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GESDAV

Risk and impact of inter-ictal depression on quality of life of Nigerian women with epilepsy of childbearing age

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ABSTRACT

Background: Depression, the most common psychiatry comorbidity in patients with epilepsy is common among women, especially those of reproductive age. Although it could be said that the female gender is a risk factor for depression, the risk of inter-ictal depression and its impact on the quality of life (QoL) of women with epilepsy (WWE) has not been sufficiently studied among Nigerians. **Materials and Methods:** In this cross-sectional case–control study, data were collected from 70 women (29 WWE and 41 women without epilepsy) within the age range ≥18 and ≤55 between July 2010 and March 2011. A questionnaire that includes items-related to demographic information, becks depression inventory-II (BDI-II) and QoL inventory in epilepsy-31 was used for data collection. **Result:** WWE had a significantly higher BDI-II score ($P = 0.001$). The frequency of depression was 37.9% in WWE and 4.9% among controls. (Odds ratio 11.9). WWE had poorer QoL score than the control ($P \leq 0.001$). Depressed WWE had poorer total QoL ($P = 0.007$) as well as poorer emotional well-being (<0.001) and social function ($P = 0.004$) compared with women without epilepsy. **Conclusion:** Depression is prevalent in this sample of Nigerian WWE of childbearing age with significant impact on their total QoL, emotional well-being and social function. Regular screening for depression among this population of PWE is imperative. Rational drug management as well as non-pharmacological treatment of depressed WWE is emphasized.

KEY WORDS: Depression, epilepsy, QoL, reproductive age, women

INTRODUCTION

In recent times, female issues in epilepsy have witnessed profound emphasis on the childbearing years; apparently because of reproductive concerns and hormonal influences on epilepsy, in addition to the efficacy and effects of anti-epileptic drug (AED) [1]. However, women with epilepsy (henceforth, WWE) of fertile age are a specific sub-group of people with epilepsy (PWE) who are at risk of comorbid depression as a consequence of adverse bio-psychosocial factors [2] such as genetics, personal attribution style, social isolation and discrimination, limited vocational opportunities, financial limitations in addition to hormonal factors [3-5]. Converging lines of evidence suggest that sex hormones, which are known to contribute to remodeling the hippocampus, play a pivotal role in both epilepsy and depression [1,6].

Being the most common psychiatry comorbidity in epilepsy, depression is a strong determinant of quality of life (QoL) of patients with epilepsy [7]. The female gender could be considered to be a risk factor for depression and poor QoL since women are twice as likely to develop depression as the male

gender [1-6]. Among Nigerian WWE, psychosocial/economic factors such as unemployment (with the attendant poor personal/household income), fewer years of formal education, physical and sexual abuse, lower marriage rates, poorer housing conditions and higher stigma scores are preponderant [8].

The aforementioned factors in addition to other putative epilepsy-related factors such as the type of seizure (partial onset seizures being a risk factor) seizure control and duration of epilepsy in themselves do foster the development of depression and poor QoL in WWE [9]. Very few information is available about female issues in Nigerian PWE, the profile of depressive symptomatology in Nigerian WWE has also not been sufficiently evaluated. The aim of this study was to determine the frequency and risk of depression among a cohort of Nigerian WWE of childbearing age, using a case–control study design and to assess the influence of depression on their perception of QoL.

MATERIALS AND METHODS

Study Design and Location

This hospital-based case–control study was carried out among WWE who were evaluated in the neurology outpatient department of the Olabisi Onabanjo University Teaching Hospital, Sagamu, South-west Nigeria. This neurology outpatient service provides epilepsy care to residents of Ogun state (and adjoining states), Nigeria. Consecutive women aged ≥18 and ≤55 years who were diagnosed as having epilepsy according to the definition and classification of International League against Epilepsy (1981) [9] were included between July, 2010 and March, 2011. Women aged <18 years or above 55 years, acute symptomatic seizures, concurrent somatic or psychiatry comorbidities (including mental retardation and dementia) and refusal to give informed consent were excluded. Age, level of education and monthly income - matched women were also recruited. These apparently healthy women served as controls, and they were drawn from relatives of patients seen at the outpatient clinic of the hospital as well as medical students and hospital workers with no personal or family history of epilepsy. Institutional Review Board approved the study and informed written consent was taken from the subjects.

Subjects Selection

Consecutive women seen at the general neurology clinic were enrolled into the study if they met inclusion criteria and gave their written informed consent. Of the 49 women seen during this period, 6 were excluded because of age (>55 years), whereas 14 had a concurrent medical or psychiatry comorbidity. The controls were randomly selected (using a simple random sampling method). To ensure that the controls were level of income matched, they were essentially drawn from female students and junior support staff of the hospital while the rest were relatives of patients attending the general outpatient clinic of the hospital.

Study Instrument and Subject Assessment

Beck depression inventory (BDI)

The BDI-II is a 21 item self-report measure that is widely used to screen for depression and assess its severity (16). Each item is scored from 0 to 3, with higher scores indicating more severe symptoms. The various scores were categorized accordingly with BDI-II scores between 0 and 9 indicated no depression while 10-18 and 19-29 indicated mild and moderate depression respectively. Any score ≥30 indicated severe depression. The control women also completed the BDI-II questionnaire. In this study, BDI-II was used to screen for depression. Respondents were categorized into two groups based on BDI-II scores. Those with BDI-II scores of 0-9 were considered non-depressed, while respondents with scores of 10 and above were grouped as depressed.

QoL

QoL was assessed using the QoL inventory in epilepsy for adults-31 (QoLIE-31, version 1.0). The QoLIE-31 instrument is a self-administered questionnaire that focuses on specific areas of concern for PWE. This questionnaire contains 31 questions and seven subscales; each of the subscales assesses a different domain of QoL: (i) seizure worry (SW), (ii) overall QoL, (iii) emotional well-being, (iv) energy/fatigue (EF), (v) cognitive functioning, (vi) antiepileptic medication effects, and (vii) social functioning. The methods for scoring of the QoLIE-31 item have already been described [10]. For the control women, QoLIE-31 questionnaire was modified to exclude seizure specific domains such as SW and medication effects while the other domains such as emotional well-being, energy and fatigue, social function, cognitive function and overall quality were included in the final QoLIE-31 version since these domains were essentially generic.

Subject's Assessment

After demographic data have been collected from eligible patients, the QoLIE-31 questionnaire was completed. The subjects also completed the BDI-II questionnaire. Thereafter, epilepsy related variables, including the type of seizures, duration of epilepsy, types and seizure frequency were collected. The number of AED as well as compliance was also recorded. Compliance with AED was defined as "good" if in the past 1 month, patient had missed 3 or fewer doses of AED in a twice a day regimen. Compliance was "fair" if 4-8 doses were missed and poor if patient had 9 or more missed doses. The number of missed doses were divided by half for patient on daily medication and multiplied by 1.5 for patients on thrice a day regimen. The case records of the patients were reviewed to verify the accuracy of the data.

Statistical Analysis

Data analyses were carried out using statistical package for the social sciences for windows (SPSS version 17.0 Inc., Chicago, IL, USA). Because the BDI-II score was not normally

distributed, it was expressed as both median and mean values with inter-quartile ranges. Comparisons were tested for statistical significance using the non-parametric Mann–Whitney *U*-test, or for categorical differences using the Chi-squared test. Univariate correlation analysis using Pearson's correlation coefficient was used to evaluate the total QoL (and the subscales) correlates of depression, while Spearman's rank correlation coefficient was used for qualitative variables to outline the factors that influenced the variance of the BDI-II scores. Pearson correlation coefficient was used to evaluate the relationship of the BDI-II scores and QoLIE-31 scores. The level of significance was set at <0.05.

RESULT

WWE and controls were similar demographically. The mean age was 29.6 years (SD = 8.22) for the subjects and 29.7 years (SD = 6.03) for controls. 17 WWE (58.6%) and 24 controls (58.6%) were currently married. 17 (58.6%) WWE and 18 (43.9%) controls earned < $133 monthly. Secondary level of education was completed by 11 (37.3%) WWE and 18 (43, 9%) the controls. Table 1 shows the demographic characteristics of the patients and controls.

Seizure was partial onset in 20 (68.96%) subjects while it became secondarily generalized in 15 (51.7%). 6 (20%) subjects had been seizure free in the preceding 6 month. Seizure was idiopathic in 23 (79.3%) subjects and carbamazepine were the most frequently used AED. Only 3 (10.3%) subjects were taking more than one AED. Table 2 shows the clinical characteristics of the WWE.

Table 1: Socio-demography characteristics and distribution of depression

Variable	WWE 29 (100%)	Controls 41 (100%)	χ^2	*P* value
Sociodemography				
Marital status			0	0.994
Currently married	17 (58.6)	24 (58.5)		
Currently not married	12 (41.3)	17 (41.5)		
Employment status			0.278	0.598
Currently employed	13 (44.8)	21 (51.2)		
Currently unemployed	16 (55.1)	20 (48.8)		
Educational level			1.87	0.609
None	4 (13.8)	2 (4.8)		
Primary	6 (20.7)	10 (24.4)		
Secondary	11 (37.9)	18 (43.9)		
Tertiary	8 (27.5)	11 (26.8)		
Family support			2.24	0.524
Excellent	21 (72.4)	28 (68.3)		
Very good	8 (27.5)	10 (24.4)		
Fair	0 (0)	3 (7.3)		
Monthly income (dollars)			5.22	0.265
No income	5 (17.2)	5 (12.2)		
≤133	17 (58.6)	18 (43.9)		
>133	7 (24.1)	18 (43.9)		
Depression			12.65	0.001†
No depression	18 (62.0)	39 (95.1)		
Mild depression	8 (27.5)	2 (4.9)		
Moderate depression	3 (10.3)	0 (0)		

WWE: Women with epilepsy, †Fishers exact *P* value

Median BDI-II score of WWE and control women were 7.0 (IQ range 0-23) and 1.0 (IQ range 0-25), respectively. WWE had a significantly higher BDI-II score than controls (Mann–Whitney *U*-test, $Z = -3.178$, $P = 0.001$). The frequency of depression (defined in this study as BDI-II ≥10) was 37.9% in WWE and 4.9% among controls. The odd ratio for inter-ictal depression was 11.9 among this cohort of WWE of childbearing age [Table 3]. Among WWE, no statistically significant relationship existed between depression and socio-demographic as well as clinical variables [Table 4].

Table 5 shows the QoL scores between WWE and controls. When compared with control women, WWE had poorer total QoLIE-31 scores ($P < 0.001$). On the other QoL domains, WWE equally had poorer scores on overall QoL domain ($P < 0.001$), emotional well-being ($P = 0.009$), EF ($P < 0.001$) and social function ($P < 0.001$). Total QoLIE-31 scores, social function ($P = 0.004$) and emotional well-being ($P = 0.001$) were significantly poorer among depressed WWE ($P = 0.007$).

DISCUSSION

This study reveals that the inter-ictal depression is prevalent among this sample of Nigerian WWE of childbearing age.

Table 2: Clinical characteristics of the WWE

Seizure related variables	Frequency (%)
Seizure type	
Simple partial	1 (3.4)
Complex partial	4 (13.8)
Secondarily generalized	15 (51.7)
Primarily generalized tonic-clonic	9 (31.0)
Seizure frequency	
1/week	3 (10.3)
<1/week but >1/month	8 (27.6)
1 in the preceding 6 months	12 (41.4)
None in 6 months	6 (20.7)
Putative etiology	
Unknown	23 (79.3)
Trauma	3 (10.3)
Infection	3 (10.3)
Type of AED	
Phenobarbitone	3 (10.3)
Carbamazepine	22 (75.9)
Valproate	1 (3.4)
Phenobarbitone and carbamazepine	2 (6.8)
Phenytoin and leveteracetam	1 (3.4)
No of AED	
One AED	26 (89.7)
>One AED	3 (10.3)
Age at seizure onset (mean±SD)	18.59±9.76
Duration of epilepsy (mean±SD)	10.96±9.79

AED: Anti-epileptic drug, SD: Standard deviation, WWE: Women with epilepsy

Table 3: Profile of depression in the study population

	WWE 29 (100%)	Controls 41 (100%)	χ^2	OR	95% CI	*P* value
Depression	11 (37.9%)	2 (4.9%)	12.65	11.91	2.39-59.42	0.001†

†Fishers exact *P* value, WWE: Women with epilepsy, CI: Confidence interval, OR: Odds ratio

When compared with women without epilepsy of the same age group, the risk of inter-ictal depression in this sample of WWE was found to be 11 times higher than age, gender and income matched control group. The frequency of inter-ictal depression (37.9%) in this study is similar to that of the survey by Beghi *et al*. [11] although these authors screened a larger patient population and used a different screening instrument for depression. We found a higher prevalence rate than the reported 30.7% by the survey of Todorova and Kaprelyan [2]. Other studies have documented depression in WWE of childbearing age to be between 20% and 50% [11]. The relatively wide range of the prevalence rate is probably due to differences in the methodology of the studies.

Mild and moderate depression was the class of depression identified in this study [Table 1]. Although our study found no subjects with BDI-II scores suggesting severe depression, the prevalence of depressive disorders among PWE could be as high as 48% (mean lifetime-to-date prevalence of 29% based on 7 studies) [12,13]. In the event of comorbid depression in PWE, a careful selection of an AED that can potentially stabilize mood is especially important. Other options to consider including the use of selective serotonin reuptake inhibitors, which control depressive symptoms without a significant increase in seizure frequency. In this respect, citalopram and paroxetine are recommended. Counseling and psychotherapeutic measures have also been found useful in the prevention and treatment of relapse of inter-ictal depression [14-16].

Table 4: Showing the correlation of some socio-demographic and seizure related variables with BDI-II score

Socio-demographic	BDI-II score
Age	
R	0.067
P	0.732
Age at seizure onset	
R	0.147
P	0.448
Family support	
R	−0.329
P	0.081
Income	
R	−0.117
P	0.547
Duration of epilepsy	
R	−0.007
P	0.971
Number of AED	
R	0.054
P	0.779
BDI-II	
R	-
P	-
Seizure frequency	
R	−0.252
P	0.187

BDI-II: Becks depression inventory-II, AED: Anti-epileptic drug

Our study found no demographic nor clinical risk for depression among this sample group. The small sample size of this study could have accounted for this outlook. However, in similar studies with larger sample sizes, factors such as low educational level, unemployment, duration of epilepsy, increased seizure frequency and severity have been implicated [2,11,17]; the aforementioned factors playing out in the background of the neurobiological association of depression and epilepsy. The neurobiology of the association of epilepsy and depression in women is not yet completely understood but overwhelming evidence points to the effects of sex hormones and their role in the hippocampal neuroplasticity with resultant alteration in seizure threshold and mood balance [6]. This neurobiological observation has lent support to the suggested bi-directional relationship between depression and epilepsy [18].

We also observed that WWE had poorer total QoL compared to control individuals [Table 5]. This same trend was observed in the other QoL domains except cognitive function. The absence of severe depression in this cohort could have explained this lack of difference in cognitive function since severe depression has been associated with poor cognitive performance [19]. When compared with WWE without depression, total QoL emotional function and social function of WWE with depression were significantly impaired [Table 5]. This finding suggests that the domains of emotionality and socialization were significantly hampered by inter-ictal depression. However, it should be noted that these domains of QoL appears to assess a construct that overlaps with that measured by BDI-II scale. Nevertheless, adequate social support in addition to other treatment modalities may improve overall QoL in WWE. Depressed patients with high social support are likely to benefit more from long-term therapy [20].

This study had its limitations. The small sample size made it difficult to test certain associations and limits generalizations. The use of BDI-II in this study may be associated with overestimation of depressive symptoms due to the presence of epilepsy. Moreover,

Table 5: QoL comparison between WWE with and without depression compared with control women

	WWE *n*=29	Control women *n*=39†	*P* value	Depressed WWE *n*=11	Non-depressed WWE *n*=18	*P* value	Depressed controls *n*=2	Non-depressed controls *n*=39†	*P* value
Overall QoL	58.01±15.35	82.26±9.55	<0.001*	54.09±13.75	60.41±16.16	0.290	78.75±8.83	82.45±9.66	0.599
Seizure worry	48.34±23.79	-	-	38.60±21.03	54.29±23.94	0.085	-	-	
Emotional	71.98±16.37	81.48±12.83	0.009*	59.27±11.21	79.75±14.11	<0.001*	72.0±16.97	82.00±12.67	0.289
Energy fatigue	72.32±19.70	78.29±12.31	<0.001*	64.54±16.98	77.08±20.16	0.097	65.00±21.21	79.01±11.71	0.118
Cognitive function	73.96±20.49	91.15±11.61	0.130	72.10±21.27	75.10±20.54	0.710	96.66±4.71	90.85±11.83	0.498
Medication effect	78.58±20.49	-	-	69.18±18.24	84.32±22.45	0.07	-	-	
Social function	65.68±18.89	96.58±6.15	<0.001*	53.27±19.26	73.27±14.44	0.004*	92.50±10.60	96.81±5.99	0.341
Total QoL	67.75±12.53	89.03±5.72	<0.001*	60.02±12.31	72.47±10.35	0.007*	86.15±9.82	89.18±5.61	0.472

†2 of the 41 control subjects were not included in the analysis because of incomplete data. **P* value<0.05, QoL: Quality of life, WWE: Women with epilepsy

depression as assessed by BDI-II may occur in varying context other than major depressive disorders. Nevertheless, the study design, use of standardized, internationally acceptable instruments and focus on a vulnerable population are some of its strengths.

In conclusion, inter-ictal depression is prevalent among this sample of Nigerian WWE (just like other epilepsy population) with significant impairment of their QoL. Prompt and regular screening for depression is recommended, while paying attention to drugs management and other treatment modalities that are capable of improving their QoL without increasing seizure frequency. Since this study was hospital based with relatively small sample size, the larger community-based studies are desirable to unravel other potential contributors to depression and poor QoL in this population.

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