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RESEARCH

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Determinants of quality of life in Nigerian female patients with epilepsy on carbamazepine and levetiracetam monotherapy

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Abstract

Background The study is aimed to identify the predictors of Quality of Life (QOL) in women with epilepsy (WWE) on carbamazepine (CBM) and levetiracetam (LTM) monotherapy. 100 WWE were recruited (50 each on CBM and LTM), after clinical diagnosis of epilepsy supported by Electroencephalography (EEG) features and seizures classification by 2017 International League Against Epilepsy (ILAE) criteria, the Quality of Life Inventory Scale 31(QOLIE-31) and Zung Self-Rating Depression Scale (ZSRDS) were used to assess QOL and depression, respectively.

Result Higher QOLIE-31 scores was seen in the LTM group across all domains except seizure worry ($p=0.051$) compared to CBM group**.** Logistic regression showed that the use of CBM ($p=0.000$), fast frequency on EEG ($p=0.005$), longer duration of epilepsy ($p=0.017$), presence of depression ($p=0.008$) and lower level of education ($p=0.003$) were predictors of QOL. Progesterone ($p=0.040$), oestradiol ($p=0.011$) and prolactin ($p=0.002$) in follicular phase showed significant association with QOLIE-total score. In the luteal phase, luteinizing hormone–follicle stimulating hormone (LH–FSH) ratio ($p=0.009$) and testosterone ($p=0.015$), FSH ($p=0.015$), prolactin ($p=0.000$), showed significant association with QOL. None of the hormones independently predicts QOL.

Conclusion LTM group appears to have better QOL than CBM group. Healthcare providers should focus on addressing these identified predictors which include medication effect, depression, Level of education, EEG background and duration of epilepsy with aim of improving QOL.

Keywords Quality of life, Epilepsy, Hormone, Anti-epileptic drug

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Introduction

People living with epilepsy experiences social consequences, cognitive impairment, mental health conditions and poor Quality of Life (QOL) [1, 2]. The QOL has been described as pragmatic end point in the management of people living with epilepsy [3, 4]. Seizure frequency, seizure severity, level of education, depression, polytherapy and adverse events profile are major determinants of QOL in Patients with Epilepsy (PWE). In addition, women with epilepsy (WWE) faces unique challenges throughout their lifespan owing to the interplay between seizures, anti-epileptic drugs (AEDs) and sex steroid hormones [5]. This tri-directional complex relationship results in the disruption of the hypothalamic pituitary ovarian axis which affects the determinants of QOL like seizure frequency, depression and adverse events profile in WWE [6, 7]. In a cross-sectional study to evaluate the use of AEDs patterns and their impacts on QOL among 200 patients, there were more cases of adverse drug reaction among those on polytherapy compared to those on monotherapy and the study concluded that selection of rational and safer AED treatment options plays a major role in achieving better QOL in patients with epilepsy [8]. However, previous studies had shown that positive effects of newer AEDs like levetiracetam (LTM) as add-on therapy on QOL but just few studies have been able to look into the actions of LTM as a sole agent on QOL of PWE [9]. Furthermore previous studies have linked AEDs especially those that interfere with cytochrome P450 to reproductive endocrine with alteration of the level of circulating gonadotropins and sex steroid hormones [5, 10]. These changes have attending effects on seizures control and frequency which are some of the major determinants of QOL especially in WWE. Previous studies have evaluated the effect of CBM as monotherapy on sex steroid hormones and its effect on QOL, but there are few data on effect of LTM as monotherapy on sex steroid hormones and attending effect on overall QOL in our environment and sub-Saharan African (SSA) by extension. This study aims to identify the predictors and compare QOL in WWE on carbamazepine (CBM) and LTM monotherapy.

Methods

This is a medical out-patient hospital-based cross-sectional study between August 2015 to August 2016. A total of 100 age-matched WWE of reproductive age group with 50 each on CBM and LTM monotherapy were randomly selected from available records in the clinic which serve as sampling frame. We excluded WWE that were currently or previously on any other AEDs apart from CBM or LTM, and those with any form of endocrinopathies, mental health issues and primary/secondary amenorrhea. The choice of CBM, was driven by the fact that it is mostly prescribed/used of the first-generation AEDs but limited by significant drug interaction and induction hepatic microsomal enzyme [11, 12]. While LTM is a newer generation drug with increasing usage, lesser drug interaction and effect on hepatic microsomal enzyme [11]. The participants on CBM were 200 mg of twice daily, while those on LTM were on 250 mg twice daily. Sample size was calculated using the formula for comparison of means average and standard deviation of Quality of Life Inventory Scale 31(QOLIE-31) among WWE from previous studies was used [13]. However, because of the non-parametric distribution of variables and the availability of small data set bootstrapping re-sampling was done. Participants for this study were fully informed on the research protocol detailing the purpose, method, risks, and benefits of the research. The risk concerning adverse reaction related to CBM and LTM, pain from blood sampling withdrawal, possible reaction to contrast during neuroimaging, and possible allergy with gel used during attachment of Electroencephalography (EEG) electrode were explained to the patients. A Phoenix digital 32-channel EEG machine made in Austria was used. Each of the participant gave a written and well understood informed consent. The consent was translated to the local language for those who did not understand English language and the services of interpreters were employed. Participants were free to decline participation or withdraw from the study at any time without reprisal or loss of benefit. After clinical diagnosis of epilepsy, seizure classification and definition of epileptiform activity on EEG were in accordance with International League Against Epilepsy (ILAE) and Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology by two different Neurologists [14–18]. An interviewer based pre-established questionnaire was used to obtain clinical information with regard to socio-demographic characteristics and medical history related to epilepsy of interest which include age of onset, aetiology, duration of epilepsy, frequency and types of AED used [19]. We used QOLIE-31, an instrument previously validated in clinical studies among Nigerian cohort to assess the QOL [13, 20]. The QOLIE-31 has good psychometric properties with test–retest reliability ranging from (0.64–0.85) and internal consistency reliability coefficient ranging from $\alpha = 0.77$ to $\alpha = 0.85$ for social functioning scale and cognitive functioning scale, respectively [3, 4, 13]. The instrument measures QOL by conversion of preceded numeric value from raw data to a scale of 0 to 100 with higher scores indicating a better QOL and places emphasize on seven domain which includes seizure worry, emotional well-being, energy/fatigue, medication effects, cognitive functioning, social functioning

and overall quality of life [13]. The Zung Self-Rating Depression Scale (ZSRDS) was used to screen for depression [21, 22]. It consist of a 20 item with Likert-type scale after each item and the score for each of item ranges from 1 to 4. The minimum possible score is 20 and 80 is the maximum possible score. A score > 50 is taken as depression [22, 23]. Hormonal sample collection, handling analysis and menstrual characteristics was as we previously described [24]. Catamenial epilepsy as a twofold increase in daily seizure frequency during specific phases of the menstrual cycle [25–27]. The Statistical Package for Social Science for windows version 22 acquired by IBM in 2013 and manufactured in Armonk, New York, was used for analysis of the data obtained after initial entering and cleaning on Microsoft Excel. The Shapiro–Wilk test was used to check for normality of data and the significant value was greater than 0.05 for all the test thus making the data a normal distribution. Socio-demographic characteristics was tested using Chi-square statistics while the association between the socio-demographic characteristics and QOLIE-31 score were tested using the independent Student's t-test and one-way analysis of variance (ANOVA) with a post hoc test using Tukey's honest significance test. The Tukey's honest was used to find means of the correlates (socio-demographic and clinical variables) that are significantly different from each other. A multiple linear regression model was used to assess the independent predictors of the QOLIE-31 total score. A level of statistical significance was set at p-value of less than 0.05 for all statistical analysis.

Results

Table 1 shows that the mean age of patients was 29.07 ± 7.55, while the mean age of onset was (20.01 ± 11.57). The largest percentage of participants had secondary education and a total of 14% had depression. Furthermore, the duration of epilepsy was more than 2 years in 77% and less than 2 years in 23% among WWE. Considering, QOLIE 31 total score, the mean score was statistically significantly higher among WWE that have postgraduate education, use of LTM, epilepsy duration of < 2 years, slow background frequency on EEG and those without depression. With regard to menstrual history, both groups had comparable age of menarche and presence of catamenial epilepsy; *p*-value: *p* (0.094, 0.092), respectively. A higher number of the LTC group had hirsutism, 10 (20.0%), inter-menstrual bleeding, 9 (18.0%), dysmenorrhea 40 (80.0) and dyspareunia, 13 (26.0%) as opposed to the CZP group (see Table 2).

Table 3 shows that the mean total score of QOLIE-31 was 49.69 ± 13.45, with the highest seen in overall QOL domain 54.56 ± 21.64 and lowest in cognitive functioning domain 46.98 ± 15.98. Higher scores was seen in LTM group with statistically significant differences across all domains except seizure worry ($p = 0.051$). The level of education is associated with seizure worry ($p = 0.020$), overall QOL ($p = 0.002$), energy ($p = 0.032$), cognitive functioning ($p = 0.000$) and social functioning (p = 0.001). Depression is associated with overall QOL ($p = 0.009$), energy ($p = 0.022$), cognitive functioning ($p = 0.016$), medication effects ($p = 0.009$), and social functioning ($p = 0.013$).

There is an association between duration of epilepsy and overall QOL ($p = 0.005$), medication effects ($p = 0.019$) and social functioning ($p = 0.015$). Family history of epilepsy is associated with seizure worry ($p = 0.022$) and cognitive functioning ($p = 0.038$). There is no significant association between last episode of seizure and epileptiform pattern with domains of cognition except for emotional well-being ($p = 0.005$, $p = 0.028$, respectively). There is significant association between types of AED and domains for cognition except for seizure worry ($p = 0.051$). EEG frequency is associated with overall QOL ($p = 0.004$), emotional well-being ($p = 0.001$), cognitive functioning ($p = 0.009$) and medication effects ($p = 0.023$) (see Table 4).

Logistic regression analysis showed that the medication ($p = 0.000$), EEG frequency ($p = 0.005$), duration of epilepsy ($p = 0.017$), depression ($p = 0.008$) and level of education ($p = 0.003$) were significant predictors of poor QOL (see Table 5).

As shown in Table 6, there was a significant correlation between prolactin and all the domains of QOLIE-31 in both follicular and luteal phase. Progesterone ($p = 0.040$), oestradiol ($p = 0.011$) and prolactin ($p = 0.002$) in the follicular phase showed a statistically association with QOLIE-total score. While FSH ($p = 0.015$), prolactin ($p = 0.000$), LH-FSH ratio ($p = 0.009$) in the luteal phase and testosterone ($p = 0.015$) showed a significant association. However, none of the hormones independently predict the quality of life on linear regression analysis (see Table 7).

Discussion

To the best of our knowledge, this is one of the very few studies aimed at identifying determinants of QOL in WWE. Identified predictors of poorer QOL in WWE from this study include medication effects, educational level, depression, background EEG frequency and duration of epilepsy. The level of education has been a consistent indicator found to be associated significantly with QOL [13, 28–30], thus it was not surprising that this study demonstrated that low QOLIE-31 total score was seen among people who had little formal education and higher among those with postgraduate education. Education is an important indicator that may directly

Table 1 relationship between socio-demographic and clinical characteristics and QOLIE-TS

Variables	Categories	*n*(%)	QOLIE total score Mean (S.D)	Statistics	Df	*p*-Value
Age range(years)	15–25	44(44)	50.78(15.55)	F = 0.923	2, 97	0.401
	26–35	30(30)	46.90(10.25)			
	36–45	26(26)	51.05(12.85)			
	Mean age ± SD (29.07 ± 7.55)					
Highest level of education	Primary	31(31)	45.06(8.65)	F = 7.872	3, 96	0.000*
	Secondary	35(35)	46.55 (12.15)			
	Tertiary	29(29)	55.32 (14.53)			
	Postgraduate	5(5%)	67.62 (17.27)			
Ethnicity	Yoruba	89(89)	49.34 (16.28)	F = 0.098	2, 97	0.906
	Hausa	5(5)	52.06 (14.60)			
	Igbo	6(6)	49.54 (13.38)			
Duration of epilepsy	< 2years	23(23)	55.69 (15.26)	t = 2.503	98	0.014*
	≥ 2years	77(77)	47.89 (12.41)			
Age of onset (years)	1–15	34(34)	45.18(9.46)	F = 2.394	3, 96	0.073
	16–30	42(42)	51.32 (15.11)			
	31–45	21(21)	54.02 (14.43)			
	46 and above	3(3)	52.49(0.00)			
	Mean Age ± SD (20.01 ± 11.57)					
Depression	Absent	86(86)	48.16 (12.62)	t = − 2.925	98	0.004*
	Present	14(14)	59.08 (15.01)			
Family history of epilepsy	Yes	14(14)	44.08(9.28)	t = − 1.698	98	0.093
	No	86(86)	50.60 (13.84)			
Last episode of seizure	Nil	3(3)	50.63(2.39)	F = 1.179	3, 96	0.322
	< 6 months	60(60)	47.81 (13.86)			
	6 months–1 year	30(30)	53.43 (13.84)			
	2–5 years	7(7)	49.28(7.92)			
Aetiology	Structural	55(55)	48.67 (13.11)	F = 1.179	3, 96	0.322
	Metabolic	3(3)	63.46 (16.06)			
	Immune	1(1)	52.53 (0.00)			
	Unknown	41(41)	49.96 (13.67)			
Type of AED	CBM	50(50)	43.50 (5.50)	t = − 5.157	98	0.000*
	LTM	50(50)	55.87 (16.04)			
Seizure type	Focal	16(16)	47.86 (13.77)	F = 0.555	3, 96	0.646
	Generalized	32(32)	52.19 (14.14)			
	FBTC	40(40)	48.75 (12.69)			
	Unknown/unclassified	12(12)	48.53 (14.40)			
EEG frequency	Fast	42(42)	54.28 (16.01)	t = 3.027	98	0.003*
	Slow	58(58)	46.36 (10.14)			
Epileptiform pattern	Nil	14(14)	50.18 (14.65)	F = 1.899	2, 97	0.155
	Focal	42(42)	52.46 (14.28)			
	Generalized	44(44)	46.88 (11.89)			
		14(14)	43.60 (7.86)	t = − 1.846		

QOLIE Quality of life in Epilepsy Inventory, *AED* anti-epileptic drug, *EEG* electroencephalography, *Df* degree of freedom, *n* number, *t* Student's independent value, *F* one-way analysis of variance (ANOVA) value, *CBM* carbamazepine, *LTM* levetiracetam

* Statistically significant

Table 2 Showing comparison of menstrual characteristics of WWE on CBM and LTM monotherapy

Variables	CBM	LTM	Test	*p*-value
Menarche mean (SD)	11.5 (1.1)	11.9 (1.4)	− 16.00	0.094
Dysmenorrhea *N*(%)	12(24.0)	40(80.0)	31.41	0.000*
Menses pattern *N*(%)			17.13	0.000*
Oligomenorrhea	13(26.0)	12(24.0)		
Hypermenorrhea	19(38.0)	3(6.0)		
Normal	18(36.0)	35(70.0)		
Hirsutism *N*(%)	1(2.0)	10(20.0)	8.27	0.004*
Dyspareunia *N*(%)	6(12.0)	13(26.0)	57.27	0.000*
Intermenstrual bleeding *N*(%)	0(0.0)	9(18.0)	70.48	0.000*
Catamenial epilepsy *N*(%)	1(2.0)	5(10.0)	2.84	0.092

CBM carbamazepine, *LTM* levetiracetam

*Statistically significant

or indirectly influence QOL through its association with employment, higher social class, and economic status. The role of education in ensuring medication adherence should not be underestimated [13, 30, 31]. Clearly the choice of anticonvulsants plays a significant role in the determination of the QOL in epilepsy [28]. Previous studies have demonstrated an improvement in QOL with use of LTM as add-on therapy. In this present study, LTM performed better than CBM across all domains of QOL except seizure worry. These findings from our study is similar to findings from another study by Rudakova and colleagues, on effect of current AEDs on quality of life of PWE which concluded that patients treated with LTM had higher scores than patients treated with CBM [32]. Studies in the past have evaluated impact of newer drugs on QOL in PWE using various tools such as SF-36, QOLA, QOLIE-89 and QOLIE-31 in variety of clinical settings and have consistently demonstrated an improvement in QOL [4, 29, 32]. On the other hand, unsatisfactory effect of CBM on QOL has been attributed to the unfavourable pharmacokinetic profile and adverse drug reaction [12, 32]. However, it will be difficult to ascribe causality and temporal relationship to sole effect of medications because the cross-sectional nature of the study design. A prospective randomised control trial or longitudinal study will be needed to deduce such causal relationship between LTM/CBM and QOL. It is rather surprising that we are unable to demonstrate any association between seizure type and QOL as it was previously demonstrated though with contrasting finding from different studies, while Herodes and colleagues reported lower scores in patients with generalized tonic–clonic seizures, Thomas and colleagues among Indian and Guekht and colleagues in Russian patients demonstrated that focal seizures had lower QOL scores than those with generalized seizures [33, 34]. A plausible reason for this difference are varied duration of seizures and gender specificity in our cohort. Another predictor of QOL identified in this study was the presence of fast frequency background on EEG. The EEG have proven to be a reliable biomarker that helps in detecting cortical abnormalities associated with cognitive decline, an important component of QOLIE-31 [35] . There was a significant association between hormones and QOLIE-31 total score, but this did not attain any significant level on regression model. We thus suggest further evaluation of this potential therapeutic implication of this finding using a larger sample size in longitudinal study. The interplay between the sex steroid hormonal, epilepsy, and AED is complex. Both interictal and ictal discharges have been proposed as altering the sex steroid hormonal axis at the level of the hypothalamus and the pituitary [26, 27]. There is large variability in reported cases due to differing definitions, however, work by Herzog and colleagues has led to a more uniform acceptance of the definition of CE as a twofold increase in daily seizure frequency during specific phases of the menstrual cycle [25–27]. This study reported a CE frequency of 6% with no significant difference in both groups. Progesterone has long been shown in several studies to have anti-seizure activities [5]. WWE are prone to seizure in response to decrease level of progesterone especially during premenstrual period [5]. The main anti-seizure effect of progesterone has been linked to its conversion to all pregnanolone, an intermediate precursor, which has positive modulatory effect on GABA-A receptors [37]. Also, progesterone may modulate signalling cascades of inflammation, apoptosis, neurogenesis, and synaptic plasticity and therefore, progesterone may directly exact disease-modifying effects on epileptogenesis [27, 37, 38]. Thus, enhancing the activity of progesterone or its derivatives might be an unexplored therapeutic end point in reducing seizures and improving QOLIE-31 in WWE. Oestrogen is generally believed to have proconvulsant and epileptogenic property in animals and humans [10]. However, some other studies have shown that the effect of oestrogen on seizure susceptibility is highly variable depending on the factors such as treatment duration, dosage, hormonal status and seizure model [7]. Harden and colleagues reported a positive correlation between seizure and the oestrogen–progesterone ratio in WWE picking in the premenstrual and pre-ovulatory period and declining during the mid-luteal phase [5]. The effect of testosterone on seizure is complex and metabolites dependent, while the aromatization metabolite 17beta oestradiol has proconvulsant effect, testosterone

Table 3 Relationship between socio-demographic characteristics and QOLIE-31 domains

Variables	Seizure worry	Overall quality of life	Emotional well-being	Energy	Cognitive functioning	Medication effects	Social functioning
Age range(years)[a]							
15–25	45.31(18.48)[c]	59.33(24.25)[d]	51.18(14.37)	50.34(9.73)	46.92(18.62)	55.62(23.11)	51.41(22.40)
26–35	51.45(15.40)	47.17(16.41)	46.00(11.35)	50.50(9.41)	45.82(12.53)	44.14(24.69)	45.34(17.98)
36–45	56.93(16.25)	55.00(20.60)	53.38(11.92)	48.46(9.98)	48.42(15.14)	47.54(26.54)	49.85(19.55)
p value	0.023*	0.058	0.087	0.679	0.834	0.123	0.450
Level of education[a]							
Primary	47.63(17.74)	47.10(14.19)[e]	49.94(10.83)	47.42(6.69)	42.46(14.55)[e]	42.47(19.60)	41.62(14.93)[e]
Secondary	45.45(18.09)	51.94(20.58)[f]	47.31(13.70)	48.86(9.78)	42.53(15.29)[g]	53.09(22.33)	45.74(17.73))[f]
Tertiary	56.31(14.91)	61.12(24.83)	52.41(12.44)	52.24(11.07)	53.90(14.34)	50.74(30.81)	57.39(22.50)
Postgraduate	63.40(13.28)	81.00(22.12)	59.20(21.98)	59.00(9.62)	66.06(13.21)	72.23(17.35)	72.60(26.17)
p value	0.020*	0.002*	0.180	0.032*	0.000*	0.056	0.001*
Ethnicity[a]							
Yoruba	50.69(17.48)	53.99(21.87)	50.20(13.21)	49.72(10.04)	46.69(15.95)	48.74(25.18)	49.36(20.07)
Hausa	43.00(17.99)	54.50(18.91)	48.00(9.38)	49.00(4.18)	49.00(21.86)	59.45(12.68)	48.44(30.27)
Igbo	48.44(19.81)	62.92(21.88)	52.00(15.80)	53.33(6.06)	49.68(13.53)	62.04(24.20)	47.17(20.24)
p value	0.619	0.625	0.883	0.663	0.871	0.309	0.965
Age of onset (years)[a]							
1–15	43.31(16.14)	47.99(16.29)	45.89(11.29)	48.75(9.66)	42.57(13.76)	45.37(22.54)	44.78(14.02)
16–30	50.79(17.53)	57.10(24.85)	51.52(14.36)	51.19(9.36)	48.47(16.95)	53.48(24.68)	50.95(23.43)
31–45	59.87(15.37)	60.83(21.32)	54.67(12.02)	49.29(10.52)	51.81(16.71)	52.53(22.95)	52.53(22.95)
46 and above	68.00(0.00)	52.50(0.00)	56.00(0.00)	50.00(0.00)	42.22(0.00)	63.00(0.00)	63.00(0.00)
p value	0.003*	0.127	0.071	0.723	0.164	0.314	0.394
Depression[b]							
Present	49.49(17.75)	52.30(20.41)	49.30(13.21)	49.01(9.10)	45.43(15.59)	47.50(24.10)	47.17(19.95)
Absent	54.37(16.09)	68.39(24.55)	55.71(11.36)	55.36(11.34)	56.49(15.58)	65.88(23.81)	61.57(19.33)
p value	0.337	0.009*	0.090	0.022*	0.016*	0.009*	0.013*
Drugs							
CBM	53.59(15.00)	41.66(11.09)	46.16(11.09)	47.10(10.22)	42.23(10.22)	33.98(20.34)	39.93(12.60)
LTM	46.75(19.30)	67.45(20.34)	54.24(13.81)	52.70(9.10)	51.73(19.12)	66.17(17.29)	58.44(22.51)
Mean SD	50.17(17.54)	54.56(21.64)	50.20(13.11)	49.90(9.64)	46.98(15.98)	50.07(24.79)	49.18(20.39)
F	3.915	54.812	10.405	9.130	9.593	72.672	25.750
p value	0.051	0.000*	0.002*	0.003*	0.003*	0.000*	0.000*

[a] ANOVA with Tukey's HSD

[b] Independent *t*-test

[c] 15–25 significantly different at $p < 0.05$ compared to ages 36–45 years

[d] 15–25 significantly different at $p < 0.05$ compared to ages 26–35 years

[e] Primary significantly different at $p < 0.05$ compared to tertiary and Postgraduate

[f] Secondary significantly different at $p < 0.05$ compared to Postgraduate

[g] Secondary significantly different at $p < 0.05$ compared to Tertiary

[p] Focal significantly different at $p < 0.05$ compared to generalized

[*] Statically significant, *CBM* carbamazepine, *LTM* levetiracetam

on other hand is converted by 5 alpha reductase to 5 alpha dihydrotestosterone and then subsequently to 3 alpha androstenediol which has anticonvulsant property through its GABA modulating effect [40]. Findings from our study was also in keeping with previous findings that depression is a significant predictor of QOLIE and a common co-morbidity among people with epilepsy [29, 31, 41]. In adults, depression and anxiety are the two most frequent mental health-related diagnoses in epilepsy [42, 43]. Depression in people with epilepsy though common sometimes escapes diagnosis

Table 4 Relationship between seizure characteristics and QOLIE-31 domains

Variables	Seizure worry	Overall quality of life	Emotional well-being	Energy	Cognitive functioning	Medication effects	Social functioning
Duration of epilepsy[b]							
< 2yrs	52.31(13.94)	65.65(22.73)	52.70(12.46)	51.52(11.22)	52.55(17.08)	60.63(22.57)	58.17(24.97)
≥ 2yrs	49.53(18.51)	51.24(20.30)	49.45(13.28)	49.42(13.28)	45.32(15.37)	46.92(24.68)	46.50(18.15)
p value	0.508	0.005*	0.300	0.360	0.056	0.019*	0.015
Family history of epilepsy[b]							
Yes	40.26(17.52)	54.64(15.31)	47.14(12.47)	47.14(8.25)	38.81(15.77)	45.83(18.71)	41.07(13.32)
No	51.79(17.10)	54.54(22.57)	50.70(13.21)	50.35(9.82)	48.31(15.71)	50.76(25.66)	50.50(21.09)
p value	0.022*	0.987	0.349	0.250	0.038*	0.493	0.109
Last episode of seizure[a]							
Nil	56.77(11.18)	50.83(15.88)	45.33(2.31)	36.67(5.77)	45.46(1.29)	63.88(4.81)	64.67(5.77)
< 6 months	46.58(18.45)	53.50(22.19)	47.20(12.88)[g]	50.17(9.61)	45.13(16.26)	52.22(24.24)	46.39(21.28)
6 months–1 year	54.92(16.04)	58.10(22.35)	57.20(12.57)	51.50(9.21)	49.87(17.20)	48.21(26.74)	53.50(19.62)
2–5 years	57.76(10.61)	50.00(16.83)	48.00(9.24)	46.43(9.45)	51.10(9.34)	33.73(20.70)	48.00(15.58)
p value	0.090	0.724	0.005*	0.057	0.523	0.205	0.240
Aetiology[a]							
Structural	51.26(17.65)	50.82(19.77)	49.16(13.15)	49.45(8.85)	46.69(15.71)	48.52(24.47)	48.04(19.43)
Metabolic	61.45(12.68)	78.33(19.09)	66.67(9.24)	51.67(12.58)	59.08(13.64)	70.38(17.65)	63.40(30.89)
Immune	64.00(0.00)	45.00(0.00)	68.00(0.00)	55.00(0.00)	54.45(0.00)	19.43(0.00)	43.00(0.00)
Unknown	47.56(17.60)	58.06(23.16)	49.95(12.56)	50.24(10.72)	46.30(16.64)	51.42(25.24)	49.83(21.30)
p value	0.399	0.086	0.071	0.910	0.573	0.277	0.629
Seizure type[a]							
Focal	51.52(18.67)	53.44(21.43)	49.50(15.45)	46.56(10.60)	43.42(17.11)	49.83(24.42)	47.76(17.79)
Generalized	50.60(17.41)	57.13(22.51)	52.75(14.53)	50.94(9.46)	50.64(16.41)	49.65(26.91)	52.19(23.10)
FBTC	48.80(18.64)	54.75(20.70)	49.60(11.49)	50.00(9.74)	44.86(15.71)	52.83(23.57)	47.85(18.40)
Unknown/unclassified	51.82(13.92)	48.54(24.11)	46.33(10.98)	51.25(8.56)	49.05(13.68)	42.36(24.74)	47.50(23.84)
p value	0.929	0.706	0.502	0.476	0.340	0.651	0.800
EEG frequency							
Fast	52.75(16.16)	61.79(24.97)	55.33(13.88)	51.79(9.87)	51.83(17.05)	56.68(29.07)	53.36(23.26)
Slow	48.30(18.38)	49.31(17.28)	46.48(11.23)	48.53(9.32)	43.47(14.31)	45.29(20.09)	46.16(17.63)
p value	0.212	0.004*	0.001*	0.096	0.009*	0.023*	0.081
Epileptiform pattern							
Nil	54.08(17.30)	52.86(20.94)	46.86(13.54)	52.86(8.25)	49.98(15.86)	42.80(30.21)	49.07(25.25)
Focal	52.89(17.74)	56.98(24.06)	54.29(13.02)[p]	50.83(9.62)	49.51(15.64)	56.81(23.83)	52.10(19.95)
Generalized	46.34(17.04)	52.78(19.59)	47.36(12.26)	48.07(9.90)	43.62(16.07)	45.96(22.76)	46.43(19.21)
p value	0.149	0.640	0.028*	0.193	0.176	0.062	0.440

[a] ANOVA with Tukey's HSD

[b] Independent *t*-test

[d] 15–25 significantly different at $p < 0.05$ compared to ages 26–35 years

[e] Primary significantly different at $p < 0.05$ compared to tertiary and Postgraduate

[f] Secondary significantly different at $p < 0.05$ compared to Postgraduate

[g] < 6 months significantly different at $p < 0.05$ compared to 6 months–1 year

[p] Focal significantly different at $p < 0.05$ compared to generalized

[*] Statically significant, *CBM* carbamazepine, *LTM* levetiracetam

even when necessary treatment is needed [44]. In many cases, a combination of anti-epileptic use, psychotherapy and antidepressants are the most effective approach [3]. The manifestation of depression in people with epilepsy has a significant negative toll on seizure control, sexual function, sleep, school or work performance,

Table 5 Showing logistic analysis of the correlates of QOLIE-TS

Variables	B	S.E	Wald	*p*-value	Odds ratio	95% CI	
						Lower	Upper
Age							
15–25	− 0.001	0.018	0.006	0.938	0.999	0.964	1.034
26–35	− 0.025	0.021	1.400	0.237	0.975	0.936	1.016
36–45	Reference						
Medication							
CBM	− 0.088	0.022	16.243	0.000*	0.915	0.877	0.956
LTM	Reference						
EEG frequency							
Fast	0.046	0.016	7.918	0.005*	1.047	1.014	1.081
Slow	Reference						
Duration of epilepsy							
< 2yrs	0.041	0.017	5.646	0.017*	1.042	1.007	1.077
≥ 2yrs	Reference						
Depression							
Present	− 0.054	0.020	7.138	0.008*	0.947	0.910	0.986
Absent	Reference						
Highest level of education							
Primary	− 0.127	0.042	9.006	0.003*	0.881	0.811	0.957
Secondary	− 0.114	0.041	7.735	0.005*	0.892	0.824	0.967
Tertiary	− 0.063	0.039	2.545	0.111	0.939	0.870	1.014
Postgraduate	Reference						

B Beta co-efficient, *S.E* standard error, *EEG* electroencephalography, *CI* confidence interval, *CBM* carbamazepine, *LTM* levetiracetam

* Statically significant

Table 6 Relationship between hormones and QOLIE-31 domains

Variables	Total QOLIE-TS	Seizure Worry	Overall quality of life	Emotional Well-being	Energy	Cognitive functioning	Medication Effects	Social Functioning
FP: FSH								
Df	62,37	62, 37	62, 37	62, 37	62, 37	62, 37	62, 37	62, 37
F	1.444	1.570	1.313	1.233	2.323	1.576	1.130	1.596
p	0.116	0.071	0.188	0.249	0.003*	0.069	0.349	0.064
FP: LH								
Df	61,38	61, 38	61, 38	61, 38	61, 38	61, 38	61, 38	61, 38
F	1.354	2.168	1.232	1.235	2.346	1.459	1.159	1.542
p	0.160	0.006*	0.248	0.245	0.003*	0.107	0.317	0.078
FP: PR								
Df	56,43	56, 43	56, 43	56, 43	56, 43	56, 43	56, 43	56, 43
F	1.674	1.610	1.226	1.202	1.718	1.548	1.114	1.957
p	0.040*	0.053	0.245	0.267	0.033*	0.069	0.358	0.012*
FP:EST								
Df	70,29	70, 29	70, 29	70, 29	70, 29	70, 29	70, 29	70, 29
F	2.185	3.702	1.260	1.718	2.665	2.345	1.102	2.707
p	0.011*	0.000*	0.248	0.054	0.002*	0.006*	0.396	0.002*
FP:PRL								
Df	52,46	52, 46	52, 46	52, 46	52, 46	52, 46	52, 46	52, 46
F	2.331	2.761	1.797	2.142	2.358	2.082	1.385	2.156
p	0.002*	0.000*	0.022*	0.005*	0.002*	0.006*	0.132	0.004*

Table 6 (continued)

Variables	Total QOLIE-TS	Seizure Worry	Overall quality of life	Emotional Well-being	Energy	Cognitive functioning	Medication Effects	Social Functioning
FP: LH:FSH								
Df	62,35	62, 35	62, 35	62, 35	62, 35	62, 35	62, 35	62, 35
F	1.350	2.063	1.186	1.167	1.783	1.573	1.015	1.451
p	0.170	0.011*	0.296	0.315	0.033*	0.074	0.492	0.118
LP: FSH								
Df	62,37	62, 37	62, 37	62, 37	62, 37	62, 37	62, 37	62, 37
F	1.959	1.786	1.550	2.012	3.482	1.610	1.633	1.827
p	0.015*	0.030*	0.077	0.012*		0.061	0.055	
LP: LH								
Df	66,33	66, 33	66, 33	66, 33	66, 33	66, 33	66, 33	66, 33
F	1.568	1.847	1.151	2.772	3.306	1.677	1.299	1.259
p	0.079	0.028*	0.335	0.001*	0.000*	0.053	0.208	0.237
LP: PR								
Df	60,39	60, 39	60, 39	60, 39	60, 39	60, 39	60, 39	60, 39
F	1.465	1.908	0.788	2.261	2.070	1.705	1.348	1.279
p	0.103	0.017*	0.801	0.004*	0.009*	0.039*	0.161	0.208
LP: EST								
Df	69,30	69, 30	69, 30	69, 30	69, 30	69, 30	69, 30	69, 30
F	1.238	2.222	1.367	2.211	5.082	1.059	1.912	1.176
p	0.263	0.009*	0.173	0.009*	0.000*	0.443	0.026*	0.318
LP: PRL								
Df	55,43	55, 43	55, 43	55, 43	55, 43	55, 43	55, 43	55, 43
F	2.718	2.332	2.177	2.664	6.420	1.823	1.748	2.180
p	0.000*	0.002*	0.005*	0.001*	0.000*	0.001*	0.030*	**0.005***
LP: LH:FSH								
Df	68,30	68, 30	68, 30	68, 30	68, 30	68, 30	68, 30	68, 30
F	2.219	1.994	1.492	3.824	3.775	1.932	1.536	1.701
p	0.009*	0.019*	0.114	0.000*	0.000*	0.024*	0.098	0.055
Testosterone								
Df	65,34	65, 34	65, 34	65, 34	65, 34	65, 34	65, 34	65, 34
F	1.998	1.567	1.585	1.879	2.295	2.125	1.812	1.971
p	0.015*	0.077	0.072	0.024*	0.005*	0.009*	0.030*	0.017*

FP follicular phase, *LP* luteal phase, *FSH* follicle stimulating hormone, *PR* progesterone, *EST* estrogen, *PRL* prolactin, *Df* degree of freedom, *F* ANOVA value

* Statistically significant

cognition and consequently on overall QOL. Our study is limited in that we restricted our cohort to females. We were able to identify determinants of QOL in WWE, but causality and relationship could not be ascertained because of the cross-sectional nature of the study especially with regard to medication effect. As such, we propose a prospective longitudinal study to further explore interplay among AEDs, hormones and QOL in WWE.

Conclusion

Overall, we demonstrated higher QOLIE-31 score in the LTM group across all domains except seizure worry. Furthermore, we identified predictors of poorer QOL in WWE from this study include medication effects, educational level, depression, background EEG frequency and duration of epilepsy. While we demonstrated association between progesterone, testosterone, prolactin and LH/FSH ratio with QOL, none of the hormones independently predicts the QOL on linear regression analysis.

Table 7 Showing linear analysis of the correlates of QOLIE-TS

Variables	B	Standardized Beta	t	*p*-value	95% CI	
					Lower	Upper
FP: Progesterone	0.149	0.136	1.355	0.178	− 0.069	0.367
FP: Oestradiol	0.612	0.060	0.594	0.554	− 1.433	2.656
FP: Prolactin	0.190	0.124	1.235	0.220	− 0.116	0.496
LP: FSH	− 0.100	− 0.133	− 1.327	0.188	− 0.250	0.050
LP: Prolactin	0.070	0.051	0.500	0.618	− 0.208	0.348
LP: LH:FSH	− 0.815	− 0.138	− 1.371	0.174	− 1.995	0.365
Testosterone	0.008	0.109	1.087	0.280	− 0.006	0.021

FSH follicle stimulating hormone, *LH* luteinizing hormone, *FP* follicular phase, *LP* luteal phase, LH:FSH: ratio of luteinizing hormone to follicle stimulating hormone, *B* Beta co-efficient, *S.E* standard error, *CI* confidence interval, *t* Student's test value

Abbreviations

QOL	Quality of Life
WWE	Women with epilepsy
CBM	Carbamazepine
LTM	Levetiracetam
EEG	Electroencephalography
ILAE	International League Against Epilepsy
QOLIE-31	Quality of Life Inventory Scale 31
QOLIE-TS	QOLIE-Total Score
ZSRDS	Zung Self-Rating Depression Scale
PWE	Patients with epilepsy
AEDs	Anti-epileptic drugs
CNS	Central nervous system
LH	Luteinizing hormone
FSH	Follicle stimulating hormone
P	Progesterone
PRL	Prolactin
E	Estradiol
T	Testosterone
FP	Follicular phase
LP	Luteal phase
ANOVA	One-way analysis of variance

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Author contributions
LO and AO conceived the idea of the study. JY, BF and LO were involved with statistical analysis. Diagnosis and classification were done by YJ and LO who are neurologist. LO, JY, AM, AA, AAR, BO, BF, AM, FF, and AO, were involved in the study design, data collection and interpretation and made significant intellectual contribution manuscript development. MO and DO performed neuroimaging, recruited patients and made significant intellectual contributions to the development of manuscripts. LO, AM, AA and OO, provided the laboratory expertise in addition to significant contribution to manuscript development. All authors read and approve the manuscript.

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Availability of data and materials
The data will be made available upon reasonable request, the principal investigator, will make the data available.

Declarations

Ethical approval and consent to participate
This was obtained from joint review board of University of Ibadan/University College Hospital with assigned number of UI/EC/15/077. Participants for this study were fully informed on the research protocol detailing the purpose, method, risks, and benefits of the research. Each of the participant then voluntarily gave a written and well understood informed consent. The consent was translated to the local language for those who did not understand English language and the services of interpreters were employed. Participants were free to decline participation or withdraw from the study at any time without reprisal or loss of benefit. There were sections for the person giving the consent, person obtaining the consent and witnesses in the informed consent.

Consent for publication
Not applicable.

Competing interests
There are no competing interest or competing interests.

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