

The impact of the Covid-19 pandemic on a Greek cohort of patients with epilepsy

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Abstract

Background: The Covid-19 pandemic, the subsequent lockdown, and the measures of social distancing may have had adverse effects on patients with epilepsy (PWE). This study was designed to assess the pandemic's psychological impact on the Greek non-infected PWE and possible changes in their seizure control.

Method: The patients were evaluated utilizing a semi-structured interview consisting of open questions regarding their demographic, social, and clinical characteristics, followed by five questions (on a scale of 0-10) related to the Covid-19 pandemic, lockdown, and social distancing measures. Anxiety and depression of PWE were screened using the Hospital Anxiety and Depression Scale (HADS), which consists of HADS-Anxiety and HADS-Depression subscales.

Results: We evaluated 65 PWE in the outpatient clinic (60 %) or via telephone interview (40 %). None of these patients experienced changes in seizure control. The mean scores of the Covid-19-related questions were 6.1 ± 2.7 (fear of getting infected), 4.7 ± 3.3 (fear of death), 7.1 ± 2.7 (fear of sickness for their relatives), 6.4 ± 3.1 (stress during lockdown), and 3.0 ± 2.9 (fear of antiepileptic drugs unavailability). Thirty-nine (60 %) patients screened positive for anxiety and thirty-three (50.8 %) for depression.

Conclusion: The psychological impact of the Covid-19 pandemic, lockdown, and social distancing measures on non-infected PWE was moderate without changes in their seizure control. HIPPOKRATIA 2021, 25 (4):145-150.

Keywords: Epilepsy, Covid-19, lockdown, psychological impact, anxiety, depression

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Introduction

The coronavirus disease (Covid-19) was first reported in December 2019. In a very brief period, it has spread worldwide and was declared a pandemic a few months later, forcing governments all over the world to implement lockdowns and social distancing measures to restrain the transmission. The pandemic and the subsequent restrictive measures affected the general population physically and psychologically, especially patients with chronic health conditions¹⁻⁴.

Epilepsy is one of the most common chronic neurological diseases⁵⁻⁸, which does not seem to be a risk factor for Covid-19^{2,3,5,7,8}. During the pandemic, several studies in different countries reported that non-infected patients with epilepsy (PWE) had a high level of anxiety and depression, resulting in increased seizure frequency⁸⁻¹⁰. It is generally accepted that many factors precipitate epileptic seizures, and psychological distress is a prominent one^{9,11-13}. However, other studies during the pandemic showed increased seizure frequency in PWE, with mild anxiety and depression symptoms^{10,13,14}.

All these studies were conducted during the first pandemic wave with inconclusive results. No study had been conducted in Greece during that period; therefore, we decided to conduct this study in a Greek cohort in the middle of the second pandemic wave. We hypothesize that the Covid-19 pandemic and the subsequent lockdown and social distancing measures may have adverse effects on PWE. This study aimed to evaluate the psychological impact of the pandemic on non-infected PWE and assess possible changes in their seizure control.

Materials and Methods

In the current study, we included all patients diagnosed with epilepsy according to the International League against Epilepsy (ILAE) classification of epilepsies¹⁵, who attended the outpatient clinic of Hippokratia Hospital in Thessaloniki for at least one year before the pandemic, with fully recorded medical history. We excluded patients younger than 18 years of age, patients with mental retardation, and patients infected with Covid-19, either themselves or their family members.

We recruited patients who attended the outpatient clinic in January 2021 and were interviewed after giving written informed consent and patients who contacted us by phone at the same time to report their clinical status after giving verbal consent for participation (followed by written consent subsequently sent). A few days later, they were interviewed via telephone, and the consultation was recorded by the study's investigators^{5,7,10}. The study was approved by the Ethical Committee of the Hippokratiko General Hospital of Thessaloniki, Greece (decision No 30330/2021).

We evaluated the patients utilizing a semi-structured interview that consisted of open questions regarding patients' demographic, clinical, and social characteristics, followed by five Covid-19 managing questions and anxiety and depression screening measurements with the Hospital Anxiety and Depression Scale (HADS)^{8,16}. The time frame of the information obtained by this interview was locked to one month earlier.

The respondents' demographic and social characteristics were age, residence (e.g., urban or rural), education, and employment status, while the selected clinical characteristics included: i) epilepsy-related such as duration of the disease, types of seizure, treatment efficacy, number of antiepileptic drugs (AED), and seizure frequency¹⁷, ii) Covid-19 infection, and iii) history of psychiatric disease or psychiatric treatment intake.

We evaluated the behavior of PWE coping with the Covid-19 pandemic and the restrictive measures, employing five scaling questions, each yielding a score ranging from zero to ten, with zero denoting no distress or fear at all and ten marking the highest level of frustration. The respondents were asked to scale their answers to the following questions: i) "Do you have a fear of getting infected from Covid-19 and the consequences of it?" ii) "Do you fear that you might die from Covid-19?" iii) "Are you worried about your relatives or caregivers getting sick from Covid-19?" iv) "How stressful are the lockdown and social distancing measures to you?" v) "How much do you worry that you may be unable to get a refill of your antiepileptic drugs?"

Finally, using HADS in the format validated for Greek patients¹⁶, we screened the PWE for anxiety and depression. The HADS comprises two subscales, each with seven questions, screening for anxiety (HADS-A) and depression (HADS-D). The answer options follow a 0-3 Likert scale. Zero corresponds to no sign, while three to the highest level of anxiety or depression for a particular question in this screening tool. For each subscale, the maximum score is 21, with a higher score indicating more severe psychological issues. A score of 0-7 on HADS-A or HADS-D is considered normal, whereas higher than seven is considered pathological for the respective condition¹⁶. A score of 8-10 is considered borderline, 11-14 moderate, and 15-21 severe^{8,16,18}.

Statistical analysis

The study's findings were analyzed using non-parametric

tests due to the non-normally distributed nature of most of the data. Comparisons between means of two unrelated variables were performed using the Mann-Whitney U test, while the Kruskal-Wallis H test was employed to compare three or more variables. Correlations between HADS scores, Covid-19-related questions scores, and various demographic, social, and epilepsy-related characteristics of PWE were calculated using Spearman's rho correlation coefficient. We set the level of statistical significance at $p < 0.05$. The IBM SPSS for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA) statistics software was employed for all calculations.

Results

A total of 65 PWE were included in this study, with demographic, social, and epilepsy-related characteristics presented in Table 1. Thirty-two patients had generalized onset seizures, and 33 had focal onset seizures. Of the 33 patients with incomplete seizure control under treatment during the last year before the pandemic, 14 had weekly seizures (1-3 per week), 11 had monthly seizures (1-3 per month), and eight had at least once a year (1-10 per year). There was no change in seizure frequency during the pandemic, and the seizure-free patients were stable both before and during the pandemic. The study sample had no change in antiseizure medication and employment status during the pandemic. None of the patients had a history of psychiatric disorders.

Thirty-nine patients (60 %) were evaluated in the outpatient clinic, and 26 (40 %) via telephone interview and answered all the Covid-19-related questions and HADS.

All Covid-19-related question scores showed a strong positive correlation to HADS total score (Figure 1, Figure 2). The first two questions related to fear of i)

Table 1: Demographic, social, and epilepsy-related characteristics of the 65 patients with epilepsy who were evaluated in the outpatient clinic or via telephone in January 2021.

Characteristics	mean \pm SD	range
Age (yrs)	45.5 \pm 14.8	18 - 72
Education (yrs)	12.7 \pm 2.7	9 - 17
Disease duration (yrs)	15 \pm 10.8	2 - 40
	number	%
Male	28	43.1
Female	37	56.9
Employed	28	43.1
Unemployed	37	56.9
Urban resident	34	52.3
Rural resident	31	47.7
Treatment Efficacy		
Seizure-free	32	49.2
No seizure-free	33	50.8
Number of AED		
One	33	50.8
Two	16	24.6
Three and more	16	24.6

SD: Standard Deviation,

AED: Antiepileptic drugs.

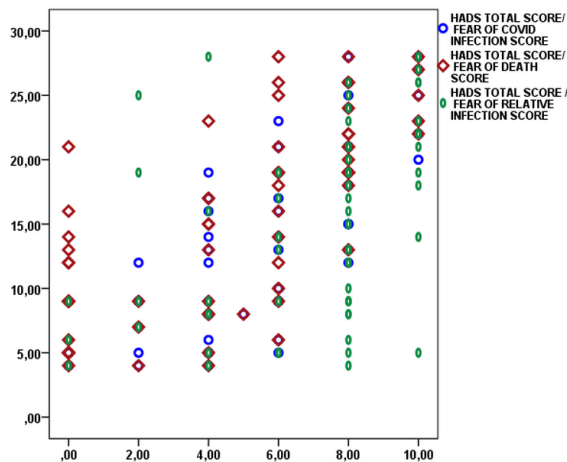


Figure 1: Scatterplot presenting the relationship between Hospital Anxiety Depression Scale (HADS) total score (y-axis values) and three Covid-19-related questions scores regarding fear of infection, death, and relative infection (x-axis values). These Covid-19-related question scores showed a strong positive correlation to HADS total score ($p < 0.001$).

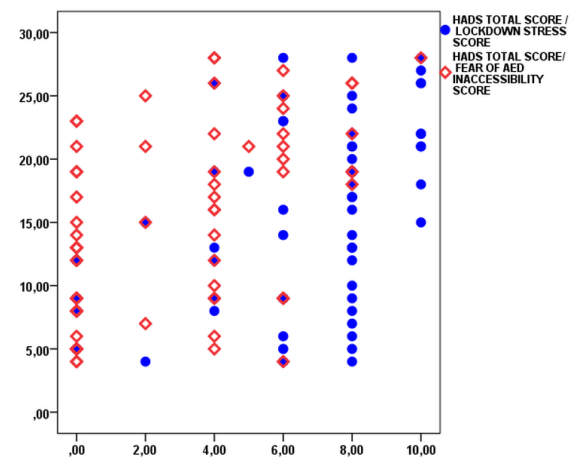


Figure 2: Scatterplot presenting the relationship between Hospital Anxiety Depression Scale (HADS) total score (y-axis values) and two Covid-19 related questions scores regarding lockdown stress and fear of antiepileptic drug unavailability (x-axis values). These Covid-19-related question scores showed a strong positive correlation to HADS total score ($p < 0.001$).

getting infected or ii) dying from Covid-19 correlated to HADS total score with a $\rho = 0.789$ ($p < 0.001$) and $\rho = 0.718$ ($p < 0.001$), respectively. The third question referring to fear of sickness from Covid-19 for their relatives yielded a $\rho = 0.489$ ($p < 0.001$), while the last two questions related to lockdown and fear for possible drug unavailability correlated to HADS total score with a $\rho = 0.496$ ($p < 0.001$) and $\rho = 0.493$ ($p < 0.001$), respectively.

Table 2 shows the study sample’s mean scores of the Covid-19-related questions. These scores indicate that the level of fear of getting infected with Covid-19, either themselves or their relatives, and stress during lockdown was moderate, and the level of fear of death or AED unavailability was mild¹⁹.

Thirty-nine patients (60 %) screened positive for anxiety, of whom 17 (44 %) were at borderline level, 17 (44 %) at a moderate level, and five (12 %) at a severe level. Thirty-three patients (50.8 %) screened positive for depression, of whom 23 (69 %) were at a borderline level and ten (31 %) at a moderate level.

Exploring the impact of the demographic, social, and epilepsy-related characteristics of PWE, contained

in Table 1, on the scores of Covid-19-related questions and the HADS, HADS-A, and HADS-D scores, we observed that age correlated positively to fear of death score ($\rho = 0.267$, $p = 0.032$), HADS total score ($\rho = 0.256$, $p = 0.039$), and HADS-D score ($\rho = 0.296$, $p = 0.01$). Employment status was related to anxiety and depression levels as well as to fear of Covid-19 infection, fear of death, and stress level due to lockdown, with unemployed patients scoring higher than employed ones (Table 3). Seizure control was related to depression, fear of death, and fear of AED unavailability. Patients with incomplete seizure control yielded higher scores than those who were seizure-free (Table 4). The remaining demographic social and epilepsy-related characteristics of patients showed no significant association to the scores of Covid-19-related questions as well as to the HADS total and subscales scores.

Discussion

This study assessed the impact of the Covid-19 pandemic in a Greek cohort of PWE. Our patients had moderate fear of getting infected with Covid-19, either themselves or their relatives, and were moderately stressed by

Table 2 : Mean scores of the Covid-19-related questions of the 65 patients with epilepsy who comprised this study’s sample.

Questions	mean ± SD	range	95% Confidence Interval	
			mean ± SD	range
Fear of getting infected	6.1 ± 2.7	2 - 10	6.1 ± 0.3	5.3 - 6.7
Fear of death	4.7 ± 3.3	0 - 10	4.7 ± 0.4	3.9 - 5.5
Fear of sickness for their relatives	7.1 ± 2.7	2 - 10	7.1 ± 0.3	6.4 - 7.7
Stress during lockdown	6.4 ± 3.1	0 - 8	6.4 ± 0.4	5.6 - 7.1
Fear of AED unavailability	3.0 ± 2.9	0 - 10	3.0 ± 0.4	2.3 - 3.7

The mean scores indicate that the level of fear of getting infected from Covid-19 themselves or their relatives and stress during lockdown was moderate, and the level of fear of death or AED unavailability was mild. The questions’ score range was 0-10.

CI: Confidence Interval, SD: Standard Deviation, AED: Antiepileptic drugs.

Table 3 : Correlation of the scores of the Covid-19-related questions (range 0-10), of the Hospital Anxiety Depression Scale (HADS; range 0-42), and HADS-Anxiety (HADS-A; range 0-21), HADS-Depression (HADS-D; range 0-21) with the employment status of the study's sample.

Questions/Tests	mean \pm SD		p-value
	Employed patients	Unemployed patients	
Fear of getting infected	5.2 \pm 2.6	6.6 \pm 2.7	0.025*
Fear of death	3.5 \pm 3.3	5.6 \pm 3.1	0.013*
Fear of sickness for their relatives	7.2 \pm 2.1	6.9 \pm 3.1	0.077
Stress during lockdown	5.1 \pm 3.3	7.3 \pm 2.5	0.005*
Fear of AED unavailability	2.2 \pm 2.6	3.6 \pm 3.1	0.066
HADS Total	11.4 \pm 5.9	18.1 \pm 7.1	<0.001*
HADS-A	6.4 \pm 3.8	9.4 \pm 4.3	0.005*
HADS-D	4.9 \pm 2.9	8.7 \pm 3.5	<0.001*

*Values of p in bold are statistically significant ($p < 0.05$).

Unemployed patients scored statistically higher than employed patients in questions regarding fear of getting infected, fear of death, stress during lockdown, HADS total, HADS-A and HADS-D.

SD: Standard Deviation, AED: Antiepileptic drugs, HADS: Hospital Anxiety Depression Scale, HADS-A: HADS-Anxiety, HADS-D: HADS-Depression.

Table 4 : Correlation of the scores of Covid-19-related questions (range 0-10), of the Hospital Anxiety Depression Scale (HADS; range 0-42), and HADS-Anxiety (HADS-A; range 0-21), HADS-Depression (HADS-D; range 0-21) with the seizure control status of the study's sample.

Questions/Tests	mean \pm SD		p-value
	seizure-free patients	no seizure-free patients	
Fear of getting infected	5.6 \pm 2.5	6.4 \pm 2.9	0.144
Fear of death	3.8 \pm 3.3	5.6 \pm 3.2	0.034*
Fear of sickness for their relatives	7.2 \pm 2.7	6.9 \pm 2.8	0.761
Stress during lockdown	6.2 \pm 3.3	6.5 \pm 2.8	0.949
Fear of AED unavailability	2.1 \pm 2.5	3.9 \pm 3.1	0.017*
HADS Total	13.3 \pm 6.7	17.1 \pm 7.5	0.026*
HADS-A	7.2 \pm 3.9	9.0 \pm 4.6	0.099
HADS-D	6.1 \pm 3.4	8.1 \pm 3.8	0.025*

*Values of p in bold are statistically significant ($p < 0.05$).

Patients with incomplete seizure control scored statistically higher than seizure-free patients in questions regarding fear of death, fear of AED unavailability, HADS total, and HADS-D.

SD: Standard Deviation, AED: Antiepileptic drugs, HADS: Hospital Anxiety Depression Scale, HADS-A: HADS-Anxiety, HADS-D: HADS-Depression.

the restrictive measures. Some studies showed that 19-39 % of PWE are afraid of getting infected^{5,9,20,21}, while Friedrich et al observed that the patients feared 50 % more for their relatives getting infected than for themselves²⁰. Stress from lockdown was moderate and severe, as reported by Alkhotani et al and Friedrich et al, respectively^{9,20}.

Sixty percent of the study sample screened positive for anxiety and 50.8 % for depression. Older, unemployed, and patients with incomplete seizure control tend to be more severely affected. Relevant studies showed that during the pandemic, PWE had anxiety and depression symptoms ranging from 9.4 % to 72.2 % and 8.6-66.2 %, respectively^{3,8,9,13,14,18,21-25}. These symptoms were mainly increased by financial problems^{8,14,23,26,27} and less by medication availability¹⁰ or the pre-existence of a psychiatric disorder^{9,22,26}.

Only three studies in the literature included a control sample. Specifically, Assenza et al showed that PWE had significantly higher levels of depression and anxiety than PWOE (both $p < 0.001$)¹⁰. Hao et al concluded the same results ($p < 0.001$) and also showed that the percentage of PWE (13.1 %) with severe psychological distress was significantly higher than the control group (1.6 %) ($p < 0.001$)²². On the other hand, Salari et al reported that PWE and the control group had similar anxiety levels ($p = 0.067$)²⁸. These data are insufficient to conclude a definite impact of the pandemic on PWE. The prevalence of anxiety and depression disorders in PWE before the pandemic ranged from 20 % to 25.6 % and 22.9-35 %, respectively^{11,29}, but these results cannot be directly compared with those after the pandemic.

None of our patients reported changes in seizure control during the pandemic, and three other studies reached

the same conclusion for 56-75 % of PWE during that period^{3,30,31}. Several researchers reported an improvement in seizure control in a very small percentage (4.3-17 %), attributed to increased sleep duration, decreased work stress, and improved AED adherence due to the restrictive measures^{10,18,25,26,30,31}.

However, many studies show that the Covid-19 pandemic exacerbates seizures in 8.6-10 % of PWE^{10,13,14,18,21,25,26,30,31}, while fewer in 23.2-31.2 % of PWE^{3,5,8,9,24,26}. Seizure worsening is more often precipitated by sleep disturbance and anxiety symptoms of PWE^{3,5,7,8,10,14,18,23-27,30,31} and less often by intractable epilepsy, intake of more than one AED, and difficulty in obtaining medication during the pandemic^{5,7,9,10,13,14,18,22,24,30}.

During the pandemic, the regular examinations of the patients were initially canceled and later performed only to a limited degree at outpatient clinics. Many researchers have found that telemedicine, i.e., the use of communication technology (telephone, video call, message, e-mail) by the patients and/or their caregivers during the confinement period, contributed effectively to solving their epilepsy-related problems, assessing their psychological distress, and helping them to cope with it^{2,3,5,7-10,14,20,21,23,25}. In our study, patients were evaluated using two different approaches; by close contact or via telephone, which has also been used in the past²⁶.

Certain limitations regarding the current study should be acknowledged. Firstly, we used scaling questions to assess Covid-19 specific psychological effects because no relevant, validated scale was available. This study did not include a control group because, amid the pandemic, it was difficult to locate and recruit healthy individuals to participate. The sample size was small due to difficulties in accessing the outpatient clinic. The patients may not have been aware of the different types of seizures that possibly occurred during the pandemic. Finally, our patients' lack of previous experience with telephone interviews may have caused some communication errors, and also, the sleep status of our patients has not been evaluated.

In conclusion, the psychological impact of the Covid-19 pandemic, lockdown, and social distancing measures on non-infected PWE was moderate without changes in their seizure control.

Conflict of interest

The authors have no conflicts of interest to disclose.

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