Original Paper

Comorbidity of Epilepsy and Depression in Al Husseini Teaching Hospital in Holy Kerbala /Iraq in 2018

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Abstract

Background: Epilepsy comorbidity with depression is well known in clinical practice. The impact of depression state is bidirectional, and similarly seizure might be causal or result of depressive state.
Material and methods: a cross-sectional study among sixty patients with epilepsy investigated the prevalence and predictors of depression among these patients. A validated well-known questionnaire form (PHQ-9) was used to assess depressive state.
Results: Very high prevalence, exceeding 80%, of depression was found and this might be related to the unstable security and economic state in the country. Significant predictors were gender, duration of disease and positive video EEG findings. While patients' age, family history of epilepsy, type of fit, the type of therapy and compliance were all not significantly associated with depression.
Conclusions: a high majority of epileptic patients suffer from depression and this might affect their response to treatment and their prognosis.
Keywords: Epilepsy, Depression, Family history, duration of disease, PHQ-9
Conflict of interest: None

Introduction

Epilepsy is a syndromes characterized by unprovoked, recurring seizures and to be epileptic should have at least more than two seizures or more [(1)].
It is frequent neurological illness affecting an estimated 50 million people in the world, characterized by unusual electrical activity in the brain that lead to change in the movement of the body or can affect the sensation, consciousness or behavior [(2, 3)]. It is regarded as one of the most common neurological illness that can affect the life adjustment [(4)]. It affects physical and psychological functions of the person [(5, 6)].
The problem in epilepsy is that seizure recurrence is unpredictable and it represents a constant threat to the patient and their family.
Epilepsy can affect the community in regard the employment and poverty; also can be associated with certain physical and mental illness affection patient quality of life [(7)]. In addition it represents a fundamental social stigma for the patients and their families resulting in social isolation due to lack of understanding [(8-10)].
The WHO has defined Quality of Life as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [(11, 12)].
Comorbid psychiatric illness might increase health care needs and socioeconomic burdens due to long-term disability and morbidity and worsen epileptic patients diagnosis and treatment, exacerbate the prognosis [(13, 14)].
The most common psychiatric disease that is associated with epilepsy is depression, and this can have negative impact on the treatment and prognosis of epilepsy [(15, 16)].

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Since long ago; Hippocrates mentioned the relationship between depression and epilepsy [17]. This association between them is under estimated in regard the diagnosis and treatment [18].

Major depression was characterized by lack of feeling pleasure , low mood, reduced energy and fatigue that persist for at least two weeks; occurring most days [19]. It is a leading cause of disability and a main cause of global burden of disease as about 350 million people are affected worldwide. According to DSM-5 criteria, major depressive disorder has nine symptoms: low mood, anhedonia, significant weight loss or gain, poor sleep or hypersomnia, psychomotor agitation or retardation, loss of energy, excessive guilt, poor concentrate, and suicidal thought. A diagnosis of major depressive disorder requires the depressive mood or the loss of interest or pleasure to persist for more than two weeks, the presence of at least five of the nine symptoms, and causing significant impairment in social and occupational functioning [20]. The depressive state in epileptic patients might have bidirectional association with the lowered sexual motivation and performance [21].

The prevalence of depressive disorders in epilepsy patients is thought to be 15–50%, depending on the methodological factors, such as study setting, socioeconomic conditions, selected measures, and definitions used [8, 22, 23]. It had been shown that low mood appears to be generally pronounced in depressed epilepsy patients when compared with idiopathic depression [24, 25]. A noteworthy point is the association between antiepileptic drugs and depression as a side effect for these medications [14].

Most reviewed bulk of literature reported greater prevalence and impact of depression on female compared to males [26, 27]. Similar gender predilection of depression among female epileptics was also reported [27, 28]. The results of this and similar studies among patients with epilepsy are important for health policy makers and physicians in order to put forwards and implement interventional programs for improving the quality of life of epileptic patients [10].

The improvement in technology had introduces valuable diagnostic tools in epilepsy management. Video EEG and neuroimaging are important investigation tools used by neurologist and psychiatrist to confirm or exclude the clinical diagnosis of a wide range of brain's abnormalities with especial rule in the diagnoses of epilepsy with/without other neurological diseases [29, 30].

Patients and methods

Institution based cross sectional study was used to explore the prevalence of depression among patients with epilepsy in Al Husseini Teaching hospital in Kerbala governorate in Iraq in 2018. The study was conducted in the period between 2nd January 2018 and 31st December 2018. Participants of this study were individuals with epilepsy receiving medical care at the wards or in the consolatory clinics (Neuro-medicine and Psychiatry) at the hospital. For assessment of depression a validated questionnaire form; Patient Health Questionnaire-9 (PHQ-9) was used for assessment. This questionnaire is nine questions with a Likert four score scale to assess patient answers. An answer of one or above was regarded as positive answer [31]. A total score of five more was considered as Positive Depression Score (PDS). Data obtained included demographic characteristics: age, gender, family history of epilepsy and other variables: seizure type, duration, type of treatment, patients' compliance and fit control. In addition, the results of investigations performed were assessed including: Video Electro-Encephalogram (EEG,) and Magnetic Resonance Imaging (MRI). Video EEG changes was regarded as positive when spikes sharp waves or complexes of spike and wave either alone or in association with slow wave activity

was detected on video EEG.

Results

The gender distribution showed that males formed one half of the sample (51.7%, 31 patient) and the remaining were females, and male to female ratio in the sample was 1:1.07 (table 1).

The mean age of the patients in the sample was 28.88 ± 14.28 year and mean duration of illness was 7.34 ± 6.46 year. The mean age patients when epilepsy started was 21.54 ±13.89 year. About one third of the sample complained from epilepsy for five years or less while the remaining two thirds complained since more than five years.

Most patients were in the age category20-39 year which is the main productive age (figure 1).

The major type of presenting fit was the generalized tonic fit (53.3%), followed by focal fit (25.0%, figure 1). EEG changes were encountered in more than three quarters (77.8%) of the patients with focal fit compared to one half (51%) of the patients with general clonic fits.

About two third (60%) of the patients were on single therapy for epilepsy, while the rest were on combined therapy (table 1).

The distribution of the type of treatment showed that for the total sample showed that three quarters of the patients were on Carbamazepine (table 3).

The men depression score ranged between and the mean was 0.817±0.390 and this represented a good to very good level. The prevalence of depression (those with PHQ-9 score of 5 or more) among epileptic patients in the sample was high (81.9%). However, two thirds of the patients complained of mild or moderate depression, while no patients suffered from severe depression (figure 2).

A clear difference was found between male (77.4%) and female (86.2%) patients (Odds ratio=1.823, 95% Confidence Interval was 0.473-7.033). In addition, the total score according to PHQ-9 was significantly higher among female epileptics than male epileptics (9.90±4.23 for females vs. 7.55± 4.79 for males. The duration of disease was a significant predictor of developing depression (p=0.022). A great majority (95%) of those with longer duration (>5 year) showed positive depression score compared to 63.6% of those with shorter duration (table 3). Similarly, uncontrolled fit was a clear predictor of positive depression score. An obvious difference was found between the group with controlled fit (84.2%) and those with uncontrolled fit (77.3%, odds ratio=1.57, 95% Confidence Interval was 0.17-2.40), however the difference was not significant (p=0.503, table 3).

Positive video EEG change was significantly associated with positive total score of depression (p=0.041). The majority (91%) of epileptics with positive EEG changes showed positive depression score compared to 70% of those with normal EEG and the odds ratio for positive EEG change was 4.211 (95% confidence interval 0.992-17.878).

The total depression score was not associated with positive family history of epilepsy (p=0.847), type of treatment (p=0.340) and patient's compliance (0.406, table 3).

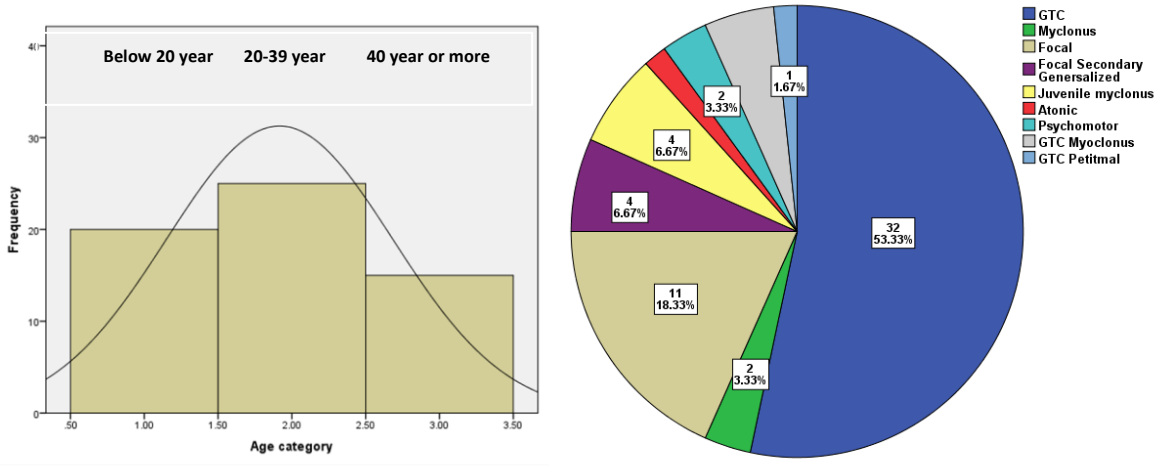
The reliability analysis of subscales of PHQ-9 showed moderate internal reliability (Cranach's alpha=0.51). Detailed analysis of the patients' answers on PHQ-9 questionnaire showed that the highest positive answer was for question 2 and 3 followed by question 9 where about one fifth of the patients reported daily complaint of these symptoms. On the other hand, the highest negative answer was for question seven and nine where about two thirds of the patients reported negative answers. A noticeable finding was that about one fifth of the epileptic patients (18.3%) complained of suicidal thoughts (table 1).

These answers showed epileptic patients suffer a lot in respect to the quality of life. For example, about one half of the patients

'had no or little interest or pleasure in doing things'. Similarly, a higher proportion (51.7%) suffered from 'Feeling tired or having little energy' and about similar proportion had positive answers for the questions six to nine (table 1).

Table 1. The demographic and other characteristics of epileptic patients in Al Husseini Teaching Hospital in Holy Kerbala /Iraq in 2018 (n=60)

Variable	Group	Frequency	Percentage
Gender	Male	31	51.67
	Female	29	48.33
Age category	Below 20 year	20	33.3
	20-39 year	25	41.7
	40 year or more	15	25.0
Duration of epilepsy	One year or less	9	15.00
	1-4 year	23	38.33
	6-10 year	17	28.33
	More than 10 year	11	18.33
Type of fit	Focal	15	25.0
	General	45	75.0
Family history	Negative	45	75.00
	Positive	15	25.00
Type of treatment	Monotherapy	36	60.00
	Combined therapy	24	40.00
Controlled fit	No	38	63.30
	Yes	22	36.70
Regular treatment	No	34	56.70
	Yes	26	43.30
EEG changes	Negative	27	45.00
	Positive	33	55.00
CT and MRI changes	Negative	49	81.70
	Positive	11	18.30
Total		60	100.00



GTC: Generalized Tonic Clonic fit

Figure 1. The age distribution and categories of epileptic patients in Al Husseini Teaching Hospital in Holy Kerbala /Iraq in 2018 (n=60)

Table 2. The types of medications given to epileptic patients in Al Husseini Teaching Hospital in Holy Kerbala /Iraq in 2018 (n=60)

Drug	Frequency (percentage)*
Carbamazepine	43 (70.49%)
levetiracetam	16 (26.23%)
Sodium valproate	14 (24.59%)
Clonazepam	5 (8.20%)
phenytoin	4 (6.56%)
Lamotrigine	3(4.92%)

* some patients were given more than one drug at the same time

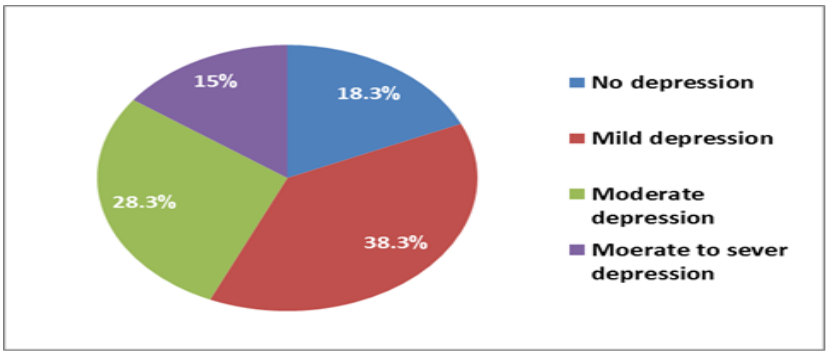


Figure 2. The severity of depression distribution among epileptic patients in Al Husseini Teaching Hospital in Holy Kerbala /Iraq in 2018 (n=60)

Table 3. The demographic and other characteristics of epileptic patients by the state of depression in Al Husseini Teaching Hospital in Holy Kerbala/Iraq in 2018 (n=60)

Variable	Group	Positive Depression Score		Negative Depression Score		Total		Sign.
		Freq.	%	Freq.	%	Freq.	%	
Gender	Male	7	63.6	24	48.98	31	51.7	0.379
	Female	4	36.4	25	51.02	29	48.3	
Age category	Below 20 year	4	36.36	16	32.7			0.925
	20-39 year	4	36.36	21	42.9			
	40 year or more	3	27.27	12	24.5			
Duration of epilepsy	Less than 5 year	8	72.7	24	49	9	15.0	0.022
	5 year or more	3	27.30	25	51	23	38.33	
Type of fit	Focal	4	36.40	11	28.21	15	25	
	General	7	63.60	28	71.79	45	75	
Family history	Negative	8	72.70	37	75.51	45	75.00	0.847
	Positive	3	27.30	12	24.49	15	25.0	
Type of treatment	Monotherapy	8	72.70	28	57.14	36	60.0	0.500
	Combined therapy	3	27.30	21	42.86	24	40.0	
Controlled fit	No	6	54.50	32	65.3	38	63.3	0.503
	Yes	5	45.50	17	34.7	22	36.7	
Regular treatment	No	5	45.50	29	59.2	34	56.7	0.406
	Yes	6	54.50	20	40.8	26	43.3	
EEG changes	Negative	8	72.70	19	38.8	27	45.0	0.041
	Positive	3	27.30	30	61.2	33	55.0	
CT and MRI changes	Negative	9	81.80	40	81.63	49	81.7	0.154
	Positive	2	18.20	9	18.37	11	18.3	
Total		11	28.21	49	71.79	60	100.0	

Table 4. The distribution of answers on pHQ-9 questionnaire of epileptic patients in Al Husseini Teaching Hospital in Holy Kerbala /Iraq in 2018 (n=60)

	Question	Never	Some days (<=3 days a week)	Most days (>3 days a week)	Every day
1.	Little interest or pleasure in doing things	34 (56.7%)	5 (8.3%)	17 (28.3%)	4 (6.7%)
2.	Feeling down, depressed, or hopeless	22 (36.7%)	9 (15.0%)	17 (28.3%)	12 (20.0%)
3.	Trouble falling or staying asleep, or sleeping too much	27 (45.0%)	7 (11.7%)	14 (23.3%)	12 (20.0%)
4.	Feeling tired or having little energy	29 (48.3%)	7 (11.7%)	14 (23.3%)	10 (16.7%)
5.	Poor appetite or overeating	30 (50.0%)	11 (18.3%)	10 (16.7%)	9 (15.0%)
6.	Feeling bad about yourself — or that you are a failure or have let yourself or your family down	28 (46.7%)	10 (16.7%)	13 (21.7%)	9 (15.0%)
7.	Trouble concentrating on things, such as reading the newspaper or watching television	38 (63.3%)	11 (18.3%)	7 (11.7%)	4 (6.7%)
8.	Moving or speaking so slowly that other people could have noticed Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	33 (55.0%)	14 (23.3%)	8 (13.3%)	5 (8.3%)
9.	Thoughts that you would be better off dead or of hurting yourself in some way	37 (61.7%)	5 (8.3%)	7 (11.7%)	11 (18.3%)

There were statistically significant correlations between large number of subscales of PHQ-9 in epileptic patients in the sample ($p<0.05$). The highest mean subscale was for 'Feeling sad' with a mean of 1.32±1.172. The total score according to PHQ-9 ranged from 0 to 19 and the mean was 8.68±4.65, while the least subscale was for 'Difficulty in concentration' with a mean of 0.62±0.94 point. No gender difference was discovered in the subscales except for question 2 and 3 –'Feeling down, depressed' and 'Trouble falling or staying asleep -($p<0.05$).

Discussion

The present study showed that a high proportion of epileptics complained from depression according to PHQ-9 tool. This high prevalence could be related to the general social burden of wars and conflicts in the country since decades. In addition, this finding might be associated with patients' compliance with treatment availability troubles and the types of the medicine available in the market and the governmental premises.

It is also important to mention that large number of internally displace population were included in the study sample and they were mostly from Mosul governorate and they had suffered a lot during ISIS attacks in 2014 which obliged them to be displaced to most other governorates.

It is important to mention that about two fifths of the sample (38.3%) complained of mild depression, while no patients showed severe depression (figure 2). Similar comorbidity was widely reported since decades [30, 32, 33], and literature review showed that Wiegartz and his colleagues in 1999 found that 43% of 76 patients with epilepsy had a major depressive disorder [34]. Similarly Ettinger and his colleagues in 1998 identified symptoms of depression in 26% of 44 children with epilepsy [35]. While in 2006 Kanner and her colleagues found that among 97 patients with refractory epilepsy, 29% met DSM-IV criteria for MDD severe enough to merit pharmacotherapy [36] . While a study among 405 epileptics in Northern Ethiopia reported a prevalence of depression at 45.2% [37].

Even population based studies in Canada revealed this positive association [14-16, 38,

[39]. Patients with epilepsy showed an odds ratio of 2.4 in comparison to non-epileptics in a large population based studies, among about 37000 people, in Canada [38], and in USA [39]. The comorbidity was also proved among a larger sample of more than one half million person in China [15].

Comorbid epilepsy and depression might be resulting from the consequence of epilepsy alone or the opposite might be true as some diseases might induce epileptic seizure [7]. In addition, seizure might be a side effect of medications [10]. Epilepsy might be caused by organic lesion which might result in depression or depressive state might result functionally from the social and behavioral impact of epilepsy on the patients. A noticeable finding reported in many published papers, is the economic impact of epilepsy as a chronic disease in need for continuous medications cost and medical supervision and follow up. This economic impact has been reported in many studies in Iraq [12], and in other countries [40].

The mean depression score was found for the participants in this study was 0.81( ) and this suggest a poor quality of life. Similar findings were reported in Basrah and Baghdad in Iraq. The study among 100 epileptics in Baghdad in 2014 reported a moderate quality of life score (55.9) was range (0.51) [41]. Significantly lower scores for the quality of life than normal people was reported in a study in Basrah [12].

Gender difference was clear in the present study and this was consistent with the findings found on literature review [28, 42, 43]. The higher prevalence of depression among females might be related the sociocultural male dominant culture in oriental communities, in addition to the worse feeling of stigma in female than that male patients in these communities.[27] It is important to notice that depression prevalence is generally higher among females than male [26].

The duration of disease was significantly associated with developing depression in the present study (table 3). A similar finding was reported in a study in Basrah/Iraq among 116 patients [12], and Iran.

Video EEG and neuroimaging represent diagnostic tools of expanding benefit and are widely used to assess brain lesions [44]. More than one half of the patients in the present study (55%) showed abnormal EEG and this was similar to the finding (57.4%) in a series of 246 firstly diagnosed epileptic patients in Iraq [29].

The association of positive EEG changes and depression found in the present study had been reported in many similar studies decades [45-47] and recent studies [30, 32, 33].

Conclusions and recommendation: The study showed that epilepsy disease has an important role in the quality of life of epileptic patients, thus some interventional programs are necessary to improve their life. Additionally, the high prevalence of depression among epileptics necessitates its treatment before or simultaneously with treating epilepsy.

References

1. Lambert MV, Robertson MM. Depression in epilepsy: etiology, phenomenology, and treatment. Epilepsia. 1999;40:s21-s47.
2. Spitzer RL, Williams JB, Kroenke K, Linzer M, Verloin deGruy F, Hahn SR, et al. Utility of a new procedure for diagnosing mental disorders in primary care: the PRIME-MD 1000 study. Jama. 1994;272:1749-56.
3. Brodie MJ, French JA. Management of epilepsy in adolescents and adults. The Lancet. 2000;356:323-9.
4. Shih C-C, Su Y-C, Liao C-C, Lin J-G. Patterns of medical pluralism among adults: results from the 2001 National Health Interview Survey in Taiwan. BMC health services research. 2010;10:191.
5. Prevots DR, Burr RK, Sutter RW, Murphy TV. Poliomyelitis Prevention in the United States: Updated Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morbidity and Mortality Weekly Report: Recommendations and Reports. 2000:i-22.
6. Forsgren L, Beghi E, Oun A, Sillanpää M. The epidemiology of epilepsy in Europe–a systematic review. European Journal of neurology. 2005;12:245-53.
7. Boylan L, Flint L, Labovitz D, Jackson S, Starner K, Devinsky O. Depression but not

seizure frequency predicts quality of life in treatment-resistant epilepsy. Neurology. 2004;62:258-61.
8. Kanner AM. Management of psychiatric and neurological comorbidities in epilepsy. Nature Reviews Neurology. 2016;12:106.
9. Keezer MR, Sisodiya SM, Sander JW. Comorbidities of epilepsy: current concepts and future perspectives. The Lancet Neurology. 2016;15:106-15.
10. Elger CE, Johnston SA, Hoppe C. Diagnosing and treating depression in epilepsy. Seizure. 2017;44:184-93.
11. Group WHOQoL. What is quality of life? World Health Organization Quality of Life Assessment. World Health Forum. 1996;17:354-6.
12. Shakir M, Al-Asadi JN. Quality of life and its determinants in people with epilepsy in basrah, iraq. Sultan Qaboos University medical journal. 2012;12:449-57.
13. Domínguez-Aguilera MC, Muñiz-Landeros CE. Prevalence of psychiatric disorders in patients with epilepsy in a tertiary level care hospital: Detection through the MINI PLUS International Structured Interview. Medicina Universitaria. 2017;19:3-6.
14. Bosak M, Turaj W, Dudek D, Siwek M, Szczudlik A. Depressogenic medications and other risk factors for depression among Polish patients with epilepsy. Neuropsychiatric disease and treatment. 2015;11:2509-17.
15. Chang H-J, Liao C-C, Hu C-J, Shen WW, Chen T-L. Psychiatric disorders after epilepsy diagnosis: a population-based retrospective cohort study. PloS one. 2013;8:e59999.
16. Fiest KM, Dykeman J, Patten SB, Wiebe S, Kaplan GG, Maxwell CJ, et al. Depression in epilepsy: a systematic review and meta-analysis. Neurology. 2013;80:590-9.
17. Hoppe C. Citing Hippocrates on depression in epilepsy. Epilepsy & behavior : E&B. 2018;90:31-6.
18. Kanner AM. Depression in neurologic disorders: why should neurologists care? Depression in neurologic disorders: diagnosis and management. 2012:1-9.
19. Barry JJ. Idiopathic depressive disorders: basic principles. Depression in Neurologic Disorders: Diagnosis and Management. 2012:28-38.
20. Association AP. Diagnostic and statistical manual of mental disorders (DSM-5®): American Psychiatric Pub; 2013.
21. Atlantis E, Sullivan T. Bidirectional Association Between Depression and Sexual Dysfunction: A Systematic Review and Meta-Analysis2012. 1497-507 p.
22. Hoppe C, Elger CE. Depression in epilepsy: a critical review from a clinical perspective. Nature Reviews Neurology. 2011;7:462.
23. Leah E, Sarah M. Manuscript Pilot Study: Evaluation of Changes in Depressive Symptoms After One Year in Patients with Refractory Epilepsy Treated with Vagus Nerve Stimulation. 2016.
24. Mula M. The interictal dysphoric disorder of epilepsy: Legend or reality? Epilepsy & Behavior. 2016;58:7-10.
25. Amiri M, Hansen CP. The interictal dysphoric disorder in patients with epilepsy: a doubtful disorder lacking diagnostic tools. Seizure. 2015;24:70-6.
26. Bogren M, Brådvik L, Holmstrand C, Nöbbelin L, Mattisson C. Gender differences in subtypes of depression by first incidence and age of onset: a follow-up of the Lundby population. European archives of psychiatry and clinical neuroscience. 2018;268:179-89.
27. Wang X, Chen Y, Lei L, Zhiyi H. Factors associated with quality of life in epileptics in northen China and the variations between men and women. Chinese Journal of Neurology. 2017;50(1):34-9.
28. Shetty PH, Naik RK, Saroja A, Punith K. Quality of life in patients with epilepsy in India. Journal of neurosciences in rural practice. 2011;2:33.
29. Qassim Hadi A-A, Ala Khalil A-B. The significance of EEG recording in confirming the diagnosis of epilepsy in cases referred for the 1st time. Mustansiriya Medical Journal. 2006;6:77-85.
30. Brown E, Clark D, Bogess M, Widge A, Ramasubbu R, Protzner A, et al. Oscillation Changes in EEG Measured in the On and Off DBS State in Patients with Treatment Resistant Depression. Biological Psychiatry. 2017;81:S401.
31. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. Journal of general internal medicine. 2001;16:606-13.
32. Stafstrom CE, Carmant L. Seizures and epilepsy: an overview for neuroscientists. Cold Spring Harbor perspectives in medicine. 2015;5:a022426.
33. Northoff G. How do resting state changes in depression translate into psychopathological symptoms? From 'Spatiotemporal correspondence'to 'Spatiotemporal Psychopathology'. Current opinion in psychiatry. 2016;29:18-24.
34. Wiegartz P, Seidenberg M, Woodard A, Gidal B, Hermann B. Co-morbid psychiatric disorder in chronic epilepsy: recognition and etiology of depression. Neurology. 1999;53:S3-8.
35. Ettinger AB, Weisbrot DM, Nolan EE, Gadow KD, Vitale SA, Andriola MR, et al. Symptoms of depression and anxiety in pediatric epilepsy patients. Epilepsia. 1998;39:595-9.

36. Kanner AM. Depression and epilepsy: a new perspective on two closely related disorders. Epilepsy currents. 2006;6:141-6.
37. Bifftu BB, Dachew BA, Tiruneh BT, Birhan Tebeje N. Depression among people with epilepsy in Northwest Ethiopia: a cross-sectional institution based study. BMC research notes. 2015;8:585-.
38. Tellez-Zenteno JF, Patten SB, Jetté N, Williams J, Wiebe S. Psychiatric comorbidity in epilepsy: a population-based analysis. Epilepsia. 2007;48:2336-44.
39. Ottman R, Lipton RB, Ettinger AB, Cramer JA, Reed ML, Morrison A, et al. Comorbidities of epilepsy: results from the Epilepsy Comorbidities and Health (EPIC) survey. Epilepsia. 2011;52:308-15.
40. Alexander HB, Broshek DK, Quigg M. Quality of life in adults with epilepsy is associated with anticonvulsant polypharmacy independent of seizure status. Epilepsy & Behavior. 2018;78:96-9.
41. Sabah Abdullah J. Quality Of Life For Patients With Epilepsy In Baghdad City. kufa Journal for Nursing sciences. 2014;4:1-9.
42. Alanis-Guevara I, Pena E, Corona T, Lopez-Ayala T, Lopez-Meza E, Lopez-Gomez M. Sleep disturbances, socioeconomic status, and seizure control as main predictors of quality of life in epilepsy. Epilepsy & Behavior. 2005;7:481-5.
43. Buck D, Jacoby A, Baker GA, Ley H, Steen N. Cross-cultural differences in health-related quality of life of people with epilepsy: findings from a European study. Quality of Life Research. 1999;8:675-85.
44. Hirsch L, Arif H. Neuroimaging in the evaluation of seizures and epilepsy. UpToDate, Pedley, TA (Ed), UpToDate, Waltham, MA Accessed. 2017;10:12.
45. Davison K. EEG activation after intravenous amitriptyline. Electroencephalography and clinical neurophysiology. 1965;19:298-300.
46. Nielsen H, Kristensen O. Personality correlates of sphenoidal EEG-foci in temporal lobe epilepsy. Acta Neurologica Scandinavica. 1981;64:289-300.
47. Ulrich G, Renfordt E, Zeller G, Frick K. Interrelation between changes in the EEG and psychopathology under pharmacotherapy for endogenous depression. Pharmacopsychiatry. 1984;17:178-83.