice except two regarding age and state of residence, and another related to leisure activities. Likert-type quality-of-life questions were based on the domains of the abbreviated World Health Organization Quality of Life (WHOQOL-BREF) instrument [18,19]. The domains evaluated were physical health, psychological sphere, social relations, and environment. Supplementary Tables 1 and 2 show the questions and domains of the survey.

2.1. Statistical analysis

Descriptive and frequency statistical analyses were obtained, and comparisons were made by the SPSS 14.0 program (SPSS Inc. - Chicago) and Statistica 7 (StatSoft Inc). Categorical variables were reported as frequencies (percentages) and continuous variables as the mean \pm standard deviation (SD). Percentages were analyzed and compared by Fisher's exact test. Statistical significance in comparisons between the quantitative variables studied was assessed using One-Way ANOVA and Logistic Regression. Odds ratios (ORs) and 95% confidence intervals (CIs) were shown in the final model and p-values <0.050 were considered statistically significant.

3. Results

3.1. Demographics and clinical data

The questionnaire was answered by 464 participants including 380 (81.9%) adult PWE and 84 (18.1%) caregivers, mainly from the richest areas in the country. Regarding adult PWE, 36.5% had college education and most lived with family, either parents (27.1%), spouse and/or children (45.2%).

Most PWE were taking 1 or 2 antiseizure medicines (ASM) as shown in Table 2. Patient's use of antidepressants was reported by 44.5% of adult PWE and 37.3% of caregivers. Healthcare providers consisted of Brazilian free universal public system in about one-third of the cases, which is different from the governmental data that report that around 70% of the Brazilian population do not have access to private or preferred provider organization (PPO) care [20]. This fact may be a bias, due to more internet access in the richest areas of the country and consequently higher rates of PWE who could afford these latter types of health care. Table 1 describes demographics and clinical data.

3.2. Epilepsy during pandemic

Increase in seizure frequency was pointed in about one-quarter of patients during pandemic. Lack of availability of ASM was reported both in public dispensing units and private pharmacies. Participants had difficulties with prescription renewals and access to the healthcare provider for epilepsy treatment and a great number of them had appointments postponed or canceled. Before the COVID-19 pandemic direct telehealth and electronic ASM prescriptions were not allowed in Brazil. After March 2020 they were available mainly in private and PPO health care. Telemedicine was unavailable for most of PWE. Epilepsy and use of ASM were considered risk factors for COVID-19 by some participants. Data about treatment during pandemic are presented in Table 2.

Table 1
Demographics and clinical data.

Participant (n)	PWE (380)	Caregivers (84)	p-value
Patient age in years (SD)	34.3 (9.76)	14.1 (10.30)	<0.001
Female % (n)	78.7 (299)	43.2 (51)	<0.001
Schooling (maximal level)			
Elementary school % (n)	3.8 (14)	-	-
High school % (n)	41.1(151)	-	-
College % (n)	36.5 (134)	-	-
Graduation/Master % (n)	8.2 (30)	-	-
Specialization % (n)	10.4 (38)	-	-
Brazilian region			0.139
West center % (n)	8.1 (30)	12.3 (14)	
North % (n)	5.1 (19)	6.1 (7)	
Northeast % (n)	10.5 (39)	13.2 (15)	
South % (n)	22.8 (85)	13.2 (15)	
Southeast % (n)	53.5 (199)	55.3 (63)	
Type of healthcare provider			0.955
Public system % (n)	36.8 (140)	38.1 (45)	
PPO % (n)	33.7 (128)	33.9 (40)	
Private % (n)	29.5 (112)	28.0 (33)	
Number of ASM			<0.001
One % (n)	40.3 (153)	32.2 (38)	
Two % (n)	32.1 (122)	19.5 (23)	
Three % (n)	17.4 (66)	23.7 (28)	
>Three % (n)	10.3 (39)	24.6 (29)	
Drug-resistant epilepsy % (n)	35.5 (135)	55.1 (65)	<0.001
Seizure Frequency before pandemic			<0.001
Every day % (n)	3.4 (13)	12.7 (15)	
Most days % (n)	3.9 (15)	8.5 (10)	
At least once a week % (n)	12.4 (47)	12.7 (15)	
Sporadic % (n)	80.3 (305)	66.1 (78)	

PWE: people with epilepsy; ASM: antiseizure medicines; PPO: preferred provider organization.

3.3. Quality-of-life aspects during COVID-19 pandemic

3.3.1. Health

Dissatisfaction with health status was reported by 36.7% and 38.1% in groups 1 and 2, and possibility of performance of usual obligations during the pandemic were reported only by 18.7% and 16.9%, respectively. Resting and relaxing was feasible in 21.8% and 17.8% in groups 1 and 2. Patient sleep deprivation was mentioned in 32.9% of PWE and by 33.9% of caregivers. Only 17.1% of PWE considered their sleep latency as adequate followed by a full night sleep, with similar values in the other group (17.8%).

3.3.2. Psychological

There were several psychological concerns of the participants who answered affirmatively some questions described in Table 3.

3.3.3. Social relations and environment

Loneliness during pandemic was reported by 30% in both groups and most related that the support from others has decreased (56.1% in group 1 and 66.1% in 2). Economic difficulties were reported by 23.5% and 30.5% of groups 1 and 2, and full isolation at home was reported by 40.8% and 55.9%, respectively. Leisure activities mostly cited were music listening, watching television and internet browsing.

3.4. Seizure worsening and COVID-19 beliefs

3.4.1. Seizure frequency increase, treatment and quality of life during pandemic

Patients who had increase in seizure frequency during COVID-19 pandemic had more frequently reported problems with treatment and quality-of-life aspects. Table 4 shows the concerns of this subgroup of participants ($p < 0.050$).

Table 2
Epilepsy treatment during COVID-19 pandemic.

Participants (n)	PWE (380) % (n)	Caregivers (84) % (n)	p-value
Increase in seizure frequency	26.3 (100)	27.9 (33)	0.188
Difficulties to access healthcare provider for epilepsy	36.8 (140)	36.4 (43)	1.000
Regular medical visits			0.021
Performed	29.7 (113)	32.2 (38)	
Postponed	12.9 (49)	21.2 (25)	
Cancelled	14.5 (55)	17.8 (21)	
Not scheduled for this period	42.9 (163)	28.8 (34)	
Prescription renewals not available	6.8 (26)	5.9 (7)	0.958
ASM not available			
Public dispensing units	21.9 (83)	28.0 (33)	0.009
Private pharmacies	19.2 (73)	17.8 (21)	0.038
Telehealth			
Visits and phone contact not available	66.6 (253)	58.5 (69)	0.071
Electronic prescriptions available	10 (38)	14.3 (17)	0.501
Concerns			
Epilepsy as risk factor for COVID-19	36.3 (138)	58.5 (69)	<0.001
ASM as risk factor for COVID-19	16.8 (64)	11 (13)	0.120
Severe COVID-19 due to epilepsy	74.5 (283)	89.8 (106)	<0.001

PWE: people with epilepsy; ASM: antiseizure medicines.

Table 3
Most frequent psychological concerns of participants during pandemic.

Questions with affirmative answers	PWE (n = 380) % (n)	Caregivers (n = 84) % (n)	p-value
Very worried about COVID-19	21.8 (83)	22.0 (26)	0.815
Too much difficulty in concentrating	25.0 (95)	22.0 (26)	0.389
Affected to make decisions	52.1 (198)	42.4 (50)	0.312
General insecurity	51.3 (195)	47.5 (56)	0.260
Not optimistic about the future	66.8 (252)	57.6 (68)	0.230
Feeling bad emotionally	48.2 (183)	37.3 (44)	0.073
Not taking care of physical appearance	18.9 (72)	26.3 (31)	0.029
Butterflies in stomach	25.8 (98)	16.1 (19)	0.093
Regarding isolation			
Frequent feelings of sadness	25.0% (95)	21.2% (25)	0.430
Joy in staying at home	8.9% (34)	9.3% (11)	0.430
Regarding epilepsy			
Insecurity in doing new activities	49.8(189)	46.7(55)	0.260

PWE: people with epilepsy.

The factors with higher risk of increase in seizure frequency during pandemic were age older than 41 years, treatment in public healthcare system, drug resistant epilepsy, daily seizures before pandemic, use of more than 3 ASM, difficulties in getting ASM in public dispensing units, need to initiate or increase the dose of antidepressant drugs, adversities with prescriptions, current financial problems and the belief that epilepsy or ASM are risk factors for contracting COVID-19. These values are shown in Table 5 and in Supplementary Fig. 1.

3.4.2. Fear of COVID-19

Some variables were associated with fear of having COVID-19 and are described in Table 6 and in Supplementary Fig. 1. There were no significant differences regarding region of residence within the country.

Table 4
Comparison of people with increased seizure frequency with those without worsening during pandemic.

Questions with affirmative answers	p-value
Difficulties of getting ASM in public dispensing units	0.044
Difficulties with prescription renewals	0.008
Difficulties with electronic prescriptions	0.004
Difficulties in usual obligations	0.018
Easily tired	<0.001
Sleep problems	0.001
Dissatisfaction with health status	0.003
Very worried, COVID-19-related thoughts all time	0.002
Too much difficulty in concentrating	<0.001
Affected to make decisions	<0.001
General insecurity	0.001
Not optimistic about the future	0.003
Feeling bad emotionally	<0.001
Not taking care of physical appearance	0.014
Butterflies in stomach	<0.001
Belief that epilepsy is a risk factor for having COVID-19	0.024
Belief that taking ASM is a risk factor for having COVID-19	0.006
Regarding isolation	
Frequent feelings of sadness	<0.001
Joy in staying at home	<0.001
Regarding epilepsy	
Insecurity in doing new activities	0.003

ASM: antiseizure medicines.

Table 5
Odds Ratio (OR) for having increase of seizure frequency during pandemic (p<0.050).

Increase of seizure frequency during pandemic	OR	IC95%	p-value
Demographic data and answers with p-value ≤0.050		min ; max	
Age >41 years	2.28	1.38 ; 3.75	0.001
Public system healthcare treatment	1.69	1.06 ; 2.68	0.027
Drug-resistant epilepsy	3.24	2.02 ; 5.20	<0.001
Seizure frequency before pandemic: daily or most days	2.64	1.21 ; 5.77	0.012
≥3 ASM	2.82	1.73 ; 4.59	<0.001
PWE with difficulties in getting ASM in public dispensing units vs PWE who buy ASM in private pharmacies	2.24	1.29 ; 3.90	0.004
Antidepressant drugs: initiation or dose increase vs no use	2.23	1.21 ; 4.12	0.009
Difficulties with prescription renewals	1.69	1.03 ; 2.75	0.037
Lack of ASM due to difficulties with prescription renewals	3.18	1.38 ; 7.32	0.005
Current financial difficulties	2.88	1.48 ; 5.61	0.001
Belief epilepsy as risk factor for COVID-19	2.16	1.21 ; 3.83	0.008
Belief ASM increase the risk for COVID-19	2.64	1.41 ; 4.93	0.002

OR: Odds Ratio.

4. Discussion

This online survey carried out during the first 6-8 months of COVID-19 pandemic with 380 PWE and 84 caregivers composed mostly by residents in the richest areas of Brazil without drug resistant epilepsy has raised several concerns, namely problems in accessing the healthcare system including ASM dispensation and telehealth and fear of having a more severe COVID-19 because of epilepsy. Increase in seizure frequency was reported by circa one-fourth of participants who had also more difficulties with prescription renewals, ASM dispensing, beliefs of higher risk of having COVID-19, psychological and physical complaints regarding health quality-of-life aspects than those without worsening of seizures.

Table 6
Odds Ratio (OR) for having fear of contracting COVID-19 (p ≤ 0.050).

Fear of contracting COVID-19	OR	IC95%	p-value
Demographic and answers with p-value ≤0.050		min ; max	
Female	2.40	1.42 ; 4.06	0.001
Elementary or High school vs College	2.09	1.27 ; 3.42	0.003
Seizure frequency before pandemic: daily or most days	4.81	1.12 ; 20.64	0.021
PWE with difficulties in getting ASM in public dispensing units during pandemic vs PWE who buy ASM in private pharmacies	2.93	1.42 ; 6.06	0.003
Current financial difficulties	1.94	0.99 ; 3.80	0.053
Belief epilepsy as risk factor for COVID-19	10.89	5.34 ; 22.19	<0.001
Belief ASM increase the risk for COVID-19	3.05	1.44 ; 6.46	<0.001

Difficulties in accessing health care for epilepsy treatment was a common finding in our survey, as well as with ASM supplies, in agreement with data published in other nations regardless of the national income [17,21,24,26,27]. Telemedicine was scarcely provided in our sample compared to other countries [11,21-25]. Interestingly, reports of low availability of ASM in private pharmacies were present in our study, which may be due to difficulties with pharmaceutical supplies and commercial logistics. These facts during the present sanitary crisis will probably increase the problems regarding the care of PWE worldwide especially in low-resource areas with possible prolonged effects. According to the Pan American Health Organization (PAHO) the estimated gap in epilepsy treatment is approximately 75% and 50%, in low and middle-income countries, respectively [28].

Increase in seizure frequency was reported by circa one-fourth of the participants of our study. These patients were older, had more frequently severe epilepsy, difficulties with prescription renewals and ASM dispensing, especially in the Brazilian public healthcare system. Seizure worsening was reported in other studies during the pandemic, which ranged from 4-35% of the surveyed population [11,20,23,25-27,29,30-32]. Physical and psychological concerns including beliefs of higher risk of having COVID-19, with new onset use of antidepressants and financial problems were also related to seizure worsening. Increase in seizure frequency due to psychological stress is well known in epilepsy, and probably played an important role during pandemic [31].

We are not aware of other studies that evaluated quality-of-life aspects during COVID-19 pandemic in PWE. Although we did not use a standardized questionnaire, our survey had questions related to the WHO-QOL BREF instrument. Dissatisfaction with health status was reported by circa one-third of the participants as well as several problems regarding physical and psychological aspects that could affect mental health issues and seizure frequency. We have no data on health satisfaction and mental health issues before the pandemic, which limits further conclusions. Other studies showed anxiety and emotional problems through validated scales in PWE attending medical visits during this period [17,33]. Sleep deprivation was reported by one-third of participants which was also mentioned in other studies [21,31] that might have affected seizure frequency.

Social relations were similarly affected with reduction of support from others. This fact is very concerning since the difficulties faced by PWE, namely in social relations, are very important in terms of quality of life and stigma [34]. Although this sample was probably biased towards a less vulnerable socio-economic group, financial difficulties were reported. This raises concerns mainly in developing countries due to inequalities, resource constraints which have been mostly affected by the impact of

COVID-19 [35]. Leisure activities were carried out at home, in a sedentary form basically involving intellectual tasks. The low levels of physical activity may have further affected mental health and aggravated seizures [36].

Fear of having a more severe COVID-19 due to epilepsy was reported in our study mainly by caregivers. Also, the fear of contracting COVID-19 was higher in females, people with low schooling and financial restrictions besides those who presented difficulties in getting ASM in public dispensing units and with more severe epilepsy. The same findings were reported by other authors [37]. The misconceptions that epilepsy and ASM are associated with an increased risk of having COVID-19 reveal a window of opportunity for patient associations to offer scientific information for promoting quality of life as well stigma reduction in PWE.

5. Limitations

Online surveys are always subject to bias considering internet access and psychological profile of the persons in adhering to this type of activity. Most of the participants were female which may reflect some of the concerns biased by sex. The poorest areas of Brazil were not well represented in the survey probably because of schooling and internet access limitations. This could have masked more specific regional difficulties with health care and quality-of-life aspects. Duration and time of the study, carried out during the pandemic, with rapidly evolving changes in the sanitary crisis, are other limitations of the present study.

6. Conclusions

During pandemic PWE and caregivers reported through an online survey of the Brazilian Association of Epilepsy seizure worsening in one-fourth of participants as well several difficulties, namely problems in accessing the healthcare system including ASM dispensation, telehealth, and fear of having a more severe COVID-19 because of epilepsy. There were also physical, psychological, and social concerns which affected quality-of-life aspects in this population. These facts may increase treatment gap in epilepsy in Brazil as well as in other developing countries and the worsening of the health conditions of this population as a public health priority should be stressed.

Declaration of Competing Interest

We have no conflicts of interest to declare. All authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yebeh.2021.108115>.

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