Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Impact of COVID-19 on quality of life in people with epilepsy, and a multinational comparison of clinical and psychological impacts

May-Yi Koh, Kheng-Seang Lim *, Si-Lei Fong, Si-Bao Khor, Chong-Tin Tan

Division of Neurology, Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

A R T I C L E I N F O

Article history:
Received 17 December 2020
Revised 2 February 2021
Accepted 3 February 2021
Available online 10 February 2021

Keywords:
COVID-19
Epilepsy
Seizure control
Quality of life
Depression
Anxiety

A B S T R A C T

Background: This study aimed to determine the relationship among the clinical, logistic, and psychological impacts of COVID-19 on people with epilepsy (PWE), and the impact of COVID-19 on the quality of life.

Method: This is a cross-sectional anonymized web-based study on PWE, using an online questionnaire to assess the clinical, logistic, and psychological impacts of COVID-19, including Hospital Anxiety Depression Scale (HADS) and Quality of Life in Epilepsy Inventory (QOLIE-31).

Result: 461 patients were recruited, with a mean age of 39.21 ± 15.88 years, majority female (50.1%), with focal epilepsy (54.0%), and experienced seizures at least once yearly (62.5%). There were 13.0% experienced seizure worsening during COVID-19 period, which were associated with baseline seizures frequency >1 per month (32.0% vs. 6.2%, p < 0.001), worries of seizure worsening (18.0% vs. 10.9%, p < 0.001), difficulty to go emergency unit (24.4% vs. 10.4%, p < 0.001), AEDs ran out of stock (23.2% vs. 11.6%, p < 0.001), self-adjustment of AED dosages (26.4% vs. 11.3%, p < 0.001), inadequate sleep (22.4% vs. 9.2%, p < 0.001), and stress (23.4% vs.10.1%, p < 0.001). Participants experiencing seizure worsening reported greater anxiety (8.10 ± 5.011 vs. 4.84 ± 3.989, p < 0.001) and depression (6.05 ± 3.868 vs. 3.86 ± 3.589, p < 0.001). Logistic regression showed baseline seizures frequency >1 per month (OR, 14.10) followed by anxiety (OR, 3.90), inadequate sleep (OR, 0.37), and treated in UMMC (OR, 0.31) as the predictors for seizure worsening during COVID-19 period. Poorer total QOLIE-31 score was noted in those with seizure worsening (48.01 ± 13.040 vs. 62.15 ± 15.222, p < 0.001). Stepwise regression highlighted depression as the main negative predictor for quality of life (b = −0.372, p < 0.001), followed by anxiety (b = −0.345, p < 0.001).

Conclusion: A significant number of PWE experienced seizure worsening during COVID-19 period, which was related to the clinical, logistic, and psychological factors. Quality of life was affected by the seizure worsening and the psychological stress.

© 2021 Elsevier Inc. All rights reserved.

1. Introduction

Epilepsy is a chronic illness requiring regular monitoring of seizure control, antiepileptic drugs (AEDs) and its side effects, and psychosocial comorbidities [1]. Since the first reported case of coronavirus disease 2019 (2019-nCoV) in Wuhan, China on 8 December 2019, the outbreak has spread around the world [2]. In Malaysia, the government took stringent precautionary measures to combat the spread of this disease by implementing the movement restriction control order (MCO) on 18th March 2020 through mandatory social distancing and lockdown [3]. The complete restriction of movement and assembly resulted in postponement of healthcare visits in Malaysia, similarly in many other countries. This unprecedented loss of access to healthcare is postulated to give rise to worsening seizure control and anxiety, which were reported in many countries in most continents, including China [4–6], Hong Kong [7], Pakistan [8], and Saudi Arabia [9] in Asia, Brazil [10] in South America, Spain [11,12] and Italy [13] in Europe, and United Stated of America [14]. However, most studies analyzes mainly the direct impact of AEDs on the psychological and clinical consequences, but not the access to emergency and outpatient services.

Therefore, we aimed to determine the relationship among the clinical, logistic, and psychological impacts of COVID-19 on people with epilepsy (PWE) in Malaysia, which is an upper middle-income country located in southeast Asia, adopting the British public-health medical services. In addition, we also aimed to study the impact of COVID-19 on the quality of life in PWE. To the best of our knowledge, the impact of COVID-19 on the quality of life in PWE has never been reported before.
2. Methodology

2.1. Sampling and framework

This is a cross-sectional anonymized web-based study involving 461 PWE, 18 years and above, can read English, Bahasa Malaysia, and Mandarin, with a diagnosis of epilepsy certified by neurologists, and were treated in adult neurology clinic in University Malaya Medical Centre (UMMC) or a member of the Malaysian Epilepsy Society (MES). MES is the national epilepsy society for PWE and their family members. Those who refused or unable to provide consent, or without a history of seizures were excluded. This study was approved by the University Malaya Medical Ethics Committee (MECID. No. 2020420–8539).

The recruitment was performed using convenience sampling. The invitation links to online questionnaires were sent via short messages (SMS), email or Facebook. Patients with epilepsy in the clinic were also approached physically. Participants have an option to leave their contact details at the end of the survey or to remain anonymous.

2.2. Measures

An online questionnaire was designed to assess the clinical, logistic, and psychological impacts of COVID-19 on PWE. Informed consent was obtained online prior to the study. Socio-demographic and clinical information were collected. The impacts of COVID-19 were assessed in 3 sections, included (1) clinical impact: seizure control, (2) logistic impact: access to clinic appointment, emergency services, and AED supply, and (3) psychological impact: assessed using validated Hospital Anxiety Depression Scale (HADS) and Quality of Life in Epilepsy Inventory (QOLIE-31). This questionnaire was sent to PWE from June 7 to July 5, 2020, 134 days after the first COVID-19 case was confirmed in Malaysia and 81 days since the implementation of MCO, with a reported 8, 663 cumulative cases as of July 5.

2.2.1. Hospital Anxiety and Depression Scale (HADS)

Hospital Anxiety Depression Scale (HADS) is used as a tool to measure anxiety and depression in patients with general medical condition [15]. It is a 14-item self-administered questionnaire consisting of two subscales, anxiety and depression. The subscale of anxiety focused on symptoms of generalized anxiety disorder and subscale of depression focused on anhedonia, and main symptoms of depression. Each item was scored on a response-scale with four alternatives ranging between 0 and 3. The responses were summed to obtain the total score for each subscale. The total score for each subscale were then categorized into normal (0–7), and abnormal – borderline (8–10) and definite (11–21). HADS was validated in epilepsy cohort, age 18 years and above, with high internal consistency reported for HAD-Anxiety (Cronbach’s α = 0.88) and HAD-Depression (Cronbach’s α = 0.82) [16].

2.2.2. Quality of Life in Epilepsy Inventory (QOLIE-31)

The QOLIE-31 has been widely cited as a reliable instrument (Cronbach’s α = 0.93) to assess epilepsy-related QOL [17]. It is a 31-item self-administered questionnaire clustered in seven subscales in the following domains: seizure worry (five items), emotional well-being (five items), energy/fatigue (four items), cognitive functioning (six items), medication effects (three items), social functioning (five items), and overall QOL (two items). The seven subscales generate a QOLIE-31 overall score representing the overall epilepsy-related quality of life. Each subscale and the overall score range from 0 to 100, with higher scores indicating better wellbeing.

2.3. Operational definition

Baseline seizure frequency was defined as the frequency of seizures in the previous 12 months before COVID-19 outbreak. Seizure control during COVID-19 period was determined based on the changes of seizure frequency, duration, or severity. Seizure worsening was defined with an increased in seizure frequency, duration, or severity.

2.4. Sample size calculation

The sample size was calculated to achieve an alpha level of 0.05 and a power of 0.80 in a two-tailed independent t-test. The effect size (Cohen’s d) was assumed to be 0.35 to detect a low to medium effect. A minimum of 260 samples were needed to achieve these parameters.

2.5. Analyses and results

Statistical analysis using IBM® SPSS® Statistics software (version 25.0) was performed with significance level defined at 0.05. All demographic data were analyzed descriptively, with nominal data presented as frequencies and percentages and continuous data presented as means and standard variations. For continuous data, independent t-tests were used for group comparison. Multivariate logistic regression analysis was carried out to ascertain the significant predictors for seizure worsening during COVID-19 period. Variables associated with a p < 0.05 in the univariate analysis were entered in a forward stepwise multiple logistic regression model. Stepwise linear regression analysis was carried out to ascertain whether seizure control during COVID-19 period and the psychological factors predicted quality of life (QOLIE-31 score).

2.6. Multinational comparison on clinical and psychological impacts on epilepsy

A literature search was performed on recent studies reporting the clinical or psychological impacts of COVID-19 on people with epilepsy. The clinical impact was defined as the percentage of participants with either increased seizure frequency or worsening seizure control. Psychological impacts were determined by the percentages of participants who were screened positive for or reported anxiety and depression using various psychological scales. The Gross Domestic Product (GDP) per capita was accessed from the International Monetary Fund report in October 2020 [18].

3. Results

A total of 461 patients were included in this study, with a respondent rate of 64.8%. The mean age was 39.21 ± 15.88 years, and 50.1% were female, majority Chinese (45.1%), single (57.5%), with secondary education level or lower (55.5%), and 39.7% employed. The mean age of seizure onset was 20.85 ± 15.72 years. Majority had focal epilepsy (54.0%), experienced seizures at least once yearly (62.5%), with abnormal EEG (67.2%) and neuroimaging results (55.1%). A hundred ninety (41.2%) had tried at least 3 types of AEDs for seizure control while another 12.4% had epilepsy surgery. None of our patients or their care takers reported being infected with SARS-CoV-2 at the time of data collection (Table 1).

3.1. Clinical, logistic, and psychological impacts

There were 11.1% reported increased seizure frequency during COVID-19 period, 4.3% and 7.4% experienced longer seizure duration and severity, respectively. In total, 13.0% experienced seizure...
Table 1

Sociodemographic and clinical characteristics of the participants, and the clinical, logistic, and psychological impacts of COVID-19 pandemic (N = 461).

| Characteristics                                      | Mean ± Standard Deviation |
|-------------------------------------------------------|---------------------------|
| **Age (Year)**                                        | 39.21 ± 15.88             |
| **Gender**                                            |                           |
| Male                                                   | 230 (49.9)                |
| Female                                                 | 231 (50.1)                |
| **Race**                                              |                           |
| Malay                                                  | 139 (30.2)                |
| Chinese                                                | 208 (45.1)                |
| Indian                                                 | 103 (22.3)                |
| Native                                                 | 2 (0.4)                   |
| Others                                                 | 9 (2.0)                   |
| **Marital Status**                                    |                           |
| Single                                                 | 265 (57.5)                |
| Others                                                 | 196 (42.5)                |
| **Highest Education Attained**                        |                           |
| Postgraduate                                           | 15 (3.3)                  |
| Degree                                                 | 115 (24.9)                |
| A Level/STPM/Diploma                                   | 75 (16.3)                 |
| Secondary                                              | 194 (42.1)                |
| Primary                                                | 31 (6.7)                  |
| No formal education                                    | 31 (6.7)                  |
| **Employment Status**                                 |                           |
| Full time student                                      | 42 (9.1)                  |
| Employed full time                                     | 162 (35.1)                |
| Employed part time                                     | 21 (4.6)                  |
| Full time house duties/Housewife                       | 22 (4.8)                  |
| Retired                                                | 63 (13.7)                 |
| Unemployed                                             | 151 (32.8)                |
| **Clinical characteristics**                           |                           |
| Frequency of seizures before COVID-19 outbreak         |                           |
| No seizure for at least a year                         | 173 (37.5)                |
| Less than once a month                                 | 166 (36.0)                |
| One or more seizures a month                           | 122 (26.5)                |
| **Type of seizure**                                   |                           |
| Focal                                                  | 249 (54.0)                |
| Generalized                                            | 193 (41.9)                |
| Unsure                                                 | 19 (4.1)                  |
| **EEG Results**                                        |                           |
| Abnormal                                               | 310 (67.2)                |
| Normal                                                 | 106 (23.0)                |
| Unsure/Not done                                        | 45 (9.8)                  |
| **CT scan/MRI Results**                               |                           |
| Abnormal                                               | 254 (55.1)                |
| Normal                                                 | 138 (29.9)                |
| Unsure/Not done                                        | 69 (15.0)                 |
| **Types of medication tried (Before and Now)**         |                           |
| 1                                                      | 144 (31.2)                |
| 2                                                      | 127 (27.5)                |
| 3 or more                                              | 190 (41.2)                |
| Surgery to control seizure                             |                           |
| Yes                                                    | 57 (12.4)                 |
| No                                                     | 402 (87.2)                |
| Unsure                                                 | 2 (0.4)                   |
| **Clinical impact**                                   |                           |
| Seizure Frequency                                      |                           |
| More frequent                                          | 51 (11.1)                 |
| No change                                              | 115 (24.9)                |
| Less frequent                                          | 79 (17.1)                 |
| No seizure                                             | 216 (46.9)                |
| Seizure Duration                                       |                           |
| Longer                                                 | 20 (4.3)                  |
| No change                                              | 157 (34.1)                |
| Shorter                                                | 63 (13.7)                 |
| No seizure                                             | 221 (47.9)                |
| Seizure Severity                                       |                           |
| More severe                                            | 34 (7.4)                  |
| No change                                              | 148 (32.1)                |
| Less severe                                            | 56 (12.1)                 |
| No seizure                                             | 223 (48.4)                |
| Seizure Worsening*                                     |                           |
| Yes                                                    | 60 (13.0)                 |
| No                                                     | 401 (87.0)                |
| Causes of seizures worsening                           |                           |

(continued on next page)
Table 1 (continued)

| Reason for Not Taking Medications | Mean ± Standard Deviation |
|-----------------------------------|---------------------------|
| Not enough sleep                  | 125 (28.3)                |
| Stress                            | 107 (24.0)                |
| Missed medication dosage          | 62 (14.1)                 |
| Inadequate medication supply      | 10 (2.3)                  |
| Fever                             | 24 (5.5)                  |
| Physical tiredness                | 86 (19.5)                 |
| Diet                              | 23 (5.2)                  |
| Unsure                            | 76 (17.2)                 |
| Seizure no change                 | 181 (40.2)                |
| No seizure                        | 18 (4.1)                  |
| Others:                           | 13 (10.4)                 |

Logistic Impact

Difficulty re-schedule clinic appointments

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Strongly disagree | 76 (16.5) |
| Disagree       | 106 (23.0)               |
| Neutral        | 159 (34.5)               |
| Agree          | 73 (15.8)                |
| Strongly agree | 47 (10.2)                |

Worries seizures get worse because my clinic appointments were postponed

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Strongly disagree | 86 (18.7) |
| Disagree       | 103 (22.3)               |
| Neutral        | 133 (28.9)               |
| Agree          | 93 (20.2)                |
| Strongly agree | 46 (10.0)                |

Access to online or tele-consultation

| Frequency | Mean ± Standard Deviation |
|-----------|---------------------------|
| Never     | 284 (61.6)                |
| Occasionally | 57 (12.4) |
| Sometimes | 69 (15.0)                 |
| Often     | 28 (6.1)                  |
| Always    | 23 (5.0)                  |

Afraid to go to Emergency Unit

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Strongly disagree | 93 (20.2) |
| Disagree       | 118 (25.6)               |
| Neutral        | 117 (25.4)               |
| Agree          | 80 (17.4)                |
| Strongly agree | 53 (11.5)                |

Difficulty to go to Emergency Unit

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Strongly disagree | 105 (22.8) |
| Disagree       | 128 (27.8)               |
| Neutral        | 142 (30.8)               |
| Agree          | 59 (12.8)                |
| Strongly agree | 27 (5.9)                 |

Understand need to go to Emergency Unit

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Yes      | 372 (80.7)                |
| No       | 89 (19.3)                 |

Adequately informed on what to do in the event of seizures

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Yes      | 363 (78.7)                |
| No       | 98 (21.3)                 |

Obtain supply of medications from

| Source | Mean ± Standard Deviation |
|--------|---------------------------|
| University Malaya Medical Centre | 407 (88.3) |
| Other university hospital       | 5 (1.1)   |
| Ministry of Health Malaysia hospital or clinic | 24 (5.2) |
| Private hospital or clinic      | 5 (1.1)   |
| Private pharmacies              | 20 (4.3)  |

Difficult to obtain medications

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Strongly disagree | 89 (19.3) |
| Disagree       | 135 (29.3)               |
| Neutral        | 125 (27.1)               |
| Agree          | 72 (15.6)                |
| Strongly agree | 40 (8.7)                 |

Procedures to arrange for medication delivery via postage are complicated

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Strongly disagree | 66 (14.3) |
| Disagree       | 106 (23.0)               |
| Neutral        | 166 (36.0)               |
| Agree          | 73 (15.8)                |
| Strongly agree | 50 (10.8)                |

Procedures to arrange for medication self-collection via “pick-and-go” or “drive-through” are complicated

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Strongly disagree | 56 (12.1) |
| Disagree       | 96 (20.8)                |
| Neutral        | 218 (47.3)               |
| Agree          | 63 (13.7)                |
| Strongly agree | 28 (6.1)                 |

Medications ran out of stock

| Response | Mean ± Standard Deviation |
|----------|---------------------------|
| Strongly disagree | 112 (24.3) |
Seizure worsening was more frequently reported in those with baseline seizures frequency ≥1 per month (32.0%) as compared to others with no seizure for at least a year (2.3%) and < 1 per month (10.2%, p < 0.001). Seizure worsening was also reported in patients who tried at least 3 AEDs (21.1% vs. 8.3% with 1 AED or 6.3% with 2 AEDs, p < 0.001), worries of seizure worsening (18.0% vs. 10.9% with no worries at all, p < 0.001), difficulty to go emergency unit (24.4% vs. 10.4% with no difficulty, p < 0.001), AEDs ran out of stock (23.2% vs. 11.6%, p < 0.05), self-adjustment of AED dosages (26.4% vs. 11.3%, p < 0.001), and inadequate sleep (22.4% vs. 9.2%, p < 0.001) and stress (23.4% vs. 10.1%, p < 0.01). Less patients in our hospital (UMMC) reported seizure worsening as compared to other hospitals (11.4% vs. 29.3%, p < 0.01). Participants experiencing seizure worsening reported greater anxiety (8.10 ± 5.011 vs. 4.84 ± 3.989, p < 0.001) and depression (6.05 ± 3.868 vs. 3.86 ± 3.589, p < 0.001) (Table 2).

A binary logistic regression analysis was conducted to investigate the predictors of seizure worsening. Among the 12 variables that correlated significantly with seizure worsening, 4 variables (stress as a precipitating factor, medication ran out of stock, difficulty to arrange self-pick-up, worries seizures get worse because of postponed clinic appointments) were excluded because of strong correlation with other independent variables. The full model containing all predictors was statistically significant, χ²(8, N = 461) = 96.49, p < 0.001. The model correctly classified 89.1% of cases. The strongest predictor for seizure worsening during COVID-19 period was baseline seizures frequency ≥ 1 per month (OR, 14.10), followed by anxiety (OR, 3.90), inadequate sleep (OR, 3.07) and treatment at UMMC (OR, 0.31) (see Table 3).

3.3. Quality of life in epilepsy

Poorer total QOLIE-31 score was noted in those with seizure worsening (48.01 ± 13.040 vs. 62.15 ± 15.222 in those with no change or improve in seizure control, p < 0.001), similarly in all subscales except medication effects (Table 2). Stepwise linear regression was conducted to determine whether seizure control predicted QOLIE-31 score in step 1, which explained 9% of the variance, F(1, 453) = 46.8, p < 0.001. Subsequent psychological factors (HADS anxiety and depression scores) were entered at Step 2, which further explained an additional 42% of the variance in predicting QOLIE-31 during COVID-19 period. All measures were statistically significant, F(3, 451) = 158.4, p < 0.001, with depression recording the highest beta value (β = −0.372, p < 0.001) (Table 4).

Table 1 (continued)

| Psychological Impact | Mean ± Standard Deviation |
|----------------------|---------------------------|
| HADS-Anxiety         |                           |
| Normal               | 334 (72.5)                |
| Borderline           | 80 (17.4)                 |
| Abnormal             | 47 (10.2)                 |
| HADS-Depression      |                           |
| Normal               | 374 (81.1)                |
| Borderline           | 55 (11.9)                 |
| Abnormal             | 32 (6.9)                  |

*Seizure worsening is defined as an increased in seizure frequency, duration, or severity.

| Question                                                                 | Mean ± Standard Deviation |
|--------------------------------------------------------------------------|---------------------------|
| I have skipped my medications to avoid running out of supply             |                           |
| Never                                                                    | 345 (74.8)                |
| Rarely                                                                   | 50 (10.8)                 |
| Sometimes                                                                | 50 (10.8)                 |
| Often                                                                    | 10 (2.2)                  |
| Always                                                                   | 5 (1.3)                   |
| I have adjusted the dose of my medications without consulting my doctor |                           |
| to avoid running out of supply                                           |                           |
| Never                                                                    | 369 (80.0)                |
| Rarely                                                                   | 39 (8.5)                  |
| Sometimes                                                                | 32 (6.9)                  |
| Often                                                                    | 11 (2.4)                  |
| Always                                                                   | 10 (2.2)                  |

| Psychological Impact | Mean ± Standard Deviation |
|----------------------|---------------------------|
| HADS-Anxiety         |                           |
| Normal               | 334 (72.5)                |
| Borderline           | 80 (17.4)                 |
| Abnormal             | 47 (10.2)                 |
| HADS-Depression      |                           |
| Normal               | 374 (81.1)                |
| Borderline           | 55 (11.9)                 |
| Abnormal             | 32 (6.9)                  |

| Question                                                                 | Mean ± Standard Deviation |
|--------------------------------------------------------------------------|---------------------------|
| Medications provided are always insufficient for the stated duration of supply |                           |
| Strongly disagree                                                       | 116 (25.2)                |
| Disagree                                                                | 204 (44.3)                |
| Neutral                                                                | 88 (19.1)                 |
| Agree                                                                   | 38 (8.2)                  |
| Strongly agree                                                          | 15 (3.3)                  |

| Question                                                                 | Mean ± Standard Deviation |
|--------------------------------------------------------------------------|---------------------------|
| I have adjusted the dose of my medications without consulting my doctor |                           |
| to avoid running out of supply                                           |                           |
| Never                                                                    | 369 (80.0)                |
| Rarely                                                                   | 39 (8.5)                  |
| Sometimes                                                                | 32 (6.9)                  |
| Often                                                                    | 11 (2.4)                  |
| Always                                                                   | 10 (2.2)                  |

| Psychological Impact | Mean ± Standard Deviation |
|----------------------|---------------------------|
| HADS-Anxiety         |                           |
| Normal               | 334 (72.5)                |
| Borderline           | 80 (17.4)                 |
| Abnormal             | 47 (10.2)                 |
| HADS-Depression      |                           |
| Normal               | 374 (81.1)                |
| Borderline           | 55 (11.9)                 |
| Abnormal             | 32 (6.9)                  |
Table 2  
Factors associated with seizure worsening during COVID-19 period (n = 461).  

| Factors | Seizure worsening during COVID-19 | p-value |
|---------|---------------------------------|---------|
|         | Yes (n = 60), n (%) | No (n = 400), n (%) |         |
| **Sociodemographic Characteristics** | | | |
| Age (Years), Mean ± SD | 37.18 ± 15.79 | 39.51 ± 15.91 | NS |
| Gender | | | |
| Male (n = 230) | 30 (13.0) | 200 (87.0) | NS |
| Female (n = 231) | 30 (13.0) | 201 (87.0) | |
| Race | | | |
| Malay (n = 139) | 21 (15.2) | 118 (84.8) | NS |
| Chinese (n = 208) | 25 (12.1) | 183 (87.9) | |
| Indian (n = 103) | 11 (18.3) | 92 (81.7) | NS |
| Native (n = 1) | 1 (1.7) | 1 (0.3) | |
| Others (n = 7) | 2 (3.3) | 7 (1.8) | |
| Marital Status | | | |
| Single (n = 265) | 38 (14.3) | 227 (85.7) | NS |
| Others (n = 196) | 22 (11.2) | 174 (88.8) | |
| Education | | | |
| Secondary or below (n = 256) | 36 (14.1) | 220 (85.9) | NS |
| Tertiary (n = 205) | 24 (11.7) | 181 (88.3) | |
| Employment | | | |
| Employed (n = 183) | 20 (10.9) | 163 (89.1) | NS |
| Others (n = 278) | 25 (16.6) | 126 (83.4) | |
| Clinical characteristics | | | |
| Age of onset (Years), Mean ± SD | 17.78 ± 14.00 | 23.14 ± 15.93 | NS |
| Seizure frequency before COVID-19 | | | |
| No seizure for at least a year (n = 173) | 4 (2.3) | 169 (97.7) | 0.001 |
| Less than once a month (n = 166) | 17 (10.2) | 149 (89.8) | |
| One of more seizure a month (n = 122) | 39 (32.0) | 83 (68.0) | |
| Seizure type | | | |
| Focal (n = 249) | 39 (15.7) | 210 (84.3) | NS |
| Others (n = 212) | 21 (9.9) | 191 (90.1) | |
| EEG | | | |
| Abnormal (n = 310) | 46 (14.8) | 264 (85.2) | NS |
| Others (n = 151) | 14 (9.3) | 137 (90.7) | |
| Imaging | | | |
| Abnormal (n = 254) | 33 (13.0) | 221 (87.0) | NS |
| Others (n = 207) | 27 (13.0) | 180 (87.0) | |
| No. of AEDs | | | |
| 1 (n = 144) | 12 (8.3) | 132 (91.7) | 0.001 |
| 2 (n = 127) | 8 (6.3) | 119 (93.7) | |
| 3 or more (n = 190) | 40 (21.1) | 150 (78.9) | |
| Surgery | | | |
| Yes (n = 57) | 6 (10.5) | 51 (89.5) | NS |
| Others (n = 404) | 54 (13.4) | 350 (86.6) | |
| Hospital | | | |
| UMMC (n = 420) | 48 (11.4) | 372 (88.6) | 0.003 |
| Others (n = 41) | 12 (29.3) | 29 (70.7) | |
| Triggers | | | |
| Reason for seizure worsening | | | |
| Stress (n = 107) | 25 (23.4) | 82 (76.6) | 0.001 |
| Inadequate sleep (n = 125) | 28 (22.4) | 97 (77.6) | 0.001 |
| Missed AEDs (n = 62) | 5 (8.1) | 57 (91.9) | NS |
| Inadequate AEDs (n = 10) | 3 (30.0) | 7 (70.0) | NS |
| Fever (n = 24) | 2 (8.3) | 22 (91.7) | NS |
| Physical tiredness (n = 86) | 16 (18.6) | 70 (81.4) | NS |
| Diet (n = 23) | 4 (17.4) | 19 (82.6) | NS |
| Clinic Appointment | | | |
| Difficulty to reschedule clinic appointments | | | |
| Yes (n = 120) | 21 (17.5) | 99 (82.5) | NS |
| No (n = 182) | 19 (10.4) | 163 (89.6) | |
| Worries seizures get worse because of postponed clinic appointments | | | |
| Yes (n = 139) | 25 (18.0) | 114 (82.0) | 0.001 |
| No (n = 322) | 35 (10.9) | 287 (89.1) | |
| Access to online or tele-consultation | | | |
| Yes (n = 341) | 20 (16.7) | 100 (83.3) | NS |
| No (n = 120) | 40 (11.7) | 301 (88.3) | |
| Emergency unit | | | |
| Afraid to go to emergency unit | | | |
| Yes (n = 133) | 19 (14.3) | 114 (85.7) | NS |
| No (n = 211) | 22 (10.4) | 189 (89.6) | |
| Difficulty to go to emergency unit | | | |
| Yes (n = 86) | 21 (24.4) | 65 (75.6) | 0.001 |
| No (n = 375) | 39 (10.4) | 336 (89.6) | |
| Understand need to go to emergency unit | | | |
| Yes (n = 372) | 47 (12.6) | 325 (87.4) | NS |
| No (n = 89) | 13 (14.6) | 76 (85.4) | |
| Knowledge on what to do during seizures | | | |
| Yes (n = 263) | 47 (12.9) | 316 (87.1) | NS |
| No (n = 98) | 13 (13.3) | 85 (86.7) | |
| Medication Supply | | | |
| Pay for your own AEDs | | | |
| Yes, fully (n = 191) | 23 (12.0) | 168 (88.0) | NS |
| Yes, partially (n = 187) | 21 (11.2) | 166 (88.8) | |
| No, fully subsidized (n = 83) | 16 (19.3) | 67 (80.7) | |
| No (n = 224) | 20 (17.9) | 92 (82.1) | NS |
| No (n = 224) | 20 (17.9) | 92 (82.1) | NS |
| Difficult to arrange AED delivery | | | |
| Yes (n = 123) | 21 (17.1) | 102 (82.9) | NS |
| No (n = 172) | 19 (11.0) | 153 (89.0) | |
| Difficult to arrange self-pick-up | | | |
| Yes (n = 91) | 18 (19.8) | 328 (80.2) | 0.016 |
| No (n = 370) | 42 (11.4) | 138 (88.6) | |
| AEDs ran out of stock | | | |
| Yes (n = 56) | 13 (23.2) | 43 (76.8) | 0.037 |
| Others (n = 405) | 47 (11.6) | 358 (88.4) | |
| Insufficient AED supply | | | |
| Yes (n = 53) | 8 (15.1) | 45 (84.9) | NS |
| No (n = 320) | 41 (12.8) | 279 (87.2) | |
| Skipped AEDs | | | |
| Yes (n = 66) | 12 (18.2) | 54 (81.8) | NS |
| Others (n = 395) | 48 (12.2) | 347 (87.8) | |
3.4. Multinational comparison of clinical and psychological impacts

Seizure worsening was reported in 8.6–29.5% of the respondents in various countries, highest in Saudi Arabia, followed by Spain and USA, Italy, China, and Malaysia. The anxiety rate ranged from 9.4 to 60.5% (highest in Italy), and depression rate from 8.6 to 46.9% (highest in Brazil and Belgium); the rates in Malaysia were within the range. Higher anxiety and depression rates (>30%) were reported in countries with >30,000 COVID-19 cases per 1 million population, including Brazil, Belgium, Spain, and Italy (Table 5).

4. Discussion

In this Malaysian nationwide study, 13.0% of the participants reported worsening of their seizure control (13.0%), 27.6% experienced anxiety, and 18.8% depression. Seizure worsening was related to clinical (uncontrolled pre-COVID seizure control and number of AEDs), logistic (difficult access to emergency, postponed clinic appointment, inadequate AED supply and self-adjustment of AEDs), and psychological (inadequate sleep and anxiety) factors. This led to poorer quality of life among PWE.

In Malaysia, seizure worsening was reported in 13% of the respondents, compatible with China but lower than the European countries and Saudi Arabia [4,6,9–13]. As shown in Table 5, the rates were higher in countries with higher percentage of COVID-19 cases, similar to the rates of anxiety and depression. These differences might also be related to the cultural differences in these countries, which influence the national policy and individual reaction toward the pandemic, but also can be disease specific [20]. As a comparison, we found different patterns in cancer studies during the pandemic, in which the rates of depression and anxiety were lower in Malaysia but not in China, whereas for European countries the rates were high but not in USA [21–24]. Stress or anxiety was commonly associated with seizure worsening [4–6,9,11], but not depression. In our study, though depression was associated with seizure worsening in univariate analysis, the association was not significant in multivariate analysis. This supports the need to screen for psychological distress routinely especially during COVID-19 pandemic.

Many studies reported logistic issues among PWE especially on the access and adjustment of AEDs [4,5,10,11], and clinic postponement [13]. It was postulated that these logistic issues may be the...
cause of seizure worsening, but only AED issues (dose adjustment and supply) were reported as a factor for seizure control during COVID-19 period [5,11]. In our study, seizure worsening was shown to be related to access of all related healthcare services including emergency, outpatient, and pharmacy services. Consequently, about 10% of the respondents adjusted their dose to avoid depletion of their AEDs and this was associated with seizure worsening, thus should be discouraged. In response to the logistic issues, immediate measures were established in our hospital (UMMC) to allow patient’s online access to the epilepsy team, pharmacy, and registration counter virtually. These measures may not be widely available in other hospitals during the early phase of the pandemic, which possibly explain more patients with seizure worsening in these hospitals.

During this pandemic, some patients (12–17%) experienced seizure improvement during the pandemic. This could be attributed to less provoking factors such as sleep deprivation and work stress in these patients, during the confinement period [11–13].

Quality of life in PWE was affected by seizure worsening during COVID-19 period, which was expected. However, the regression analysis in our study showed a higher impact of psychological stress, including both anxiety and depression, on the quality of life.

4.1. Implications

This study showed that the rights and needs of patients with chronic illness have not been silenced by the COVID-19 pandemic, and the need for the Health Authorities to re-organize the healthcare services to ensure continuity of care.

For some patients, delayed medical attention from the fear of contracting COVID-19 might have life-threatening consequences. Therefore, it is vital for us to understand and address their needs in a timely manner. A balance must be achieved between the required safety measures to prevent further spread of this virus and adequate care to patients with chronic illnesses [25]. As an alternative, telemedicine was frequently discussed and was shown to be practical and effective [26]. Epilepsy Electronic Patient Portal was also proposed to improve seizure care [27]. Another suggestion would be to allocate staggered clinic hours to less provoking factors such as sleep deprivation and work stress worsening in these hospitals.

Further research is warranted to help design platform that caters to the diversified communities and countries, especially in the resource limited areas while reducing the negative impact of COVID-19. Algorithms should be designed to prevent sudden loss of access to healthcare in the event of a public health emergency.

4.2. Limitations

As the web-based study was conducted in urban and semi-rural areas, the findings may not be representative of the rural or underprivileged settings with no access to internet. Future studies involving these underprivileged communities should be conducted to assess their continuity of care in a resource-limited driven setting.

5. Conclusion

A significant number of PWE experienced seizure worsening during COVID-19 period, which was related to the clinical, logistic, and psychological factors. Quality of life was affected by seizure worsening and psychological stress. This study highlights the impact of the COVID-19 faced by people with epilepsy and the importance to understand their needs.

Author contributions

MY designed the project, wrote the protocol, obtained the data, performed the statistical analysis, interpreted the data, and drafted the manuscript. KS designed the study, reviewed the study protocol, supervised the execution, and coordinated the data analysis plan. SL reviewed the study protocol, supervised the execution, and interpreted the data. All authors reviewed, revised, and approved the manuscript.

Funding

This study was supported by University of Malaya Faculty of Medicine Postgraduate Scheme (FOMPSS) and Impact Oriented Interdisciplinary Research Grant (IIRG) Programme (IIRG003A-2020HWB).

Declaration of Competing Interest

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

Acknowledgement

We would like to acknowledge the University of Malaya Faculty of Medicine Postgraduate Scheme (FOMPSS) and Impact Oriented Interdisciplinary Research Grant (IIRG) Programme (IIRG003A-2020HWB).
