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RESEARCH

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Impact of COVID-19 pandemic on the care of people with epilepsy and predictors of epilepsy worsening: Aswan/upper Egypt hospital-based study

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Abstract

Background During the Coronavirus disease pandemic "COVID-19", epilepsy was one of many chronic neurological diseases in which treatment was neglected. This study aimed to evaluate the impact of the pandemic on people with epilepsy and identify potential predictors of seizure worsening through a face-to-face hospital survey. During the study period, 245 participants were recruited: 124 people with epilepsy (PwE) and 121 people without epilepsy (PwoE) age and sex-matched. Both groups were compared using sociodemographic COVID-19-related questionnaires and Hamilton Anxiety and Depression scales. PwE also completed epilepsy-specific questionnaires. Subsequently, we subdivided the PwE group into people with worsening epilepsy (WPwE) and those without (NWPwE).

Results Compared with PwoE, PwE had significantly higher rates of COVID-19 infection (59.7% versus 41.3%, $p=0.004$), and 69.4% of them (86/124) reported WPwE. WPwE had significantly higher rates of COVID-19 infection (75.6% versus. 23.7%, $p<0.0001$), emergency room visits (69.8% versus 42.1%, $p=0.004$), delayed neurology appointments (69.8% versus 42.1%, $p=0.004$), and difficulties accessing medication (69.8% versus 47.4%, $p=0.02$) and being less likely to be vaccinated (39.5% versus 68.4%, $p=0.003$) than NWPwE. Depression and anxiety rates increased significantly during the pandemic compared with prior pandemics in both PwE and PwoE ($p<0.0001$ for each). Moreover, the WPwE showed a significant increase in depression rates (33.7–60.5%, $p<0.0001$) and higher mean anxiety scores compared to the NWPwE ($p=0.029$). A multivariate binary logistic regression analysis showed that having a COVID-19 infection (AOR: 12.086, $p<0.0001$), being laid off (AOR: 0.024, $p=0.001$), or having more seizures before the pandemic (AOR: 3.366, $p=0.009$) were all strong predictors of seizures getting worse.

Conclusions Nearly 69% of PwE experienced pandemic-related seizures worsening, along with deterioration of mental health. Factors such as personal COVID-19 infection, unemployment, work interruption, and higher pre-COVID seizure frequency were identified as key predictors of seizure worsening. Mitigating these predictors could strengthen resilience among PwE during future widespread crises.

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Keywords Anxiety, COVID-19, Depression, Epilepsy, Seizure worsening

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Introduction

Epilepsy is one of the chronic neurological illnesses that had an increased risk of inadequate levels of medical care during the Coronavirus disease (COVID-19) [1]. COVID-19, caused by severe acute respiratory syndrome coronavirus 2, spread rapidly around the world after its first report in Wuhan, China, on December 12, 2019 [2]. Neurologists faced a huge challenge in providing quality care to patients with chronic diseases, particularly those with migraine, tension headaches, and epilepsy, while working to minimize the spread of the COVID-19 outbreak. Those patients were thought to have experienced increased psychological distress, such as despair or depression, during the COVID-19 pandemic, which could have resulted in non-compliance, potential relapse, and worsening of the condition [3–6].

People with epilepsy are particularly vulnerable to the negative impacts of the pandemic, such as heightened levels of psychosocial stress, social isolation, and disruption of sleep and dietary habits, since they are susceptible to physical and emotional disturbances or environmental and lifestyle changes. Many factors can increase the risk of seizures, illness and fever, stressful events, sleep deprivation, changes in antiseizure medications (ASM), and the use of proconvulsive treatments. Some of these factors are unavoidable during a socio-sanitary crisis like that experienced during COVID-19 [7–9].

Because of the exponential rise in infections, the Egyptian government declared a nationwide emergency; this entailed restricting public movement, mandating home confinement, and imposing social isolation. Flights to China were first suspended, followed by all international flights being suspended. Schools, universities, and public venues, along with mosques and churches, were closed by March 21. In summary, Egypt suspended travel, closed public spaces, and enforced social isolation policies to swiftly address the viral outbreak [10]. This nationwide lockdown, in addition to the direct effects of COVID-19, dramatically altered the lifestyle and regular routines of the entire population. Therefore, in addition to the risk of neurological involvement that COVID-19 itself poses, changes in the social environment may also negatively impact seizure control in people with epilepsy.

The present study aimed to evaluate the impact of the COVID-19 pandemic on people with epilepsy and to identify potential predictors of seizure worsening through a face-to-face hospital survey.

Methods

This study was a cross-sectional survey with some questions pertaining to earlier experience with the COVID-19 pandemic for all participants, with some items being of a retrospective nature (prior to COVID-19). The study was done at the epilepsy outpatient clinic of Aswan University Hospital in Aswan. People with epilepsy (PwE) were recruited consecutively during the period from June 2021 to June 2022. The inclusion criteria were (a) patients with epilepsy diagnosed according to the International League Against Epilepsy (ILAE), whether infected or not infected with COVID-19. (b) age ≥ 18: 50 years old, (c) both sexes were included, (d) with no history of trauma, cerebrovascular disease, metabolic, endocrinal, addiction, or other neurological disorders.

For the control group: People without epilepsy (PwoE), age and sex-matched healthy controls were recruited from the relatives of the participating people with epilepsy to be under the same environmental condition with the same exclusion criteria of people with epilepsy.

The study was approved by the ethical committee of the Faculty of Medicine, Aswan University, with Institutional Review Board (IRB) number: (547/7/21). The research complied with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from all participants to participate in the study after all the study points were explained before the start.

All participants were assessed with structured questionnaires, including the following:

Sociodemographic, COVID-19 related questions if they or members of their family were infected with COVID-19 or had COVID-19 illness symptoms, and psychiatric assessment using Hamilton Anxiety and Hamilton Depression scales (Arabic version) [11, 12]. Scores were collected retrospectively 6 months prior to and during the COVID-19 pandemic at the same session. The diagnosis of anxiety and depression was made according to the Diagnostic and Statistical Manual of Mental Disorders (5th ed; DSM–5) [13].

Hamilton Depression Scale (HDRS) is a 17-item scale designed to diagnose depression and estimate its severity. The degree of depression severity is extracted according to the following criteria: (0–7 no depression), (8–13 mild depression), (14–18 moderate depression), (19–22 severe depression), (23 and above very severe depression) [14]. Arabic version is used, as it was found to be reliable and valid [12].

Hamilton Anxiety Scale (HARS) is a 14-item scale designed to measure the severity of psychological and physical symptoms of anxiety [15]. The degree of anxiety severity was extracted according to the following criteria: Scores (8–14, mild anxiety); (15–23, moderate anxiety); and (≥ 24, severe anxiety) [16]. Arabic version is used, as it was found to be reliable and valid [11].

People with epilepsy were subjected to epilepsy-related questions that included the duration of their epilepsy, change in frequency and severity during the lockdown period, number of antiseizure medications (ASM),

difficulty in getting medications, disturbance of sleep and eating habits, work, and overall worries during the pandemic.

People with epilepsy were classified into two subgroups: people with worsening epilepsy (WPwE) and people without worsening epilepsy (NWPwE), according to the increase in seizure frequency and/or duration of seizure. The average frequency per month during the last 6 months prior and 6 months during COVID-19 was calculated. Any increase in the frequency of seizure or duration is considered worsening.

Statistical analysis: The data were analyzed using IBM SPSS Statistics (Version 26). The Shapiro–Wilk test for normality was used to check if data was normally distributed. Qualitative data were summarized in frequency and percentage, while the median was used for quantitative data as the current data were non-normally distributed. The categorical variables were compared using the chi-square test. The Mann–Whitney *U* test was used to compare mean values between two different groups. The Wilcoxon signed-rank test was used to compare measurements before and after treatment in the same group. McNemar testing was used to compare the proportion of depression and anxiety prior to and during COVID-19 in each group. A forward conditional stepwise binary logistic regression analysis was conducted to determine predictors of seizure worsening during the COVID-19 pandemic after adjusting for age and gender. Additional variables that were assumed or previously found to impact seizures were further assessed in later steps. A *p*-value of 0.05 or less was considered to be statistically significant.

Results

A total of 245 participants, 124 PwE and 121 PwoE, were included in the study (see Flowchart Fig. 1).

Table 1 shows the comparison between PwE and PwoE in sociodemographic characters and COVID-19-related experiences. The data shows similar age and gender distributions across both groups. Notably, PwE had a significantly higher rate of COVID-19 infection (59.7%) compared to PwoE (41.3%), which was significant ($p=0.004$). However, there were no substantial differences between the groups in terms of COVID-19 symptoms, family infections, vaccination rates, or healthcare utilization patterns.

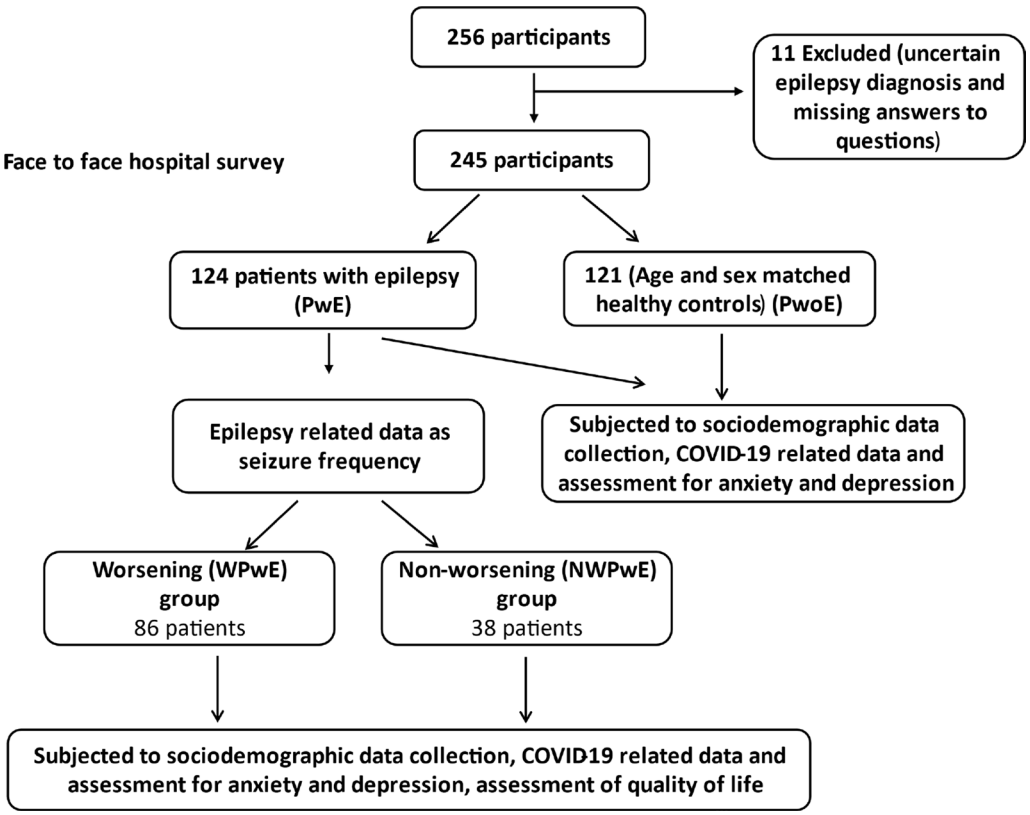

Fig. 1 Flowchart describes the study design, including the total number of people who participated in the study and their classification into people with epilepsy and without epilepsy and structured questionnaires applied for each group with subgroup analysis of people with epilepsy (people with worsening versus non-worsening epilepsy)

Table 1 Sociodemographic characteristics of people with epilepsy (PwE) and people without epilepsy (PwoE) and the influence of COVID-19 infection and confinement issues among studied groups

	PwE (*n* = 124)	PwoE (*n* = 121)	U/X^2 value	*P*- value
Sociodemographic characteristics				
Age in years				
Mean ± SD	28.69 ± 6.93	28.07 ± 6.72	7122.50	0.49
Median (IQR)	28.00 (9)	27.00 (9)		
Gender M/F: number (%)	77/47 (62.1%: 37.9%)	63/58 (52.1%: 47.9%)	2.52	0.11
Marital status: number (%)				
Single	59 (47.6%)	49 (40.5%)	1.26	0.53
Married	62 (50.0%)	69 (57.0%)		
Divorced	3 (2.4%)	3 (2.4%)		
Occupation: number (%)				
Unemployed	73 (58.9%)	57 (47.1%)	3.40	0.07
Employed	51 (41.1%)	64 (52.9%)		
COVID-19 infection questions: number (%)				
Have you passed the COVID-19 infection? (confirmed cases)				
Yes	74 (59.7%)	50 (41.3%)	8.25	0.004
No	50 (40.3%)	71 (58.7%)		
Have you symptoms of COVID-19 infection? (suspected cases)				
Yes	28 (22.6%)	23 (19.0%)	0.47	0.49
No	96 (77.4%)	98 (81.0%)		
Have some family members who live with you passed COVID-19? (confirmed cases)				
Yes	60 (48.4%)	56 (46.3%)	0.12	0.74
No	64 (51.6%)	65 (53.7%)		
Have some family members who live with you had symptoms of COVID-19? (suspected cases)				
Yes	67 (54.0%)	69 (57.0%)	0.22	0.64
No	57 (46.0%)	52 (43.0%)		
COVID-19 vaccination				
Yes	60(48.4%)	52 (43.0%)	0.72	0.40
No	64 (51.6%)	69 (57.0%)		
Health care attendance: number and %				
Have you been to the health center or hospital emergency room?				
Yes	76 (61.3%)	70 (57.9%)	0.30	0.58
No	48 (38.7%)	51 (42.1%)		
Did you avoid going to the emergency room, even though you needed to?				
Yes	70 (56.5%)	58 (47.9%)	1.78	0.18
No	54 (43.5%)	63 (52.1%)		
COVID-19 confinement issues: number (%)				
Have you strictly respected the confinement?				
Yes	67 (54.0%)	56 (46.3%)	1.47	0.23
No	57 (46.0%)	65 (53.7%)		
During this time, I have no problem going to work				
Yes	89 (71.8%)	79 (65.3%)	1.20	0.27
No	35 (28.2%)	42 (34.7%)		

The chi-square test was used to compare differences in frequency between groups. The Mann–Whitney test was used to compare differences in means between the two groups

IQR interquartile range, *PwE* People with epilepsy, *PwoE* People without epilepsy, *F* female, *M* male

Table 2 illustrates sociodemographic and epilepsy-related characteristics in the PwE group after being classified according to epilepsy frequency into WPwE and NWPwE. Out of 124 people with epilepsy, 86 (69.35%) developed worsening during the COVID-19 pandemic (increase in the frequency and/or duration of attacks), while the remaining 38 cases (30.65%) had no change in the number and duration of attacks. There was no significant difference in age or gender between the two groups, although more of the WPwE were single (60.5%), and more of the NWPwE were married (81.6%) ($p < 0.0001$). Also, for occupation, the WPwE were more likely to be unemployed (70.9%) ($p < 0.0001$). The table also shows the differences between the two groups in terms of epilepsy-related characteristics. There were no statistical differences between both groups in terms of duration of disease, duration of attack, epilepsy type (generalized versus focal), and number of ASMs. However, the epilepsy frequency almost doubled during COVID-19 in WPwE, whereas it remained unchanged in NWPwE, with a *P* value < 0.0001.

Table 3 compares COVID-19 experiences and healthcare issues between WPwE and NWPwE. WPwE had significantly higher rates of COVID-19 infection (75.6% versus 23.7%, $p < 0.0001$) and family member infections but lower rates of COVID-19 symptoms. They were less likely to be vaccinated (39.5% versus 68.4%, $p = 0.003$) and more likely to visit emergency rooms (69.8% versus 42.1%, $p = 0.004$). WPwE experienced more delays in neurology appointments and

Table 2 Sociodemographic and epilepsy characteristics in the worsening people with epilepsy and non-worsening people with epilepsy (WPwE and NWPwE)

		WPwE ($n = 86$)	NWPwE ($n = 38$)	U/X² value	*P*- value
Age in years:	Mean ± SD	28.08 ± 6.74	30.08 ± 7.25	1368.00	0.15
	Median (IQR)	27.00 (10)	29.00 (9)		
Gender M/F: number (%)		50/36 (58.1%: 41.9%)	27/11 (71.1%: 28.9%)	1.87	0.17
Marital status: number and %					
Single		52 (60.5%)	7 (18.4%)	22.05	< 0.0001
Married		31 (36.0%)	31 (81.6%)		
Divorced		3 (3.5%)	0 (0.0%)		
Occupation: number (%)					
Unemployed		61 (70.9%)	12 (31.6%)	16.86	< 0.0001
Employed		25 (29.1%)	26 (68.4%)		
Duration of disease in years:	Mean ± SD	8.21 ± 2.33	9.47 ± 3.53	1295.00	0.06
	Median (IQR)	8.00 (4)	9.00 (5)		
Duration of attack (min):	Mean ± SD	1.82 ± 1.02	1.68 ± 0.96	1499.00	0.51
	Median (IQR)	2.00 (2)	2.00 (2)		
Number of ASMs:	Mean ± SD	1.47 ± 0.55	1.39 ± 0.50	1542.00	0.56
	Median (IQR)	1.00 (1)	1.00 (1)		
One ASM		48 (55.8%)	23 (60.5%)	1.02	0.60
Two or more ASM		38 (44.19%)	15 (39.5%)		
Epilepsy type					
Generalized		45 (52.3%)	20 (52.6%)	1.39	0.50
Focal		41 (47.67%)	18 (47.4%)		
Epilepsy frequency (per month):					
6-months prior COVID -19:	Mean ± SD	1.65 ± 1.17	1.29 ± 1.06	1346.00	0.11
	Median (IQR)	2.00 (2)	1.00 (2)		
During COVID-19:	Mean ± SD	2.90 ± 1.37	1.29 ± 1.06	630.00	< 0.0001
	Median (IQR)	3.00 (2)	1.00 (2)		
Wilcoxon Signed Ranks Test: Z, *p*-value		− 8.536, < 0.0001	0.00, 1.00		

The Mann–Whitney test was used to compare differences in means between the two groups

Wilcoxon Signed Ranks Test was used to compare differences in means in the same group (prior to and during COVID-19)

IQR interquartile range, *WPwE* Worsening people with epilepsy, *NWPwE* Non-worsening people with epilepsy, *ASMs* anti-seizure medications

Table 3 COVID-19 Questions and health care and confinement issues of the people with worsening epilepsy versus non-worsening (WPwE and NWPwE)

	WPwE($n=86$)	NWPwE($n=38$)	X^2	*P*- value
COVID-19 infection questions: number (%)				
Have you passed the COVID-19 infection? (confirmed cases)				
Yes	65 (75.6%)	9 (23.7%)	29.50	< 0.0001
No	21 (24.4%)	29 (76.3%)		
Have you symptoms of COVID-19 infection? (suspected cases)				
Yes	14 (16.3%)	14 (36.8%)	6.38	0.012
No	72 (83.7%)	24 (63.2%)		
Have some family members who live with you passed COVID-19? (confirmed cases)				
Yes	52 (60.5%)	8 (21.1%)	16.39	< 0.0001
No	34 (39.5%)	30 (78.9%)		
Have some family members who live with you had symptoms of COVID-19? (suspected cases)				
Yes	51 (59.3%)	16 (42.1%)	3.14	0.08
No	35 (40.7%)	22 (57.9%)		
COVID-19 vaccination				
Yes	34 (39.5%)	26 (68.4%)	8.81	0.003
No	52 (60.5%)	12 (31.6%)		
Have you been to the health center or hospital emergency room?				
Yes	60 (69.8%)	16 (42.1%)	8.50	0.004
No	26 (30.2%)	22 (57.9%)		
Health care attendance: number and %				
Has your neurology consultation appointment been delayed due to COVID-19?				
Yes	60 (69.8%)	16 (42.1%)	8.50	0.004
No	26 (30.2%)	22 (57.9%)		
Did you avoid going to the emergency room even though you needed to?				
Yes	50 (58.1%)	20 (52.6%)	0.33	0.57
No	36 (41.9%)	18 (47.4%)		
COVID-19 confinement issues: number (%)				
Have you strictly respected the confinement?				
Yes	47 (54.7%)	20 (52.6%)	0.04	0.84
No	39 (45.3%)	18 (47.4%)		
During it have any problem for going to the pharmacy				
Yes	60 (69.8%)	16 (42.1%)	8.50	0.004
No	26 (30.2%)	22 (57.9%)		
During this time, do you have any problem finding drugs at the pharmacy?				
Yes	60 (69.8%)	18 (47.4%)	5.67	0.02
No	26 (30.2%)	20 (52.6%)		
During it, do you have any problem going to work?				
Yes	72 (83.7%)	17 (44.7%)	19.78	< 0.0001
No	14 (16.3%)	21 (55.3%)		

The chi-square test was used to compare differences in frequency between groups

WPwE Worsening people with epilepsy, *NWPwE* Non-worsening people with epilepsy

faced greater challenges in accessing pharmacies and finding medications. They also reported more work-related problems during confinement (83.7% versus 44.7%, $p < 0.0001$).

Table 4 shows the comparison between the prior and after COVID-19 pandemic among PwE versus PwoE, as well as between WPwE versus NWPwE in both depression and anxiety. Depression severity was notably higher in PwE than in PwoE. Both groups experienced a significant increase in depression frequency and severity during COVID-19 ($p < 0.0001$ for each group). Regarding anxiety, there was a marked increase in the percentage of patients with anxiety during the pandemic in both PwE and PwoE ($p < 0.0001$ for each group), with no statistical difference between groups.

Comparing WPwE and NWPwE, there were no significant differences in the frequency or the degree of depression between these groups, either before or during the pandemic. However, WPwE experienced a significant increase in the percentage of individuals with depression during the pandemic ($p < 0.0001$), while this remained unchanged in the NWPwE group ($p = 0.063$). Regarding anxiety, no significant differences in frequency were observed between WPwE and NWPwE either before or during the pandemic. Both groups experienced a significant increase in anxiety scores during the pandemic ($p < 0.0001$ for each). Interestingly, during the pandemic, WPwE exhibited higher mean anxiety scores compared to NWPwE ($p = 0.029$).

Table 5 outlines the most salient multivariate predictors of epilepsy worsening during COVID-19 as determined by forward stepwise binary logistic regression modeling. Additional models that included variables that did not significantly contribute to the multivariate model were removed. All the first four models were statistically significant ($p < 0.01$) with each additive step. The ultimate model identified four key risk factors as potential predictors for seizure worsening during the COVID-19 pandemic.

Unemployed patients (OR = 0.024; 95% CI 0.002–0.234) had 97.6% lower odds compared to employed patients, suggesting work exposures increase risk. COVID-19 infection history (OR = 12.09; 95% CI 3.09–47.21) conferred over 12 times higher odds of seizure worsening. Difficulty going to work (OR = 248.87; 95% CI 11.32–5469.87) was linked to over 200 times higher odds of worsened seizures. Higher pre-COVID seizure frequency (OR = 3.37 per month higher; 95% CI 1.36–8.32) with every additional month of seizures pre-pandemic was associated with 3.4 times higher odds of worsening seizures.

Table 4 Depression and anxiety prior to and during COVID-19 in people with epilepsy and people without epilepsy (PwE and PwoE) and in people with worsening epilepsy and non-worsening people without epilepsy (WPwE and NWPwE)

		PwE($n=124$)	PwoE($n=121$)	X^2/ U value	*P*- value	WPwE ($n=86$)	NWPwE ($n=38$)	U/ X^2 value	*P*- value
Hamilton depression rating scale									
Depression 6 months prior to COVID-19: number (%)									
Yes		73 (58.9%)	58 (47.9%)	2.94	0.09	48 (55.8%)	25 (65.8%)	1.08	0.29
No		51 (41.1%)	63 (52.1%)			38 (44.2%)	13 (34.2%)		
Degree of depression									
Mild depression		40 (32.3%)	46 (38.0%)	11.95	0.008	29 (33.7%)	11 (28.9%)	5.01	0.17
Moderate depression		27 (21.8%)	11 (9.1%)			17 (19.8%)	10 (26.3%)		
Severe depression		6 (4.8%)	1 (2.5%)			2 (2.3%)	4 (10.5%)		
Depression during COVID-19: number (%)									
Yes		92 (74.2%)	81 (66.9%)	1.55	0.21	62 (72.1%)	30 (78.9%)	0.64	0.42
No		32 (25.8%)	40 (33.1%)			24 (27.9%)	8 (21.1%)		
Degree of depression									
Mild depression		43 (34.7%)	55 (45.5%)	13.9	0.008	31 (36.0%)	12 (31.6%)	2.25	0.69
Moderate depression		28 (22.6%)	21 (17.4%)			19 (22.1%)	9 (23.7%)		
Severe depression		17 (13.7%)	5 (4.1%)			10 (11.6%)	7 (18.4%)		
Very severe depression		4 (3.2%)	0			2 (2.3%)	2 (5.3%)		
McNemar testing (prior to and after COVID-19)		< 0.0001	< 0.0001			< 0.0001	0.063		
6-months prior COVID -19:	Mean ± SD	9.67 ± 5.08	7.74 ± 3.94	5993.00	0.006	8.90 ± 3.93	11.42 ± 5.50	1216.50	0.023
	Median (IQR)	8.00 (8)	7.00 (5)			8.00 (6)	11.00 (9)		
During COVID -19:	Mean ± SD	12.15	9.9	5933.50	0.005	11.63 ± 4.87	13.32 ± 6.09	1367.50	0.15
	Median (IQR)	12.00 (10)	9.00 (6)			10.00 (8)	13.00 (10)		
Wilcoxon Signed Ranks Test (prior versus during COVID-19): Z, *p*-value		− 8.411, < 0.0001	− 7.656, < 0.0001			− 6.985, < 0.0001	− 4.741, < 0.0001		
Hamilton anxiety rating scale									
Anxiety 6 months prior COVID-19: number (%)									
Yes		6 (4.8%)	2 (1.7%)	1.96	0.16	5 (5.8%)	1 (2.6%)	0.58	0.45
No		118 (95.2%)	119 (98.3%)			81 (94.2%)	37 (97.4%)		
Degree of anxiety									
Mild anxiety		6 (4.8%)	2 (1.7%)	1.96	0.16	5 (5.8%)	1 (2.6%)	0.58	0.45
Anxiety during COVID-19: number (%)									
Yes		50 (40.3%)	40 (33.1%)	1.39	0.24	38 (44.2%)	12 (31.6%)	1.74	0.19
No		74 (59.7%)	81 (66.9%)			48 (55.8%)	26 (68.4%)		
Degree of anxiety									
Mild anxiety		50 (40.3%)	40 (33.1%)	1.39	0.24	38 (44.2%)	12 (31.6%)	1.74	0.19
McNemar testing (prior to and after COVID-19)		< 0.0001	< 0.0001			< 0.0001	0.001		

Table 4 (continued)

		PwE($n=124$)	PwoE($n=121$)	X^2/ U value	*P*- value	WPwE ($n=86$)	NWPwE ($n=38$)	U/ X^2 value	*P*- value
6-months prior COVID -19:	Mean ± SD	3.91 ± 1.98	3.54 ± 1.73	6771.50	0.18	4.09 ± 1.97	3.50 ± 1.94	1389.00	0.18
	Median (IQR)	4.00 (3)	4.00 (3)			4.00 (3)	4.00 (3)		
During COVID -19:	Mean ± SD	6.90 ± 2.21	6.31 ± 2.24	6565.00	0.09	7.19 ± 2.17	6.26 ± 2.20	1235.00	0.029
	Median (IQR)	7.00 (4)	6.00 (3)			7.00 (3)	6.00 (3)		
Wilcoxon Signed Ranks Test (before versus during): Z, *p*-value		− 8.887, < 0.0001	− 8.453, < 0.0001			− 7.40, < 0.0001	− 4.961, < 0.0001		

Table 5 Forward stepwise multivariate binary logistic regression analysis results for significant predictors (Steps 1–4) for people with worsening epilepsy during the COVID-19 pandemic

	Potential predictors	B	S.E	Wald	df	Sig	Exp(B)	95% C.I. for EXP(B)	
								Lower	Upper
Step 1	Have you passed the COVID-19	2.284	0.457	24.989	1	< 0.0001	9.820	4.01	24.05
	Constant	− 0.323	0.287	1.269	1	0.260	0.724		
Step 2	Occupation	− 2.434	0.601	16.417	1	< 0.0001	0.088	0.03	0.28
	Have you passed the COVID-19	2.959	0.606	23.843	1	< 0.0001	19.287	5.88	63.26
	Constant	0.532	0.366	2.117	1	0.146	1.703		
Step 3	Occupation	− 4.175	1.119	13.923	1	< 0.0001	0.015	0.00	0.14
	Have you passed the COVID-19	2.414	0.637	14.362	1	< 0.0001	11.180	3.21	38.96
	During it have any problem in going to work	3.471	1.105	9.860	1	0.002	32.171	3.69	280.81
	Constant	− 0.599	0.487	1.517	1	0.218	0.549		
Step 4	Occupation	− 3.740	1.167	10.268	1	0.001	0.024	0.00	0.23
	Have you passed the COVID-19	2.492	0.695	12.851	1	< 0.0001	12.086	3.09	47.21
	During this time, I have no problem going to work	5.517	1.577	12.245	1	< 0.0001	248.869	11.32	5469.87
	Epilepsy frequency during 6 months prior to COVID	1.214	0.462	6.905	1	0.009	3.366	1.36	8.32
	Constant	− 3.931	1.458	7.267	1	0.007	0.020		

The reference category for categorical variables is:

Unemployed, no personal symptoms of COVID-19, no problem in going to work

Exp (B): Adjusted odds ratio (AOR), CI: confidence interval

Discussion

The COVID-19 pandemic posed numerous challenges for healthcare systems and patients worldwide. Our study aimed to assess the impacts on people with epilepsy and identified the predictors of seizure worsening. The Key Findings in this study were: 1- Significantly higher rates of COVID-19 infection among PwE than PwoE. 2- Significantly increased symptoms of depression and anxiety in both groups. 3- A high percentage (69.35%) of people with epilepsy reported seizure worsening.

All subjects were consecutively recruited in the current study, and as a result, there were no significant sociodemographic differences between the groups (PwE and PwoE), indicating a lack of selection bias. This result is consistent with previous studies [9, 17, 18]. However, previous studies that collected data via online/web-based surveys reported some sociodemographic differences, such as a predominance of female participants (> 63–79%) [1, 17, 19]. This finding is likely related to the methodology of data collection and the characteristics of respondents who participate in online surveys.

As reported by Zhou and colleagues (2023), the present study found that PwE had significantly higher COVID-19 infection rates compared with PwoE. Cabezudo-Garcia and colleagues (2020) reported similar findings and suggested that respiratory comorbidities, such as the increased risk of aspiration pneumonia in generalized seizures, may increase infection susceptibility [20].

Also, Wang and colleagues (2022) reported that PwE had a lower level of awareness regarding certain COVID-19 preventive measures and control strategies than healthy controls [18], which could make them more vulnerable to getting the infection. In contrast, Asadi-Pooya and colleagues (2021 and 2022) found no differences in infection rates or severity between people with epilepsy and others [21, 22]. Asadi-Pooya and colleagues (2022) reported that people with epilepsy were not more prone to contracting COVID-19 than others and that COVID-19 in people with epilepsy is not associated with a more severe illness or a poorer prognosis [23].

A high percentage (69.35%) of PwE reported seizure worsening during COVID-19. This rate is higher than that reported in previous studies: 30 and 23.2% of respondents used online surveys in the data collection [17, 24]. Our rates also exceed Italian [1], Saudi [25], Spanish [26], and Malaysia [27] studies. Moreover, unlike previous reports [1, 23, 28], none of our cohort showed improvement in seizure frequency during the pandemic. Differences in sample sizes, regional responses, data-gathering approaches, and different healthcare strategies during the COVID-19 pandemic could contribute to inconsistencies.

This study demonstrated significant differences in the marital and employment statuses between WPwE and NWPwE despite no age or gender differences. WPwE were more likely to be single and unemployed, while NWPwE were married and employed. This finding aligns with previous research, which reported that lack of seizure control and early onset negatively correlated with marriage [29]. Additionally, a previous study demonstrated that frequent seizures have been linked to higher unemployment and early retirement rates among PwE. Conversely, the only predictor of job retention was the remission of seizures [30]. These findings can be explained by: In times of societal constriction, marriage may improve seizure outcomes by increasing social support. Moreover, spouses often care for PwE [31], which enhances ASM adherence and seizure control. Furthermore, epilepsy worsening was linked to employment status for numerous reasons and was bidirectional. Higher infection risks and diminished work capability make commuting to work difficult, potentially leading to frequent work interruptions and job loss. Unemployment may lead to financial constraints [9], which might affect ASM adherence [32], leading to the worsening of epilepsy. This complicated interaction between socioeconomic characteristics and epilepsy outcomes emphasizes the need for a comprehensive approach to epilepsy care that considers clinical and social issues.

In this study, the WPwE group exhibited higher percentages in the majority of COVID-19-related issues, such as the significant rate of personal and family members' COVID-19 infection, increased emergency care usage, delayed neurology consultation appointments, and more difficulty going to the pharmacy with reduced access to ASM. This finding suggests that COVID-19 disproportionately impacted those with worsening seizure control. These findings are consistent with previous reports from earlier studies [1, 26, 32–36]. Furthermore, the significantly lower rate of vaccination in the WPwE in the present study aligns with the results of the prior study conducted by Zhou and colleagues in 2023 [34]. The current study also found that work difficulties were more pronounced among WPwE, consistent with a general effect of increased seizure rate on patients' daily activities. Previous studies also report alterations in work-related activities during the COVID-19 pandemic, wherein 25.2% of employees operated remotely [17] reported work interruptions between March and May 2020 [37].

The association between COVID-19 infection and epilepsy worsening in people with epilepsy (PwE) may be explained through several mechanisms: (1) COVID-19 virus interacts with angiotensin-converting enzyme 2 (ACE2), potentially affecting seizure frequency through cytokine storms, blood–brain barrier damage, and dysregulation of renin-angiotensin and kallikrein-kinin systems [38, 39]; (2) Post-infection fever and elevated Interleukin-6 (IL-6) levels may exacerbate seizures[40–42], however, direct detection of the COVID-19 virus in cerebrospinal fluid is limited [43], warranting further research; (3) Other COVID-19-related factors such as hypoxia or cerebrovascular events could increase the epilepsy frequency [44]; (4) The COVID-19 illness itself may result in psychological stress, non-adherence to antiseizure medications (ASMs) or their unavailability, disrupted sleep cycles, ultimately contributing to epilepsy worsening [33, 45, 46].

The findings of the current study of significantly lower vaccination rates among WPwE compared to NWPwE provide insights into COVID-19 vaccination's role in epilepsy outcomes. A growing body of evidence supports the protective effect of COVID-19 vaccination for epilepsy patients: Some studies report post-vaccination seizure increases in only 5–7.65% of vaccinated PwE [47, 48], which are significantly lower than those associated with COVID-19 infection. Other studies show that only 2.5% of vaccinated PWE experienced seizure exacerbations, occurring solely in those with pre-existing seizures [49], and vaccinated PwE who contracted COVID-19 mostly had lower frequency seizures than unvaccinated individuals [34]. Multiple studies confirm good vaccine tolerability and effectiveness in preventing severe disease progression [50–52]. These findings suggest that the

benefits of vaccination for PwE significantly outweigh the minimal risks of seizure exacerbations [49].

The significant impact of "Not going to work" on epilepsy worsening can be attributed to the mandatory social isolation measures and increased frequency of emergency care visits that disrupted normal daily activities and interfered with work attendance [9]. These factors act as stressful conditions, consequently leading to exacerbation of symptoms and increased seizure frequency.

In this study, there is a significant increase in depression and anxiety in both subgroups (PwE compared to PwoE) during COVID-19, which suggests that the impact of the pandemic was similar across the population and led to significant stress, anxiety, and fear of catching the infection. Several previous studies have reported a higher prevalence of anxiety and depression among PwE than PwoE [1, 18, 32]. The severity of depression among people with epilepsy increased following the outbreak of COVID-19. This finding may be due to seizure-related fears, limited access to medical resources, heightened challenges in accessing medical care, financial strain, prolonged isolation, apprehension towards COVID-19, and diminished psychological coping skills and adjustment capabilities [34, 53].

Moreover, the current study revealed that COVID-19 significantly increased the incidence of depression and anxiety in both WPwE and NWPwE. Similar findings were reported by previous studies [1, 28, 54]. Potential reasons for worse mental health include social isolation, fears related to COVID-19 contraction, and coping deficiencies when managing stress and epilepsy self-care [55, 56]. Additionally, the increase in drug load and seizure severity that often accompanies uncontrolled seizures may directly worsen anxiety and depression in patients with epilepsy [57].

In this study, personal COVID-19 infection, unemployment, work interruption, and higher pre-COVID seizure frequency emerged as potential predictors of seizure worsening. Previous studies investigated the predictors of seizure worsening; Assenza and colleagues in 2020 indicated that chronic ASMs and the Pittsburgh Sleep Quality Index (PSQI) substantially affected seizure worsening [1]. Unfortunately, we did not assess sleep disorders among participants. Koh and colleagues (2021) identified baseline seizure frequency > 1 per month, anxiety, and sleep issues as key predictors [27]. Abokalawa and colleagues 2022 found that retirement or joblessness, moderate or severe stress, poor sleep quality, and others were potential predictors for worsened seizures [17]. Furthermore, despite the rate of vaccination being significantly lower in WPwE than in NWPwE in the univariate analysis, vaccination was not detected as a predictor of seizure worsening in the multivariate analysis. In general, the identification of these potential predictors of seizure worsening and the implementation of policy, workplace, and community modifications to mitigate these risks should enhance the resilience of individuals with epilepsy in the face of future mass crises.

The strength of this study was patient assessment through face-to-face hospital interviews. However, it had some limitations, including a relatively small sample size, lack of assessment of sleep, comorbidities, and compliance with ASM, which could be among the factors that result in seizure worsening.

Conclusion

In summary, nearly 69% of people with epilepsy experienced pandemic-related seizure worsening, accompanied by reduced mental health and quality of life. Personal COVID-19 infection, unemployment, work interruption, and higher pre-COVID seizure frequency appear to be potential predictors for seizure-worsening. Mitigating these risks through workplace, community, and policy changes could strengthen resilience among people with epilepsy during future widespread crises.

Abbreviations

ACE2	Angiotensin-converting enzyme 2
ASM	Antiseizure medication
COVID-19	Coronavirus disease of 2019
HARS	Hamilton anxiety rating scale
HDRS	Hamilton depression rating scale
ILAE	International League against epilepsy
IL-6	Interleukin-6
NWPwE	Non-worsening people with epilepsy
PwE	People with epilepsy
PwoE	People without epilepsy
WpwE	Worsening people with epilepsy

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Author contributions

E.M.K: study conception, design of the work, statistical analysis, and critical revision of the manuscript and editing. N.A.H: statistical data analysis, original draft writing, manuscript reviewing and editing. M.N.O: study conception, design of the work, data analysis, manuscript reviewing and editing. G.K.A: data analysis, manuscript reviewing and editing. A.S.E: Acquisition of data, data analysis, manuscript reviewing and editing. B.M.A: study conception, design of the work, data analysis, manuscript reviewing and editing. All authors have read and approved the final version of the manuscript to be published.

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Availability of data and materials

All data generated or analysed during this study are available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

The study was approved by the ethical committee of the Faculty of Medicine, Aswan University with IRB number: (547/7/21). This study was registered in a clinical trial registry with the identification number (ID): NCT05205590. The research adhered to the ethical principles outlined in the World Medical Association's Declaration of Helsinki. After explaining all aspects of the study prior to commencement, written informed consent to participate was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

All authors disclose no competing interests related to this study.

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