Prevalence and determinants of depression in patients with epilepsy during the COVID-19 pandemic

Mohammad Gamal Sehlo1*, Wafaa Samir Mohamed2, Usama Mahmoud Youssef1, Shrouk Esam Lotfi3 and Ghada Mohamed Salah El-deen1

Abstract

Background: Epilepsy is one of the commonest and most serious neurological conditions. It is frequently associated with one or more medical or psychiatric comorbidities. Depression is one of the most common comorbidities. Patients with epilepsy (PWE) are expected to suffer from a high level of depression during the COVID-19 pandemic. This cross-sectional study was applied to 290 PWE. Data was collected by personal interviews with each patient using the Patient Health Questionnaire 9 (PHQ 9) scale for the diagnosis of depression and assessing its severity. We aimed to assess the prevalence and the risk factors of depression in PWE during the COVID-19 pandemic.

Results: We found that 70.3% of PWE suffered from depression. Low financial status, refractory seizures, fear of infection and death by COVID-19, had close relatives died by COVID-19, had a sleep disturbance, a decreased family support, increased seizure rate during the pandemic, increased ER visits during the pandemic, lack of drug adherence, and decreased epilepsy-related follow-up visits during the pandemic were significantly associated with increased risk of depression in PWE during the pandemic.

Conclusions: The COVID-19 pandemic has a serious effect on the psychological and physical well-being of PWE. There was an increased rate of depression during the COVID-19 pandemic in PWE with its subsequent burden on those patients. So, these patients are in a high need of care and support during the pandemic.

Keywords: COVID-19, Epilepsy, Depression

Background

Epilepsy is one of the most frequent major brain disorders, affecting more than 70 million individuals worldwide [1]. Epilepsy contributes to 0.7% of the global burden of medical disorders [2].

Psychiatric comorbidities, such as mood, anxiety, and psychotic disorders, are common in epileptic patients, with rates that are often 2–3 times higher than in the general population [3]. Depression is the leading cause of poor quality of life in epileptic patients, and one of the most frequent psychiatric comorbidities [4].

The lifetime risk of depression in the general population is 15–18%, with almost one in five people experiencing one episode at some point in their lifetime [5]. Up to 30–50% of individuals with epilepsy have a depressive symptom, which often complicate seizure management and reduce overall quality of life [6].

The comorbidity of depression with epilepsy can be explained with several etiologies, including neurobiological mechanisms such as a hyperactive hypothalamic–pituitary–adrenal axis (HPA), neuroinflammatory mechanisms (IL-1b, IL-2, IL-6, interferon-g, and tumor necrosis factor-a) [7], neurotransmitter disturbance.

*Correspondence: sehlo68@gmail.com
1 Psychiatry Department, Faculty of Medicine, Zagazig University, PO Box 44519, Zagazig, Egypt
Full list of author information is available at the end of the article
(serotonin and norepinephrine) [8], and anatomical abnormalities (prefrontal cortex and paralimbic structures) [9], also the social burden of the epilepsy itself on the patients.

The COVID-19 pandemic incorporates a lot of new stressful situations: loss of employment, the death of family members and colleagues, financial insecurity, and isolation from others, especially for people who live alone [10]. That can lead to a higher level of depression in PWE.

The frequency of depressive symptoms in the general population in the USA was found to be more than 3-fold higher during COVID-19 than before the pandemic. Individuals with fewer financial resources and more stressor exposure (such as job loss) reported more depressive symptoms [11].

Patients with epilepsy are expected to suffer from a high rate of depression during the COVID-19 pandemic. It was found that the prevalence of depression among patients with epilepsy (PWE) increased to 42.3% during the period of the pandemic [12].

The aims of this study were to assess the prevalence and the risk factors of depression in PWE during the COVID-19 pandemic. To our knowledge, this is the first study that had been conducted to assess depression among PWE in Egypt.

Methods
Participants
A sample of 290 consecutive patients diagnosed with epilepsy according to the International League Against Epilepsy (ILAE) classification 2017 were included in this cross-sectional study. The patients were recruited from the outpatient clinic and the inpatient ward of the Neurology Department, Zagazig University Hospital, Zagazig, Egypt, between August 2020 and September 2021.

Both male and female patients with an age range from 19 to 60 years were included in the study.

Exclusion criteria were patients with a past history of psychiatric illness, substance abuse, intellectual disability, chronic major medical disorders other than epilepsy, and previous or current infection with COVID-19.

Measures
Sociodemographic and clinical data form
The sociodemographic and clinical data form is composed of questions related to personal and clinical characteristics of the patients and questions related to the COVID-19 pandemic. Including age, gender, marital status, employment status, number of children, educational degree, financial status, where and with whom the patient lives, family history of epilepsy, and psychiatric illness. Epilepsy-related data: type of seizures, response to antiepileptic drugs (AEDs) whether respondent or resistant, age of onset, time of seizure occurrence, number of drugs taken, rate of seizures before and during the pandemic, number of previous ER visits by a seizure, number of ER visits by a seizure during the pandemic, fear of having an uncontrolled seizure during the pandemic, drug adherence during the pandemic, routine follow-up during the pandemic. COVID-19-related data: closed people infection or death, following news about the pandemic, sleep disturbance during the pandemic, family support during the pandemic, job changes during the pandemic, financial changes during the pandemic, fear of job loss during the pandemic, fear of infection or death by COVID-19, fear of closed one’s infection or death by COVID-19, and sense of the end of the world.

Patient Health Questionnaire 9
The Patient Health Questionnaire (PHQ 9) will be used to assess depressive symptoms [13]. The PHQ 9 is a widely used measure for identifying depressive symptoms and diagnosing depressive disorders and has excellent psychometric properties when used in medical and psychiatric patients. The PHQ 9 incorporates DSM-IV diagnostic criteria for major depressive disorder, assessing the presence and severity of the nine primary symptoms of major depression. This enables not only the determination of the severity of depression but also the presence of depressive disorder. Scores of 5, 10, 15, and 20 represent mild, moderate, moderately severe, and severe depression respectively [14].

The validated Arabic version of the scale was used in this study [15].

Statistical analysis
The data analysis and sample size calculations (with 80% power) were performed using the statistical package for social sciences (SPSS version 20). The categorical data were presented in the form of number and percentage. Continuous data were expressed as mean ± SD (standard deviation) and median with the interquartile range (IQR). Chi-square was used as a test of significance of the differences among groups. Binary logistic regression analysis was used to assess the predictors of depression. A P value < 0.05 was considered to indicate statistical significance.

Results
Table 1 shows that the age of the studied group ranged from 18 to 60 years with a mean of 33.69 years. Regarding sex, more than half of them were male (52.4%). About 50% of them live in urban areas; 55.9% live with their spouse and siblings. 56.2% of them were married. Regarding education and occupation, 54.1% had secondary education. 40.3% of them were working. Low financial status was found among 39% of them, while financial
status was satisfying among 54.1% of them. Finally, 37.6% of them had no children and 39.6% had 1 to 2 children.

Table 2 shows that the median age of onset of epilepsy among the studied group was 17 years while duration was 14 years. About 21.4% of them had a positive family history of epilepsy, 2.8% had a positive family history of psychiatric disease, and 8.3% had a positive past history of psychiatric disease. The most frequent type of seizures found among the studied groups was generalized (43.4%); also 69.3% of the cases were responsive. Almost 89% of the studied group take more than one AEDs. Finally, 83.3% of the cases had seizures at any time.

Table 3 shows that 28.3% of the studied group had moderately severe and 21% had severe depression according to the PHQ 9 score.

Table 4 shows that there was a statistically significant increase in the frequency of moderately severe to severe depression among persons who fear COVID-19 infection, had close people infected, had close people dead, had financial changes during the pandemic, had sleep disturbances during the pandemic, had decreased family support during the pandemic, and continuously follow news about the pandemic.

Table 5 shows that there was a statistically significant increase in the frequency of moderately severe to severe depression among patients who had increased seizure rate, increased ER visits during the pandemic, patients who reported lack of drug adherence, and patients who reported decreased follow-up visits during the pandemic.

Table 6 shows that not working, low financial status, refractory seizures, fear of infection and death by...
COVID-19, had close people dead by COVID-19, had
sleep disturbance, decreased family support, increased
seizures rate during the pandemic, increased ER vis-
its during the pandemic, lack of drug adherence, and
decreased epilepsy-related follow-up visits increase the
risk of depression by 5.83-, 11.90-, 14.60-, 4.99-, 3.65-, 12.71-, 3.95-, 7.10-, 5.76-, 4.3-, and 3.8-fold (odds ratio)
respectively.

Table 4  The relationship between depression and COVID-19 among the studied group

| Variable                             | N     | None (n = 86) | Mild to moderate (n = 61) | Moderately severe to severe (n = 143) | χ² | P    |
|--------------------------------------|-------|--------------|--------------------------|--------------------------------------|----|------|
|                                      | No.   | %            | No.                      | %                                     |    |      |
| Fear of infection by COVID-19        | No    | 136          | 51                       | 37.5                                 | 24 | 17.6 | 61   | 44.9 | 7.74 | 0.02* |
|                                      | Yes   | 154          | 35                       | 22.7                                 | 37 | 24   | 82   | 53.2 | 6.63 | 0.04* |
| Fear of death by COVID-19            | No    | 125          | 46                       | 36.8                                 | 20 | 16   | 59   | 47.2 | 6.36 | 0.009* |
|                                      | Yes   | 165          | 40                       | 24.2                                 | 41 | 24.8 | 84   | 50.9 | 6.36 | 0.009* |
| Closed people infection              | No    | 135          | 50                       | 37                                  | 20 | 14.8 | 65   | 48.1 | 9.36 | 0.009* |
|                                      | Yes   | 155          | 36                       | 23.2                                 | 41 | 26.5 | 78   | 50.3 | 9.36 | 0.009* |
| Closed people death                  | No    | 272          | 81                       | 29.8                                 | 61 | 22.4 | 130  | 47.8 | 6.1  | 0.04* |
|                                      | Yes   | 18           | 5                        | 27.8                                 | 0  | 0    | 13   | 72.2 | 6.1  | 0.04* |
| Fear of job loss in the pandemic     | No    | 203          | 55                       | 27.1                                 | 40 | 19.7 | 108  | 53.2 | 4.15 | 0.13 NS |
|                                      | Yes   | 87           | 31                       | 35.6                                 | 21 | 24.1 | 35   | 40.2 | 4.15 | 0.13 NS |
| Job changes by the pandemic          | No    | 205          | 54                       | 26.3                                 | 41 | 20   | 110  | 53.7 | 5.63 | 0.06 NS |
|                                      | Yes   | 85           | 32                       | 37.6                                 | 20 | 23.5 | 33   | 38.8 | 5.63 | 0.06 NS |
| Financial changes in the pandemic    | No    | 62           | 36                       | 58.1                                 | 6  | 9.7  | 20   | 32.3 | 30.95| < 0.001** |
|                                      | Yes   | 228          | 50                       | 21.9                                 | 55 | 24.1 | 123  | 53.9 | 30.95| < 0.001** |
| Sleep disturbance during the pandemic| No    | 213          | 77                       | 36.2                                 | 48 | 22.5 | 88   | 41.3 | 22.67| < 0.001** |
|                                      | Yes   | 77           | 9                        | 11.7                                 | 13 | 16.9 | 55   | 71.4 | 22.67| < 0.001** |
| Follow news about the pandemic       | Not follow | 54            | 25                       | 46.3                                 | 17 | 31.5 | 12   | 22.2 | 27.95| < 0.001** |
|                                      | Low   | 73           | 22                       | 30.1                                 | 8  | 11   | 43   | 58.9 | 27.95| < 0.001** |
|                                      | Moderate | 89          | 27                       | 30.3                                 | 20 | 22.5 | 42   | 47.2 | 27.95| < 0.001** |
|                                      | Continuous | 74            | 12                       | 16.2                                 | 16 | 21.6 | 46   | 62.2 | 27.95| < 0.001** |

χ² chi-square test, NS nonsignificant (P > 0.05); *significant (P < 0.05), **highly significant (P < 0.001)

Table 5 The relationship between depression and epilepsy during the pandemic among the studied group

| Variable                             | N     | None (n = 86) | Mild to moderate (n = 61) | Moderately severe to severe (n = 143) | χ² | P    |
|--------------------------------------|-------|--------------|--------------------------|--------------------------------------|----|------|
|                                      | No.   | %            | No.                      | %                                     |    |      |
| Rate of seizures after COVID-19:     | No change | 233         | 86                       | 36.9                                 | 40 | 17.2 | 107  | 45.9 | 32.23| < 0.001** |
|                                      | Increase | 57          | 0                        | 0                                    | 21 | 36.8 | 36   | 63.2 | 32.23| < 0.001** |
| Rate of ER visits after COVID-19:    | No change | 109         | 38                       | 34.9                                 | 35 | 32.1 | 36   | 33   | 21.17| < 0.001** |
|                                      | Increase | 118         | 48                       | 26.5                                 | 26 | 14.4 | 107  | 59   | 21.17| < 0.001** |
| Drug adherence during the pandemic   | No change | 212         | 74                       | 34.7                                 | 44 | 20.9 | 94   | 44.4 | 7.68 | 0.005* |
|                                      | Lack    | 78           | 12                       | 14.8                                 | 22 | 28.6 | 44   | 56.6 | 7.68 | 0.005* |
| Routine follow-up during the pandemic| No change | 128         | 49                       | 38.3                                 | 25 | 19.5 | 54   | 42.2 | 8.35 | 0.02* |
|                                      | Lack    | 162          | 37                       | 22.8                                 | 36 | 22.2 | 89   | 54.9 | 8.35 | 0.02* |

χ² chi-square test, NS nonsignificant (P > 0.05); *significant (P < 0.05), **highly significant (P < 0.001)
To our knowledge, this is the first study that had been conducted to assess depression among PWE in Egypt. In our study, we assessed the prevalence and the determinants of depression in patients with epilepsy (PWE), during the COVID-19 pandemic.

In our study, the prevalence of depression in patients with epilepsy during the pandemic is 70.3%. 6.2% of the participants had mild depression, 14.8% had moderate depression, and 28.3% had moderately severe depression, while 21% had severe depression. Few studies have investigated the relationship between depression and COVID-19 in PWE, and all of them are consistent with our results about the increased prevalence of depression in those patients during the COVID-19 pandemic with varying percentages and this can be explained by the severe stress of the COVID-19 pandemic added to the burden of epilepsy itself.

The prevalence of depression in patients with epilepsy varied largely across the studies. In a meta-analysis of 51 cross-sectional studies published between 1999 and 2018 with sample sizes ranging from 36 to 1763, Yang et al. found that the prevalence of depression among patients with epilepsy (PWE) ranged greatly from 5.09 to 85.5% largely depending on the used diagnostic criteria [16].

The prevalence of depression in patients with epilepsy varied also during the pandemic. Sun et al. found that

| Variable | B   | SE  | Wald  | P     | OR   | 95% CI  |
|----------|-----|-----|-------|-------|------|---------|
| Age > 40 | 0.134 | 0.150 | 0.793 | 0.373 | 0.875 | 0.651  1.175 |
| Female sex | 1.774 | 1.016 | 2.456 | 0.060 | 0.062 | 0.009  0.457 |
| Divorced | 1.623 | 0.42 | 1.796 | 0.616 | 1.439 | 0.234  5.314 |
| Residence | 0.776 | 0.562 | 0.195 | 0.681 | 0.368 | 0.098  1.359 |
| Live alone | 1.179 | 0.42 | 1.098 | 0.250 | 3.250 | 0.614  2.317 |
| Illiterate | 1.282 | 0.90 | 1.424 | 0.11 | 9.794 | 1.677  57.180 |
| Not working | 8.671 | 2.059 | 17.736 | < 0.001** | 5.831 | 1.030  32.985 |
| > 2 children | 1.041 | 0.848 | 1.508 | 0.219 | 2.832 | 0.538  14.909 |
| Low financial status | 2.476 | 0.689 | 12.898 | < 0.001** | 11.896 | 3.080  45.949 |
| Positive family history of epilepsy | 0.770 | 0.738 | 0.109 | 0.745 | 0.502 | 0.036  1.557 |
| Positive family history of psychiatric disorder | 3.389 | 1.476 | 0.098 | 0.752 | 0.33  30.57 |
| Positive past history of psychiatric disorder | 0.020 | 0.030 | 0.043 | 0.836 | 0.98  1.08 |
| Age of onset < 17 years | 0.242 | 0.160 | 0.026 | 0.873 | 0.65  1.07 |
| Duration >4years | 0.061 | 0.154 | 0.022 | 0.883 | 0.98  1.05 |
| Generalized seizures | 0.957 | 0.580 | 2.233 | 0.136 | 2.59  0.87  8.00 |
| Refractory | 6.016 | 1.375 | 19.732 | < 0.001** | 14.60 | 7.31  59.93 |
| > 1 AEDs | 1.109 | 0.917 | 0.224 | 0.639 | 0.67  1.92 |
| Any time seizures | 0.074 | 1.267 | 0.003 | 0.955 | 0.99  1.00 |
| Fear of infection by COVID-19 | 12.06 | 2.764 | 19.664 | < 0.001** | 5.06 | 2.12  20.001 |
| Fear of death by COVID-19 | 5.608 | 2.102 | 5.85 | 0.044* | 4.992 | 2.181  32.071 |
| Closed people infection | 0.470 | 0.698 | 0.635 | 0.428 | 0.635 | 0.27  1.53 |
| Closed people death | 7.046 | 3.132 | 1.060 | 0.11 | 3.652 | 1.476  13.216 |
| Fear of job loss in the pandemic | 1.717 | 3.435 | 0.076 | 0.783 | 1.076 | 0.28  4.43 |
| Job changes by pandemic | 3.801 | 2.385 | 2.684 | 0.105 | 2.738 | 0.460  14.349 |
| Financial changes in the pandemic | 0.344 | 1.102 | 0.597 | 0.441 | 0.624 | 0.19  1.93 |
| Sleep disturbance during the pandemic | 4.287 | 1.092 | 15.414 | < 0.001** | 12.713 | 3.556  61.953 |
| Decrease family support during the pandemic | 3.058 | 1.706 | 10.006 | 0.03* | 3.945 | 1.237  23.772 |
| Continuous Follow news about the pandemic | 0.615 | 0.737 | 0.286 | 0.600 | 0.401 | 0.07  5.57 |
| Increase seizure rate | 10.207 | 2.102 | 5.85 | 0.044* | 5.761 | 1.468  26.762 |
| Increase ER visit rate | 8.566 | 1.676 | 3.701 | 0.004* | 5.761 | 1.468  26.762 |
| Lack of drug adherence during the pandemic | 4.207 | 1.105 | 5.523 | 0.02* | 4.270 | 2.438  22.627 |
| Lack of routine follow-up during the pandemic | 3.278 | 1.800 | 4.121 | 0.03* | 3.757 | 1.158  16.635 |

| OR  | odds ratio; CI confidence interval; *significant (P < 0.05), **highly significant (P < 0.001) |

**Discussion**

To our knowledge, this is the first study that had been conducted to assess depression among PWE in Egypt. In our study, we assessed the prevalence and the determinants of depression in patients with epilepsy (PWE), during the COVID-19 pandemic.

In our study, the prevalence of depression in patients with epilepsy during the pandemic is 70.3%. 6.2% of the participants had mild depression, 14.8% had moderate depression, and 28.3% had moderately severe depression, while 21% had severe depression. Few studies have investigated the relationship between depression and COVID-19 in PWE, and all of them are consistent with our results about the increased prevalence of depression in those patients during the COVID-19 pandemic with varying percentages and this can be explained by the severe stress of the COVID-19 pandemic added to the burden of epilepsy itself.

The prevalence of depression in patients with epilepsy varied largely across the studies. In a meta-analysis of 51 cross-sectional studies published between 1999 and 2018 with sample sizes ranging from 36 to 1763, Yang et al. found that the prevalence of depression among patients with epilepsy (PWE) ranged greatly from 5.09 to 85.5% largely depending on the used diagnostic criteria [16].

The prevalence of depression in patients with epilepsy varied also during the pandemic. Sun et al. found that
the prevalence of depression among PWE increased to 42.3% during the period of the pandemic [17]. Abokalawa et al. found that two-thirds of their sample of PWE (66.2%) reported depression during the pandemic [18]. Van Hees et al. found that 159/399 (39.8%) PWE scored positive for depression during the pandemic [19].

In our study, we found that a lot of factors related to the COVID-19 pandemic are significantly associated with increased frequency of moderately severe to severe depression. Patients who were afraid of COVID-19 infection, afraid of death from COVID-19 infection, had closed people infected or dead, had financial changes during the pandemic, had sleep disturbances during the pandemic, and continuously followed the pandemic news clearly suffered from more depression during the pandemic.

So, the COVID-19 pandemic is highly associated with increased prevalence and severity of depression among PWE which in turn has a severe burden on the patients.

These findings are consistent with other studies. Van Hees et al. reported increased depression severity with low financial status in PWE during the pandemic [19]. Sonbol et al. found that PWE who were concerned about the COVID-19 pandemic news and spent 3 h or more following the news had higher depression than the less concerned ones [20]. Kaya et al. reported increased depression levels in PWE if they encountered a COVID-19 patient or had a relative with COVID-19 [21]. Cülliler and Güven and Stauder et al. found that poor sleep quality was associated with higher depressive symptoms in PWE [22, 23].

In our study, there was a statistically significant association between increased depression severity and increased seizure rate, increased ER visits, decreased drug adherence, and decreased routine follow-up during the pandemic.

Our study is consistent with other studies who reported increased severity of depression in PWE is associated with decreased drug adherence in PWE during the pandemic [19, 24]. Other studies found that there was a significant relationship between increasing seizure frequency in PWE and increased depression severity during the pandemic [25, 26].

Depression itself is associated with depressed mood, lack of interest, and lack of activity that leads to decreased drug adherence which in turn leads to increased seizure frequency and increased rate of ER visits, so it is a bidirectional relationship. Our study is consistent with other studies who demonstrated a 2-way relation between a broad spectrum of psychiatric disorders (i.e., depression, anxiety, psychosis) and epilepsy [27, 28]. The bidirectional relationship suggests that common pathogenetic mechanisms are operant in both conditions, with the presence of one disorder potentially increasing the severity of the other [29]. Also, there is a decreased routine follow-up during the pandemic which in turn leads to worse control of the epilepsy.

Inconsistent with our results about the aspect of increased ER visits in PWE during the pandemic is Bamaga et al. [30] who found a 24% reduction in the number of ER visits for common neurological symptoms during the pandemic time in comparison to pre-pandemic. They explained this result by the public anxiety about the pandemic.

This inconsistency with our result can be explained by the fact that in our study 15.2% of the patients are illiterate and 54.1% are secondarily educated. This lack of education makes it hard for the patient's caretaker to fully understand how to support the patient during acute seizures and how to perform simple life-saving maneuvers like CPR which actually can be performed by many of the public in other communities. Moreover, this lack of education and low socioeconomic levels in our sample, along with the added financial problems during the pandemic, make it hard for these patients to access telemedicine services on the internet and mobile applications.

Using binary logistic regression analysis of the predictors of depression among the studied group during the pandemic, we found that these factors are significantly associated with increased frequency of depression in PWE during the pandemic: refractory seizures (more than 14-fold increase in the risk of depression, as a bidirectional link between depression and epilepsy), sleep disturbance (more than 12-fold increase in the risk of depression), low financial status (more than 11-fold increase in the risk of depression), increased seizures' frequency in PWE during the pandemic, low socioeconomic levels in our sample, along with the added financial problems during the pandemic, fear of COVID-19 infection (5-fold increase in the risk of depression), fear of death by COVID-19 infection (4.9 increase in the risk of depression), lack of drug adherence during the pandemic (4.2-fold increase in the risk of depression), decreased epilepsy-related follow-up consultations (3.7 increase in the risk of depression), and closed people death by COVID-19 infection (3.6 increase in the risk of depression).

Our results are consistent with other studies. Zis et al. found in their regression analysis model that unemployment and increased seizure frequency, in turn, increase the risk of depression in PWE [31]. Bifftu et al. found in their regression analysis model that perceived stress, seizure frequency of $\geq$ 1 per month, and difficulties of adherence to antiepileptic drugs were independently associated with depression in PWE [32]. Dos Santos
Lunardi et al. found in their regression analysis model that increased seizure frequency, difficulties to access their physicians and anti-seizure drugs, and unemployment increase the risk of depression in PWE during the pandemic [24]. Yang et al. found that the most significant factors associated with an increased risk of depression in PWE during the pandemic were unemployment and poor antiepileptic drug (AED) adherence [16]. Our study is the first to assess a lot of predictors for depression in PWE during the pandemic, while the previously mentioned studies assessed only a few predictors that were consistent with our results.

The present study has some limitations; as the cross-sectional design of the study prevents causal conclusions, it just proves an association between depression with its determinants and COVID-19 pandemic and opens the floor for further longitudinal studies to prove causality. There are also several strengths of this study as it is the first study in Egypt that assessed the association between depression with its determinants and the COVID-19 pandemic and also the first study that examined a lot of determinants for depression in PWE during the COVID-19 pandemic.

Conclusions
Our study revealed a high prevalence of depression in PWE during the COVID-19 pandemic. During the pandemic, patients with refractory seizures, sleep disturbance, low financial status, increased seizures’ rate, being unemployed, increased ER visits, fear of COVID-19 infection, fear of death by COVID-19 infection, lack of drug adherence, decreased epilepsy-related follow-up consultations and closed people death by COVID-19 were the most significant predictors for depression in PWE. So, these risk factors must be evaluated and adjusted as this will be reflected in the improvement of the depression which in turn will be reflected in the improvement of epilepsy and on the quality of life of PWE.

Limitations of the study
Our study has some limitations. Because the exposure and outcome are examined concurrently in a cross-sectional study, there is often no evidence of a causation link between exposure and outcome and longitudinal studies are recommended. However, we have many strengths in our study as our results are useful in focusing on PWE who are already under severe stress that increased more in the pandemic. Our study was performed by direct doctor–patient interview, not online or self-submitted questionnaires, which guarantees correct understanding of the patients to the questions and good interpretation of the results. Our study was performed in an epilepsy clinic and not in primary care clinic, allowing us to reach the medical records of the patients, which was very important to confirm the diagnosis, the type of seizures, the duration of illness, the number of anti-seizure medications, and the past medical history.

Recommendations
We recommend that PWE should be regularly screened for depression especially during unusual circumstances like the COVID-19 pandemic. Early detection of depression in PWE and early adjustment of its risk factors helps for early treatment and better outcomes that will be reflected also on better management of epilepsy and better quality of life for those patients.

Acknowledgements
The authors would like to show their gratitude to all the study participants.

Authors’ contributions
MS: concept and design. MS, WM, UY, SL, and GE: data collection and interpretation of the data, writing of the draft. All authors read and approved the study.

Funding
None.

Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Declarations
Ethics approval and consent to participate
After a complete description of the study to the participants, informed written consent was obtained. Ethical approval was obtained from the Research Ethics Committee of the Faculty of Medicine, Zagazig University, under number ZU-IRB#6316.

Consent for publication
Not applicable.

Competing interests
The authors declare no conflict of interest.

Author details
1Psychiatry Department, Faculty of Medicine, Zagazig University, PO Box 44519, Zagazig, Egypt. 2Neurology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt. 3Neuropsychiatry Department, Abbaseya Hospital for Mental Illness, Cairo, Egypt.

Received: 25 January 2022 Accepted: 6 March 2022
Published online: 15 March 2022

References
1. Thijs RD, Surges R, O’Brien TJ, Sander JW (2019) Epilepsy in adults. Lancet (London, England) 393(10172):689–701
2. Mbizvo GN, Bennett K, Simpson CR, Duncan SE, Chin R (2019) Epilepsy-related and other causes of mortality in people with epilepsy: a systematic review of systematic reviews. Epilepsy Res 157:106192
3. Josephson CB, Jetté N (2017) Psychiatric comorbidities in epilepsy. Int Rev Psychiatry (Abingdon, England) 29(S):409–424
4. Vallée C, Braben A, Nic A, Loiseau M (2019) Épidémiologie et facteurs associés au syndrome dépressif chez les patient·s suivis au centre hospitalo-universitaire de Rennes pour une épilepsie [Epidemiology and factors associated with depression in patients followed at the hospital-university centre of Rennes for epilepsy]. Medicine (Baltimore) 58(18):e16091.
and associated factors with depression among people suffering from epilepsy: a transversal French study in a tertiary center. L’Encephale 45(1):40–45
5. Malhi GS, Mann JJ (2018) Depression. Lancet (London, England) 392(10161):2299–2312
6. Jamal-Omidi S, Collins C, Fulchiero E, Liu H, Colon-Zimmermann K, Fuentes-Casiano E, Tatsucka C, Cassidy KA, Lhatoo S, Sajatovic M (2018) Assessing depression severity with a self-rated vs. rater-administered instrument in patients with epilepsy. Epilepsy Behav 85:52–57
7. Blaszczuky B, Czaczwor SJ (2016) Epilepsy coexisting with depression. Pharmacol Rep 68(5):1084–1092
8. Dean J, Keshavan M (2017) The neurobiology of depression: an integrated view. Asian J Psychiatry 27:101–111
9. Gold PW, Machado-Vieira R, Pavlatou MG (2015) Clinical and biochemical manifestations of depression: relation to the neurobiology of stress. Neural Plast. 2015:581976
10. Salpekar JA, Mula M (2019) Common psychiatric comorbidities in epilepsy: how big of a problem is it? Epilepsy Behav 98(Pt B):293–297
11. Shader RI (2020) COVID-19 and depression. Clin Ther 42(6):962–963
12. Ettman CK, Abdalla SM, Cohen GH, Sampson L, Vivier PM, Galea S (2020) Prevalence of depression symptoms in US adults before and during the COVID-19 pandemic. JAMA Netw Open 3(9):e2019686
13. Kroenke K, Spitzer RL, Williams JB (2001) The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 16(9):606–613
14. Kroenke K, Spitzer RL, Williams JB, Lowe B (2010) The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. Gen Hosp Psychiatry 32(4):345–359
15. Al-Hadi AN, AlAtteeq DA, Al-Sharif E et al (2017) An Arabic translation, reliability, and validation of the Patient Health Questionnaire in a Saudi sample. Ann Gen Psychiatry 16:32
16. Yang Y, Yang M, Shi Q, Wang T, Jiang M (2020) Risk factors for depression in patients with epilepsy: a meta-analysis. Epilepsy Behav 106:107030
17. Sun L, Mo Q, Sun H, Niu Y, Si Y (2021) Depression in patients with epilepsy during the COVID-19 pandemic based on longitudinal self-reporting. Epileptic Disord 23(2):268–273
18. Abokalawa F, Ahmad SF, Al-Hasheli J, Hassan AM, Arabi M (2021) The effects of coronavirus disease 2019 (COVID-19) pandemic on people with epilepsy (PwE): an online survey-based study. Acta Neurol Belg:1–8 Advance online publication
19. Van Heers S, Siewe Fodjo JN, Wijtvliet V, Van den Bergh R, de Moura F, Villela E, da Silva CF, Weckhuysen S, Colebunders R (2020) Access to healthcare and prevalence of anxiety and depression in persons with epilepsy during the COVID-19 pandemic: a multicountry online survey. Epilepsy Behav 112:107350
20. Sonbol H, Alahdal HM, Alnazi RA, Alsamihary K, Ameen F (2021) COVID-19 pandemic causing depression in different sociodemographic groups in Saudi Arabia. Int J Environ Res Public Health 18(13):6953
21. Kaya Y, Bostan S, Kaya A, Karaman Ö, Karatay A, Dereli S (2021) Effect of COVID-19 pandemic on anxiety depression and intention to go to hospital in chronic patients. Int J Clin Pract 75(7):e14219
22. Çilliler AE, Güven B (2020) Sleep quality and related clinical features in patients with epilepsy: a preliminary report. Epilepsy Behav 102:106661
23. Stauder M, Vogel AC, Niroa DK, Tshering L, Dema U, Dorji C, Dorji L, Mateen FJ, Bhutan Epilepsy Project (2020) Depression, sleep quality, and social isolation among people with epilepsy in Bhutan: a cross-sectional study. Epilepsy Behav 112:107430
24. Dos Santos Lunardi M, de Carvalho RM, Alencastro Veiga Domingues Carneiro R, Giacomini F, Valente KD, Lin K (2021) Patients with epilepsy during the COVID-19 pandemic: depressive symptoms and their association with healthcare access. Epilepsy Behav 122:108178 Advance online publication
25. Lacey CJ, Salzberg MR, D’Souza WJ (2016) What factors contribute to the risk of depression in epilepsy? Tasmanian Epilepsy Register Mood Study (TERMS). Epilepsia 57(3):516–522
26. Dehn LB, Pfafflin M, Brückner S, Lutz MT, Steinhoff BJ, Mayer T, Bien CG, Nussbeck FW, May TW (2017) Relationships of depression and anxiety symptoms with seizure frequency: results from a multicenter follow-up study. Seizure 53:103–109
27. Mula M, Schmitz B (2009) Depression in epilepsy: mechanisms and therapeutic approach. Ther Adv Neurol Disord 2(5):337–344
28. Hesdorffer DC, Ishihara L, Myrenealli L, Webb DJ, Welj J, Hauser WA (2012) Epilepsy, suicidality, and psychiatric disorders: a bidirectional association. Ann Neurol 72:184–191 S1 Hesdorffer DC, Hauser WA, Olafsson E, Ludwigson P, Kjartansson O. Depression, and suicide attempt as risk factors for incident unprovoked seizures. Ann Neurol 2006; 59: 35–41
29. Kanner AM (2006) Depression and epilepsy: a new perspective on two closely related disorders. Epilepsy Curr 6(5):141–146
30. Bamaga AK, Alharbi O, Bajuafier M, Batarfi A, Althobaiti KH, AlQuaisib B (2020) The effect of the COVID-19 Pandemic on emergency department visits for neurological diseases in Saudi Arabia. Cureus 12(12)e12200. https://doi.org/10.7759/cureus.12200
31. Zis P, Yanti P, Siatouni A, Tavernarakis A, Gatzonis S (2014) Determinants of depression among patients with epilepsy in Athens, Greece. Epilepsy Behav 33:106–109
32. Bifftu BB, Dachew BA, Tiruneh BT, Birhan Tobeje N (2015) Depression among people with epilepsy in Northwest Ethiopia: a cross-sectional institution-based study. BMC Res Notes 8:585

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.