



# Depression in Patients with Epilepsy in Nigeria: Phenomenology and Predictors

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## Abstract

**Objectives** In this article, we aimed to determine the correlates of depression among patients with epilepsy in Neuropsychiatric Hospital, Aro, Abeokuta, Nigeria.

**Methods** 270 patients with epilepsy attending the outpatient clinic of the hospital were recruited and assessed using sociodemographic questionnaire, MINI-Plus, and BDI-II.

**Results** The mean (standard deviation [SD]) age of the respondents was 32 (9.9) years, 45.6% were females, and 38.5% were married. Thirty-two (11.9%) patients had a diagnosis of major depressive disorder (MDD) and 13 (4.8%) had a diagnosis of dysthymia. The most common depressive symptoms were loss of pleasure (84.4%), crying (84.4%), self-dislike (81.3%), and loss of energy, tiredness/fatigue, indecisiveness and punishment feelings (78.1% each). Vegetative symptoms such as changes in appetite and sleep and loss of interest in sex were the least common depressive symptoms. In the logistic regression, seizure frequency was the single predictor of MDD and dysthymia. Patients who had at least one seizure per week were five times more likely to develop MDD (OR = 5.1,  $p = 0.014$ ) and 16 times likely to have dysthymia (OR = 16.0,  $p = 0.0007$ ). Patients who had at least one seizure per month were 3 times more likely to develop MDD (OR = 3.3,  $p = 0.029$ ).

**Conclusion** Seizure frequency is an independent predictor of depression among patients with epilepsy. Patients with poor seizure control are at higher risk of developing depression and should be routinely screened for depression.

## Keywords

- epilepsy
- major depressive disorder
- Nigeria
- dysthymia
- depression

## Introduction

Globally, about 50 million people suffer from epilepsy, with the majority living in developing countries and receiving little or no treatment.<sup>1</sup> Epilepsy is associated with a lot of physical, social, and psychological comorbidities including a high risk for suicide.<sup>2,3</sup> Depression is the most common psychiatric comorbidity in patient with epilepsy.<sup>4,5</sup> About a third of patients with epilepsy have comorbid major depressive disorder (MDD),<sup>6</sup> and a still much larger proportion experience

other forms of depression such as dysthymia, minor depression, and other depressive symptoms that do not meet the diagnostic criteria for mood disorders (termed subsyndromic mood disorders).<sup>7,8</sup> However, depression is still largely unrecognized and treated among this population, leading to poor treatment outcomes and quality of life.<sup>9</sup> Depression in patients with epilepsy has been associated with work absenteeism, increased health care system utilization and direct medical cost, and a poorer quality of life.<sup>10–12</sup>

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This makes the recognition and treatment of depression in patients with epilepsy paramount. In Nigeria, as in other parts of Sub-Saharan Africa, depression in patients with epilepsy goes largely undetected and untreated. This study aims to determine the correlates (sociodemographic and clinical) of depression among patients with epilepsy attending an outpatient clinic in a tertiary hospital in Nigeria.

## Methods

The study was conducted among patients with Epilepsy attending the outpatient clinic of the Neuropsychiatric Hospital, Aro, Abeokuta, Nigeria. The study is part of a larger study and the first part of the study has been published elsewhere.<sup>13</sup> The inclusion criteria included patients with a clinical diagnosis of epilepsy, aged between 18 and 64 years; comorbid chronic medical and/or psychiatric illnesses, comorbid alcohol and substance use disorder, and a diagnosis of intellectual disability were exclusion criteria.

### Study Instruments

**Sociodemographic questionnaire:** This was designed to gather data on participants' sociodemographic and clinical variables such as age, gender, age of onset of seizures, types and number of medications, duration of illness, etc.

**Mini international neuropsychiatric interview (MINI Plus):** Developed by Sheehan and colleagues in 1998 and found to have high validity and reliability scores or kappa values for all diagnoses above 0.70 (~70% being above 0.90) when compared with the structured clinical interview for the DSM-IV patient version and the composite international diagnostic interview (CIDI).<sup>14</sup> The depression disorder module of the MINI Plus was used in this study.

**Beck's depression interview 2nd edition (BDI-II):** A revised version of the 21-item Beck depression inventory (BDI), suitable for use in adults and adolescents, was altered to correspond to DSM-IV criteria for major depressive disorder and improve the content-validity.<sup>15</sup> Each item is scored on a scale value of 0 to 3. Higher total scores indicate more severe depressive symptoms. The standardized cutoffs used differ from the original: 0 to 13 = minimal depression; 14 to 19 = mild depression; 20 to 28 = moderate depression; 29 to 63 = severe depression. Reported psychometric properties include sensitivity and specificity of 81% and 92%, respectively, test-retest reliability of 0.93, and internal consistency (Cronbach's  $\alpha$ ) of 0.92.<sup>16</sup>

### Data Collection

On each clinic day, case notes of patients were screened and those meeting the inclusion criteria identified and recruited after duly explaining the purpose of the research, explicitly stating the voluntary nature of participation and that no disadvantage will be conferred by deciding not to participate. Following a signed informed consent, the questionnaires were administered, while they waited to be seen by a doctor. To avoid sampling a patient twice, the case notes were marked

with pencils and serial numbers were assigned to each participant to ensure confidentiality. Seizure frequency in the past month was defined as very frequent if seizures occurred daily or > 1/week; frequent if seizures occurred 1/week or >1/month; occasional if seizures occur 1/month; and none if no seizures in the past month.

### Data Analysis

The data was analyzed using the Statistical Package for Social Sciences (SPSS) version 21. Continuous variables such as age, duration of illness, duration of treatment, etc., were converted into categorical variables. Chi-square test (with Fischer's exact tests used when appropriate) was used to test the association between categorical variables and MDD. Next, a multiple logistic regression analysis was performed to determine the independent predictors of MDD and dysthymia. The level of statistical significance was set at  $p$  value < 0.05 at 95% confidence interval for all statistical tests.

## Results

Of the 270 participants, 123 (45.6%) were females, 104 (38.5%) were married, 39 (14.4%) were unemployed, with a mean age of 32 years (standard deviation [SD] = 9.9 years); 133 (49.3%) developed epilepsy at less than 18 years; 151 (55.9%) had over 10 years of illness duration; 159 (58.9%) had no seizures in the past month; 64.4% ( $n = 174$ ) had bilateral tonic clonic seizures, 12.6% ( $n = 34$ ) had focal with impaired awareness; 44.1% ( $N = 119$ ) were on carbamazepine, 89.6% ( $n = 242$ ) were on monotherapy; the mean duration of treatment was 6.1 (SD = 6.5) years with 80.7% ( $n = 218$ ) receiving treatment for less than 10 years. The prevalence of MDD was 11.9% ( $n = 32$ ), while that of dysthymia was 4.8% ( $n = 13$ ).

There was an association (–**Table 1**) between younger age ( $\chi^2 = 11.808$ ,  $df = 2$ ,  $p = 0.002$ ); being single ( $\chi^2 = 9.787$ ,  $df = 3$ ,  $p = 0.016$ ); earning less than N5,000 ( $\chi^2 = 12.077$ ,  $df = 4$ ,  $p = 0.012$ ); younger age of onset ( $\chi^2 = 3.890$ ,  $df = 1$ ,  $p = 0.049$ ); having very frequent seizures ( $\chi^2 = 19.668$ ,  $df = 4$ ,  $p = 0.001$ ); having uncontrolled seizures ( $\chi^2 = 5.83$ ,  $df = 1$ ,  $p = 0.012$ ) and MDD. There was no association between gender, type of seizures, types and number of automated external defibrillator (AED), duration of illness, duration of treatment, and MDD. In the bivariate analysis, only seizure frequency was associated with dysthymia ( $\chi^2 = 16.64$ ,  $df = 3$ ,  $p = 0.0026$ ); age, gender, seizure type, duration of illness, duration of treatment, employment and marital status, and type and number of AED were all not statistically significant.

Regarding the phenomenology of depression (–**Table 2**), the most common depressive symptoms were loss of pleasure (84.4%), crying (84.4%), self-dislike (81.3%), and loss of energy, tiredness/fatigue, indecisiveness and punishment feelings (78.1% each). Vegetative symptoms such as changes in appetite and sleep and loss of interest in sex were the least common depressive symptoms.

**Table 1** Relationship between sociodemographic and clinical characteristics and current major depressive disorder<sup>b</sup>

Variable	Major depressive disorder		$\chi^2$	df	p-Value
	Yes (n/%)	No (n/%)			
Age			11.808	2	<b>0.002</b>
15–24	17 (21.5)	62 (78.5)			
25–44	15 (9.3)	146 (90.7)			
45–64	0 (0.0)	30 (100.0)			
Marital status			9.787	3	<b>0.016</b>
Single	23 (16.0)	121 (84.0)			
Married	5 (4.8)	99 (95.2)			
Separated	3 (16.7)	15 (83.3)			
Widowed	1 (25.0)	3 (75.0)			
Employment status			11.218	4	<b>0.019</b>
Paid employment	11 (6.9)	149 (93.1)			
Unpaid	7 (22.6)	24 (77.4)			
Retired	0 (0.0)	2 (100.0)			
Unemployed	6 (15.4)	33 (84.6)			
Student	8 (21.1)	30 (78.9)			
Monthly income			12.077	4	<b>0.012</b>
Less than 5,000	23 (18.7)	100 (81.3)			
5,000–9,999	3 (8.1)	34 (91.9)			
10,000–19,999	5 (10.9)	41 (89.1)			
20,000–49,999	1 (2.2)	45 (97.8)			
> 50,000	0 (0.0)	18 (100.0)			
Age of onset			3.890	1	<b>0.049</b>
< 18	21 (15.8)	112 (84.2)			
> 18	11 (8.0)	126 (92.0)			
Seizure frequency past month			19.668	4	<b>0.001</b>
Daily or > 1/week	6 (35.3)	11 (64.7)			
1/week or > 1/month	10 (26.3)	28 (73.7)			
1/month	6 (10.7)	50 (89.3)			
None	10 (6.3)	149 (93.7)			
Seizure control (n = 228)			5.830	1	<b>0.012</b>
Controlled (< 1/year)	24 (13.7)	151 (85.7)			
Uncontrolled (> 1/year)	1 (1.9)	52 (98.1)			

<sup>a</sup> Fischer's exact values for cells with expected count less than 5.

<sup>b</sup> Only statistically significant variables reported ( $p < 0.05$ ).

In the multiple binary logistic regression analysis (**Table 3**), only seizure frequency in the past month emerged as the single independent predictor of MDD, with respondents with very frequent seizures in the past month having five times the risk of developing MDD when compared with those who had none (OR = 5.1,  $p = 0.014$ , 95% CI = 1.4–18.7), and those with frequent seizures in the past month having three times the risk of having

MDD (OR = 3.3,  $p = 0.029$ , 95% CI = 1.1–9.5). Similarly, a multi-variable logistic regression analysis of predictors of dysthymia (**Table 4**) showed seizure frequency in the past month as the only significant predictor of dysthymia. Patients who reported daily seizures or more than one seizure episode per week had 16 times odds of developing dysthymia compared with those with no seizures (OR = 16.0,  $p = 0.0007$ , 95% CI = 3.2–79.3).

**Table 2** Frequency distribution of depressive symptoms in patients with epilepsy with MDD (*n* = 32)

BDI items	Depressive symptoms	<i>n</i> (%)
4	Loss of pleasure	27 (84.4)
10	Crying	27 (84.4)
7	Self-dislike	26 (81.3)
6	Punishment feelings	25 (78.1)
13	Indecisiveness	25 (78.1)
15	Loss of energy	25 (78.1)
20	Tiredness/fatigue	25 (78.1)
2	Pessimism	24 (75.0)
8	Self-criticalness	24 (75.0)
12	Loss of interest	24 (75.0)
14	Worthlessness	24 (75.0)
1	Sadness	23 (71.9)
3	Past failure	23 (71.9)
5	Guilty feelings	23 (71.9)
19	Poor concentration	21 (65.6)
17	Irritability	19 (59.4)
9	Suicidal thoughts	18 (56.3)
11	Agitation	18 (56.3)
21	Loss of interest in sex	17 (53.1)
18	Loss of appetite	15 (46.9)
16	Too little sleep	13 (40.6)
18	Increased appetite	7 (21.9)
16	Excessive sleeping	6 (18.8)

Abbreviation: MDD, major depressive disorder.

## Discussion

This study aimed at determining correlates of depression in patients with epilepsy attending an outpatient clinic in Nigeria. In this study, only seizure frequency in the past month emerged as an independent predictor of depression. Interictal depression is common in patients with epilepsy and often goes unrecognized.<sup>17</sup> When researchers use a screening instrument such as BDI-II,<sup>18,19</sup> the reported prevalence of MDD in patients with epilepsy is often higher than when a diagnostic instrument is used to make a diagnosis of MDD in patients with epilepsy.<sup>20-22</sup> Regardless of the methodology, the prevalence of MDD in patients with epilepsy is higher than the prevalence in the general population.<sup>23</sup> Apart from MDD, patients with epilepsy also have other forms of mood disorders such as dysthymia, and clusters of symptoms that do not meet the diagnostic criteria for a depressive disorder; these have been called “subsyndromic” mood disorders.<sup>24</sup> The prevalence of dysthymia reported by participants in this study is lower than those reported in other studies;<sup>5-27</sup> differences in methodology, study setting, and patient characteristics could account for this difference. In this study, majority of the participants had generalized tonic clonic seizures, were on one AED, and had controlled seizures; this may account for the low rates of dysthymia. Patients with

refractory seizures and temporal lobe epilepsy are more likely to have higher rates of dysthymia-like depressive symptoms.<sup>8</sup>

There is a high comorbidity between depression and epilepsy and many studies have posited a bidirectional link between the two conditions.<sup>28-30</sup> Probable underlying mechanisms that have been postulated as causes of depression in patients with epilepsy include the following: abnormal activities of GABA, glutamate, serotonin, noradrenaline and dopamine in the central nervous system; decreased binding of serotonin to 5HT1a receptors in the dorsal raphe nucleus, thalamus and cingulate gyrus; HPA axis dysfunction; and atrophy of frontal and temporal lobes.<sup>28</sup> Depression can also cause seizures by causing sleep deprivation.<sup>31</sup> This makes the evaluation and treatment of depression an important part of the treatment of patients with epilepsy, as depression in people with epilepsy is often underrecognized and untreated, with an attendant negative effect on medication adherence, seizure control, and an increased risk of suicide.<sup>17,32,33</sup>

With regard to semiology, the most common depressive symptoms reported by our sample include crying, loss of pleasure, self-dislike, loss of energy, tiredness/fatigue, indecisiveness, and punishment feelings. Vegetative symptoms such as changes in appetite and sleep and loss of interest in sex were the least common depressive symptoms. This is consistent with the literature regarding manifestations of depression among patients with epilepsy.<sup>7,8</sup>

In this study, seizure frequency emerged as the single independent predictor of MDD in keeping with other studies.<sup>21,34-36</sup> The study found that those who had at least one seizure per week were five times more likely to develop MDD and those who have at least one seizure in a month were three times more likely to develop MDD when compared with those who had good seizure control. This makes it important for clinicians to optimize treatment regimen of patients with epilepsy to achieve good seizure control. In addition, patients who have not gained seizure control are at higher risk of developing MDD and therefore should be routinely screened for MDD and treated appropriately. Selective serotonin reuptake inhibitors (SSRIs) and other newer antidepressants have been proven to be effective in treating comorbid depression in patients with epilepsy and this can be commenced as soon as a diagnosis of depression is made.<sup>30,37</sup> In addition to pharmacotherapy, there is increasing evidence of the benefit of psychological therapies such as cognitive behavioral therapy delivered in person or online for patients with epilepsy.<sup>31,38</sup>

Other clinical variables such as type of epilepsy, duration of epilepsy, and type and number of antiepileptic medications were not found to be associated with major depression or dysthymia in the final regression analysis. This finding is similar to other studies<sup>39-41</sup> but different from others.<sup>42,43</sup> It is possible that the relationship between these clinical variables is mediated or moderated by seizure control,<sup>36,44</sup> and as majority of the participants had good seizure control, these clinical variables did not attain statistical significance. There could be also be methodological differences between these studies and this study—differences in participant characteristics according for the disparity.

**Table 3** Logistic regression analysis of the sociodemographic and clinical correlates of MDD

Variable	B	Wald	p value	OR	95% CI	
					Lower	Upper
Marital status						
Married	-0.528	0.750	0.387	0.590	0.179	1.947
Separated	0.041	0.003	0.957	1.042	0.236	4.593
Widowed	1.273	0.833	0.361	3.570	0.232	54.877
Single	Reference					
Seizure frequency past month						
Very frequent (daily or > 1/week)	1.630	6.064	<b>0.014</b>	5.104	1.395	18.677
Frequent (1/week or > 1/month)	1.184	4.764	<b>0.029</b>	3.266	1.128	9.456
Occasional (1/month)	0.283	0.229	0.632	1.327	0.417	4.221
None	Reference					
Age of onset (years)						
< 18 years	0.155	0.114	0.736	1.167	0.475	2.870
> 18 years	Reference					
Seizure control						
Uncontrolled seizure	1.579	2.073	0.150	4.849	0.565	41.584
Controlled seizure	Reference					
Employment status						
Unpaid employment	0.777	1.509	0.219	2.176	0.630	7.520
Unemployed	-0.140	0.054	0.816	0.869	0.265	2.844
Retired/Student	0.451	0.540	0.462	1.570	0.471	5.232
Paid employment	Reference					
Monthly income						
< 20,000	1.657	2.333	0.127	5.243	0.626	43.942
> 20,000	Reference					

Abbreviation: MDD, major depressive disorder.

**Table 4** Stepwise logistic regression analysis of independent predictors of dysthymia in patients with epilepsy

Variable	B	OR	p value	CI (lower, upper)
Seizure frequency in past month				
Daily or > 1/week	2.8	16.0	<b>0.0007</b>	3.2, 79.3
1/week or > 1/month	1.1		0.25	0.5, 17.9
1/month or > 1/year	1.4	2.9	0.08	0.9, 18.5
None	Reference	4.0		
Summary of variables removed in each step				
Step 1	Number of AED			
Step 2	Duration of treatment			
Step 3	Seizure control			
Step 4	Type of AED			
Step 5	Age of onset			
Step 6	Duration of illness			
Step 7	Employment status			
Step 8	Marital status			
Step 9	Seizure type			
Step 10	Gender			
Step 11	Monthly income			

Abbreviation: AED, automated external defibrillator.

The cross-sectional nature of the study design, and the fact that it is a single-site study limits the generalization of the study findings to other populations. However, it does contribute to the literature coming out of Nigeria and Sub-Saharan Africa on the prevalence and correlates of depression among patients with epilepsy. The small sample size also led to a wider confidence interval for some of the measures of association, especially for those with dysthymia. A much larger study with a much larger sample size is needed to increase the confidence in the magnitude of risk that seizure frequency poses to the development of dysthymia in patients with epilepsy. The study highlights the need for clinicians treating patients in these locations to be aware of comorbid depression and to routinely screen patients, especially high-risk patients—those with poor seizure control. It also lends urgency to the need for optimizing treatment for patients with epilepsy to achieve good seizure control.

#### Ethical Approval

The study was granted ethical approval from the Research and Ethical Committee of the Neuropsychiatric Hospital, Aro, Abeokuta, Ogun state, Nigeria.

#### Conflict of Interest

None declared

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