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# Determinants of depression among patients with epilepsy in Athens, Greece

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ABSTRACT

*Objective:* Depression is common among patients with epilepsy. The aim of our study was twofold: to estimate the prevalence of a major depressive episode and to identify its determinants among patients with epilepsy treated in the largest Greek hospital in Athens.
*Methods:* All consecutive patients with epilepsy that visited the epilepsy outpatient clinic of Evangelismos General Hospital were invited to participate in the study. Ninety-four patients met our inclusion criteria.
*Results:* A diagnosis of a current major depressive episode was established in 21 out of 94 eligible to participate (22.3%) patients. Being a female was associated with a 19.68-fold increase in the odds of having a major depressive episode (95% CI 3.39–114.14, $p = 0.001$); being unemployed was associated with a 6.46-fold increase in the odds of having a major depressive episode (95% CI 1.23–34.07, $p = 0.028$), and each extra seizure experienced per month was associated with a 1.38-fold increase in the odds of having a major depressive episode (95% CI 1.03–1.85, $p = 0.031$).
*Conclusion:* Unemployment, female gender, and seizure control are important determinants of a major depression episode among patients with epilepsy.



## 1. Introduction

Psychiatric disorders are common among patients with epilepsy. Extensive research has been conducted to study the coexistence of neuropsychiatric symptoms with epilepsy [1]. The prevalence of a current depressive episode in patients with epilepsy ranges from 11% to 62% [2] and represents the most common psychiatric comorbidity in epilepsy [3]. The variance in the frequency of depression may stem from the use of differing patient samples. Regardless of this fact, depression in epilepsy is a pervasive problem and frequently goes unrecognized and untreated [4].

Often, depression is viewed as a reaction to epilepsy's stigma and the associated poor quality of life. However, the manifestation of depression in epilepsy is multifaceted with many interacting neurobiological and psychosocial determinants, including clinical features of epilepsy (seizure frequency, type, foci, or lateralization of foci) and neurochemical or iatrogenic mechanisms [5]. Moreover, treatment with antiepileptic drugs (AEDs) and social coping and adaptation skills have also been identified as risk factors of depression associated with epilepsy [6].

Until now, depression in patients with epilepsy in Greece has not been adequately studied. In a previous study, Kimiskidis et al. investigated the association of interictal mood disorders with various demographic and seizure-related variables in patients with newly diagnosed and chronic epilepsy. The authors concluded that female gender, high seizure frequency, and a symptomatic epilepsy syndrome are independent risk factors for the development of anxiety and/or depression [7].

The aims of our study were twofold: to estimate the prevalence of a major depressive episode and to identify its determinants among patients with epilepsy treated in the largest Greek hospital in Athens.

## 2. Methods

### 2.1. Participants

All consecutive patients with epilepsy that visited the epilepsy outpatient clinic of Evangelismos General Hospital were invited to participate in the study.

To be enrolled, the patients had to meet the following inclusion criteria: (1) confirmed diagnosis of any type of epilepsy according to the International League Against Epilepsy (ILAE) criteria [8,9], documented clinically and confirmed with the EEG studies; (2) age equal to or greater than 18 years; (3) no gross cognitive deficits or intellectual disability; (4) absence of life threatening or severely disabling medical diseases (i.e., cancer, stroke, etc.); (5) a native Greek speaker; and (6) willing to provide a written informed consent to undergo the experimental procedures.

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### 2.2. Psychiatric evaluation

All subjects were assessed using the following instruments on the same visit.

#### 2.2.1. Mini International Neuropsychiatric Interview (MINI — Greek version 5.0.0.)

The MINI is an internationally validated, brief structured interview that has been used extensively as a diagnostic tool for Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition (DSM-IV) and International Classification of Diseases-10 (ICD-10) psychiatric disorders. The reliability and validity of this instrument have been established [10]. The MINI was administered by the same investigator (PY) to all patients.

#### 2.2.2. Psychiatric interview

A detailed psychiatric assessment was completed by the main investigator (PZ) to diagnose if the patient was currently experiencing a major depressive episode. The DSM-IV criteria for a major depressive episode were used [11].

### 2.3. Statistical analyses

A database was developed using the Statistical Package for Social Science (version 16.0 for Mac; SPSS). Frequencies and descriptive statistics were examined for each variable. Comparisons between patients with a current major depressive episode and patients without a current major depressive episode were made using Student's t-tests for normally distributed continuous data, Mann-Whitney's U test for non-normally distributed data, and chi-square test for categorical data.

Where statistically significant differences were found, correlations were carried out to identify variables that could be entered into a logistic regression model to identify determinants of depression among the patients with epilepsy. Where variables were correlated, the most clinically relevant was selected for inclusion in the model. The variables were entered as independent variables, and current major depressive episode was entered as the dependent variable.

A value of $p < 0.05$ was considered to be statistically significant.

## 3. Results

Between February 2013 and July 2013, 97 individuals fulfilled the abovementioned inclusion criteria. Out of them, 3 patients did not have an identical diagnosis according to the MINI questionnaire and the psychiatric interview. Therefore, our final study population consisted of 94 patients. A diagnosis of a current major depressive episode was established in 21 (22.3%) patients. The severity of the episode was evaluated to be mild in 10 patients (47.6% of the subgroup with current major depressive episode), moderate in 4 patients (19.0%), and severe in 7 patients (33.3%). In total, 13 patients of the subgroup (61.9%) had active suicidal ideation, but no patients had made any attempt to commit suicide.

Table 1 summarizes the AEDs used and their corresponding psychotropic effects on depression as reported in the literature. The most widely used antiepileptic drug was levetiracetam (29.8%), followed by sodium valproate (28.7%), carbamazepine (24.5%), and oxcarbazepine (24.5%).

Clinical and demographic characteristics of the study's total population and the two subgroups (depressed and nondepressed patients) are shown in Table 2. Regarding the clinical characteristics, the depressed patients were more likely to be females, had fewer years of education, and were more likely to be unemployed. Regarding the epilepsy-related characteristics, the depressed patients had a longer history of epilepsy, were experiencing seizures more frequently, were receiving more AEDs, and were more likely to receive AEDs with negative psychotropic effects. There were no other statistically significant differences regarding the clinical and demographic characteristics between the two groups.

**Table 1**
Antiepileptic agents used in our study group, and their correspondent psychotropic effects [34,35] regarding depression.

| Antiepileptic drug | Number | Percentage | Psychotropic effects [34,35] |
|---|---|---|---|
| Levetiracetam | 28 | 29.8% | Negative |
| Sodium valproate | 27 | 28.7% | Neutral |
| Carbamazepine | 23 | 24.5% | Neutral |
| Oxcarbazepine | 23 | 24.5% | Neutral |
| Topiramate | 22 | 23.4% | Negative |
| Benzodiazepines | 15 | 16.0% | Negative |
| Lacosamide | 12 | 12.8% | Limited experience |
| Lamotrigine | 9 | 9.6% | Positive |
| Pregabalin | 8 | 8.5% | Negative |
| Phenytoin | 7 | 7.4% | Neutral |
| Primidone | 6 | 6.4% | Negative |
| Phenobarbital | 6 | 6.4% | Negative |
| Zonisamide | 4 | 4.3% | Negative |

The following independent variables were entered into the multivariate logistic regression model: age, sex, education years, employment status (being unemployed or not), duration of epilepsy, seizure frequency, number of AEDs, and type of AEDs (negative psychotropic effect or not). The results of the multivariate logistic regression are shown in Table 3. Adjusted odds ratios are presented. The full model significantly predicted a major depressive episode ($\chi^2 = 37.95$, df = 8, $p < 0.001$) with the majority of the variance (34 to 52%) being explained by three variables: gender, employment status, and seizure frequency. Being a female was associated with a 19.68-fold increase in the odds of having a major depressive episode (95% CI 3.39–114.14, $p = 0.001$); being unemployed was associated with a 6.46-fold increase in the odds of having a major depressive episode (95% CI 1.23–34.07, $p = 0.028$), and each extra seizure experienced per month was associated with a 1.38-fold increase in the odds of having a major depressive episode (95% CI 1.03–1.85, $p = 0.031$).

## 4. Discussion

Our cross-sectional study has estimated that the prevalence of a major depressive episode among the patients with epilepsy treated in the largest Greek hospital in Athens is 22.3%. Moreover, we showed that female gender, unemployment, and increased seizure frequency are factors associated with a major depressive episode.

The novelty of our study is that this is the first Greek study that aimed to investigate the prevalence of a major depressive episode and to identify its determinants among patients with epilepsy. Apart from its epidemiological importance for Greece, our study was conducted in an era of a severe financial crisis, which has already led to a dramatic increase of unemployment in the general population.

The effects of unemployment on mental health are well described [12]. Depression tends to be more common among the long-term unemployed [13]. In 2011, in the beginning of the crisis, Economou et al. showed that the prevalence of major depression in the general population of Greece had already increased by almost 3 times, jumping from 3.3% to 8.2% [14]. This has also led to a substantial increase in the prevalence of suicidal ideation and reported suicide attempts [15].

Patients with epilepsy may have difficulty in finding and maintaining regular employment. They face appropriate restrictions, such as those relating to driving or working in situations in which they might be liable to injury. They may also be the victims of ignorance and stigma [16]. Additionally, a clear relationship between current seizure frequency and employment status has been demonstrated [17]. However, in our study, we showed that unemployment is independently associated with a major depressive episode after having adjusted for seizure frequency.

Seizure frequency has been associated with psychological disturbances in a number of studies. Dias et al. concluded that major