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Original Article

Prevalence and predictors of psychiatric comorbidities in epilepsy: A cross-sectional stud

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Abstract

Background:

Anxiety and depression are common psychiatric comorbidities with epilepsy. We aim to evaluate the prevalence and possible risk factors for these comorbidities in people with epilepsy. A sample of 106 epileptic patients attending neuropsychiatry out-patients clinic from August 2022 to June 2023. Neurological Disorders Depression Inventory for Epilepsy (NDDI-E, cut-off ≥ 15) and the Generalized Anxiety Disorder 7-Item scale (GAD-7, cut-off > 9) were used to assess depression and anxiety in epileptic patients. Psychiatric history, socio-demographics, and epilepsy data were obtained by a semi-structured interview. Patients with and without anxiety and depressive symptoms were compared.

Result

The prevalence of depression and anxiety among patients with epilepsy (PWE) is 31.1%, and 30.2% respectively, whereas generalized anxiety disorder was the most common subtype of anxiety disorders (20.8%). The tonic-clonic, symptomatic, and focal seizures were the most frequent semiology associated with depression and anxiety. Older age, and female patients were statistically related to depression. However, no risk factors were statistically associated with anxiety.

Conclusion

The extent of depression and anxiety disorders comorbidities is reasonably high among PWE. Early identification and management might affect the magnitude of the problem.

Keywords: Epilepsy, Depression, Anxiety

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Introduction

Epilepsy is a brain disorder described as a persistent tendency to produce epileptic seizures with psychological, cognitive, and social consequences, and requires the occurrence of two or more unprovoked seizures occurring more than 24 hours apart.[1]

Epilepsy is one of the most common neurological conditions, with an estimated 50 million people suffering from its worldwide.[2] The most prevalent psychiatric co-morbidity among epileptic patients is depression; Focal seizures, temporal lobe lesions and poorly controlled seizures are the prevalent risk factors. Depression coupled with insomnia may increase the frequency of seizures, [3] and failure to detect depression or receiving inadequate treatment could lead to suicide. [4]

Anxiety affects about 25% of patients with epilepsy, but in secondary care and specialist centers, its prevalence exceeds 50%. [5] The prevalence rates for depression and anxiety disorders in patients with epilepsy (PWE) range from 18.2–28.4% and 15.3–26.0% respectively, according to a meta-analytic study conducted in 2017. [6]

Comorbid anxiety and depression disorders are linked to decreased quality of life, and higher healthcare costs, and may also have an impact on some medical outcomes, such as inadequate seizure control and more antiepileptic drug side effects. Understanding, identifying, and managing these comorbidities in PWE is so crucial.[7]

Epidemiological data on depression and anxiety among Egyptians with epilepsy are insufficient. Deter-mining the prevalence and associated factors of depression and anxiety among epileptic patients was the purpose of this study.

Methods

An institutional-based cross-sectional study, Data was collected over ten month periods (August 2022 - June 2023) from all epileptic patients attending the neurology outpatient clinic- Qena university hospital. Patients who meet the diagnosis of epilepsy according to the international league against epilepsy (ILAE) criteria,[8] and with age > 18 years with no upper limit were included in our study and evaluated for comorbid psychiatric diseases. Patients with cognitive disorders, psychotic symptoms or chronic comorbid diseases that might affect psychological assessment as stroke and severe organic brain dis-orders were excluded from our study. The sample size was calculated by using the proportion formula: N = (Zα/2)2 p (1-p)/ d2), with a 95% confidence interval, a margin of error = 10, and fr-om a previous study that assesses the prevalence of depression around 30% a minimum 100 num-ber of epileptic patients were required.

Demographic data as marital status, gender, residence, occupation, education, age, history of depression and anxiety and Arabic validated socio-economic status scale [9] were collected. Epilepsy data as seizure semiology, disease duration, etiology, history of status epilepticus, history of seizures in the last month preceding interview, anti-epileptic drugs used, and whether patients on mono or poly-therapy were collected by an semi structured interview then electroencephalogram and brain imaging were ordered for syndrome and etiological classification. Psychiatric comorbidities were screened by validated scales for the epilepsy:1-Validated Arabic translation of (NDDI-E) score is a brief, six-item questionnaire scored on a 4-point scale from 1 to 4, with a total score range (6 – 24), with a higher score signifying more depressive symptoms with a cut- off score 15 for depressive disorders. [10] 2- Validated Arabic translation of (GAD-7) is a questionnaire scored on a 4-point scale from 0 to 3, with total score range (0 - 21) and also a higher score signifying more anxiety symptoms with a cut-off score of >9 for anxiety disorders during 2 weeks preceding the assessment. [11] Diagnostic and Statistical Manual of Mental Disorders (DSM-5) classification used to categorize anxiety and depressive disorders by structured psychiatric interview.

SPSS software, version 21 was used to analyze all the data. Frequency and percentage and chi-square test were used for qualitative data. The mean, standard deviation and student t test were used for quantitative data. Multivariate logistic regression analysis was performed to identify factors associated with depression and anxiety in epilepsy. P-values less than 0.05 are considered significant.

Results

One hundred and six patients with epilepsy were enrolled in our study, with mean age 33.11 ± 1.53 years. The majority of participants 65/106 (61.3%) were males. All Socio-demographic characteristics are revealed in **Table 1**. The mean treatment duration with antiepileptic drugs was 15.52 ± 8.75 years. Clinical Characteristics of epilepsy

were determined in **Table 2**. Our results, regarding depression, revealed that 21 patients (19.8%) had major depressive disorder and 13 patients (12.8%) with minor depressive disorder, and 72 patients (67.9%) had no depressive disorders. Twenty-two patients (20.8%) with generalized anxiety disorder, 4/106 (3.8%) with panic disorder, 2/106 (1.9%) with agoraphobia, 3/106 (2.8%) with obsessive-compulsive disorder, 4/106 (3.8%) with social phobia, and 1/106 (0.9%) with specific phobia**.** Our results, reported that the prevalence of anxiety disorders in PWE was 32/106 (30.2%) and the prevalence of depression according to the NDDI-E was 33/106 (31.1%). Older age and female patients were more in depressed PWE and had statistically significant difference between depressed and non-depressed PWE (p-value = 0.03, p-value = 0.04 respectively). Multivariate logistic regression analysis of these variables revealed that older age was a predictor of depression with p value= 0.04 (OR: 1.2; CI: 1.1-1.3). ROC curve analysis revealed the best cut-off value of age for prediction of depression in PWE was 23 years (AUC: 0.648; 95% confidence interval 0.535–0.760; p < 0.015; 79 % sensitivity, 55 % specificity) **Figure 1**.

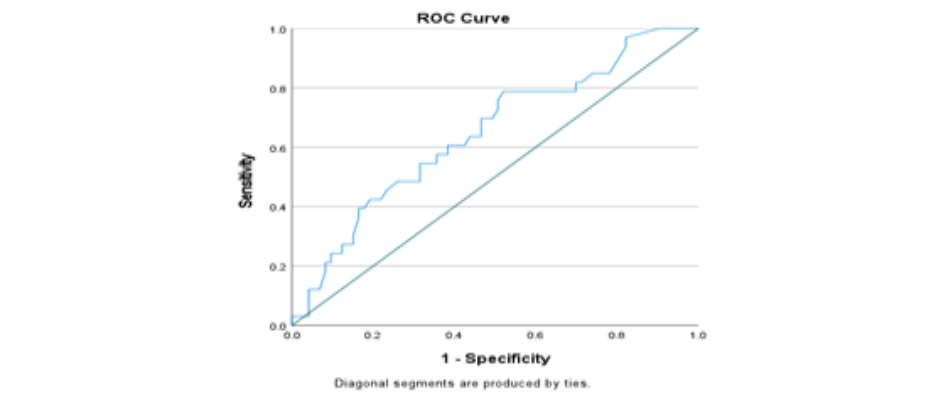

Figure 1: ROC curve analysis of age for prediction of depression in PWE

Table 1. Socio-demographic distributions of people with epilepsy

Variables	Categories	Frequency (n=106)	Patients with anxiety (n = 32)	P-value	Patients with depression (n = 33)	P-value
sex	Male Female	65 (61.3%) 41 (38.7%)	18 (56%) 14 (44%)	0.068	17 (51%) 16 (49%)	**0.044***
Residence	Urban Rural	57 (53.8%) 49 (46.2%)	17 (53%) 15 (47%)	0.548	14(42%) 19(58%)	0.482
Occupation	Employed Unemployed	45 (42.5%) 61 (57.5%)	11 (34%) 21 (66%)	0.323	22(67%) 11(33%)	0.249
Education	Literate Illiterate	74 (69.8%) 32 (30.2%)	19 (59%) 13 (41%)	0.096	13(39%) 20(61%)	0.156
Social status	Low Middle High	31 (29.2%) 66 (62.3%) 9 (8.5%)	8 (25%) 11 (34%) 13 (41%)	0.697	11(33%) 20 (61%) 2 (6%)	0.231
Marital status	Single Married Divorced	44 (41.5%) 51 (48.1%) 11 (10.4%)	16 (50%) 11 (34%) 5 (15%)	0.078	14 (42%) 15 (46%) 4 (12%)	0.456
handedness	Right Left	103 (97.2%) 3 (2.8%)	32 (100%) 0 (0%)	0.336	32(97%) 1(3%)	0.095
Consanguinity	Yes No	39 (36.8 %) 67 (63.2 %)	13(41%) 19(59%)	0.290	12 (36%) 21(64%)	0.348
Family history of epilepsy	Yes No	19 (17.9%) 87 (82.1 %)	5 (15%) 27(85%)	0.679	6 (18%) 27(82%)	0.446
Past history of anxiety	Yes No	6 (5.7 %) 100 (94.3%)	2 (6%) 30 (94%)	0.478	1 (%) 32(%)	0.082
Past history of depression	Yes No	21 (19.8 %) 85 (80.2 %)	4 (13%) 28(87%)	0.165	8(24%) 25(76%)	0.095

(*) statistically significant.

Table 2: Clinical features and related risk factors in people with epilepsy

variables	categories	Frequency (n=106)	Patients with anxiety (n = 32)	P-value	Patients with depression (n = 33)	P-value
Semiology of seizure	Absence Myoclonic Tonic- clonic Tonic Atonic Simple partial Complex partial Focal evolving Mixed Symptomatic	1 (0.9%) 5 (4.7%) 36 (33.9%) 4 (3.7%) 3 (2.8%) 6 (5.6%) 7 (6.6%) 9 (8.4%) 4 (3.7%) 31 (29.2%)	0 (0%) 1(3%) 11 (34%) 1 (3%) 1 (3%) 0 (0%) 5 (16%) 2 (6%) 1 (3%) 11 (34%)	0.115	0 (0%) 1 (3%) 11 (33%) 1 (3%) 0 (0%) 1 (3%) 5 (15%) 2 (6%) 1 (3%) 11 (33%)	0.395
Disease duration	1 < 10 years 2 = 10 -19 years 3 = 20 - 29 years 4 > 30 years	16 (15.1%) 41 (38.7%) 38 (35.8%) 11 (10.4%)	6 (19%) 6 (19%) 17 (53%) 3 (9%)	0.125	5 (15%) 10 (30%) 13 (39%) 5 (15%)	0.560
Etiology	unknown Cerebral Palsy Chemical toxins encephalitis Metabolic Post stroke Head trauma Brain tumor post operative	75 (70.8%) 6 (5.7%) 1 (0.9%) 2 (1.9%) 3 (2.8%) 9 (8.5%) 7 (6.6%) 1 (0.9%) 2 (1.9%)	21 (66%) 2 (6%) 0 (0%) 1 (3%) 1 (3%) 3 (9%) 3 (9%) 0 (3%) 1 (3%)	0.942	22 (68%) 2 (6%) 0 (0%) 1 (3%) 1 (3%) 4 (12%) 3 (9%) 0 (0%) 0 (0%)	0.804
(Nocturnal /Diurnal)	Diurnal&nocturnal Diurnal only Nocturnal only On awakening	69 (65.1%) 21 (19.8%) 13 (12.3%) 3 (2.8%)	20 (62%) 6 (19%) 5 (16%) 1 (3%)	0.921	23 (70%) 6 (18%) 3 (9%) 1 (3%)	0.887
seizures in last year	No Yes	83 (78.3%) 23 (21.7%)	22 (69%) 10 (31%)	0.096	23 (70%) 10 (30%)	0.118
Serial seizures	No Yes	99 (93.4%) 7 (6.6%)	30 (94%) 2 (6%)	0.645	33 (100%) 0 (0%)	0.067
Status epilepticus	No Yes	102(96.2%) 4 (3.8%)	31 (97%) 1 (3%)	0.649	32 (97%) 1 (3%)	0.632
Number medication	≥ 2 drugs Monotherapy No drug	30 (28.3%) 72 (67.9%) 4 (3.8%)	11 (34%) 20 (61%) 1 (3%)	0.666	12 (36%) 20 (61%) 1 (3%)	0.472
Anti-epileptic drug	Na valproate Carbamazepine OxeCarbamazepine Levitiracetam Lamotrigine	62(58.5%) 31 (29.2%) 21 (19.8%) 14 (13.2%) 5 (4.7%)	20 (62%) 9 (28%) 7 (22%) 5 (16%) 2 (6%)	0.370 0.531 0.458 0.421 0.478	20 (61%) 11 (33%) 8 (24%) 5 (15%) 1 (3%)	0.468 0.344 0.301 0.454 0.503
Abnormal EEG	No Yes	61(57.5%) 45 (42.5%)	16 (50%) 16 (50%)	0.206	20 (61%) 13 (39%)	0.416
Abnormal CT/MRI	No Yes	85 (80.2%) 21(19.8%)	27 (84%) 5 (16%)	0.335	24 (73%) 9 (27%)	0.151

Discussion

Our study determined the overall prevalence of depression and anxiety among PWE in a sample of the population from Egypt was 31.1 % and 30.2 % respectively, this percentage demonstrates the high magnitude of the

problem among epileptic patients, as the prevalence of these psychiatric comorbidities remains higher than the age-matched non-epileptic individuals (8%). [(2)] Therefore, attention should be paid to epileptic adults and the urgency for early identification of these psychiatric comorbidity and related risk factors and early management to eliminate these conditions. There are few studies in our region were published in this field, However, we revealed that our prevalence is higher than that estimated in the United Arab Emirates (26.9% and

25.8%), [5] and in France (25.5% and 22.1%). [13] But nearly similar to studies published in Brazil (24.4% and 39.4%), [14] in Oman (27% and 45%), [15] and lower than the study published in china (52.6% and 33.4%)[16] for depression and anxiety respectively.

The prevalence discrepancy might be a result of differences in the assessment parameters, as some studies use the Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A) but others used the Hamilton Rating Scale for Depression and anxiety [17] and other studies used (GAD-7) and (NDDI-E) scales like us. [5,13,16]Other possible reasons might be different cultural characteristics and socioeconomic status of the participants; also, study design could be another reason for this discrepancy as we found an institutional-based case-control study in Assiut, Egypt [18] and a community-based case-control study in Brazil [14] though, a community-based study in Canada with the prevalence of (17.4%, and 22.8%). [19]

Concerning the risk factors that influence depression and anxiety in PWE, Our sample determined that age and sex were risk factors for depression and we did not find any detectable risk factors for anxiety in PWE. A statistically significant difference in the age mean between depressed and non-depressed epileptic patients, older patients have been associated with more depressive symptoms and when we used roc curve analysis for confirming the cut-off value for the age, it was estimated at 23 years, Age is a considerable risk factor for depression in PWE as established by **Alsaadi** *2015* ,[5] **Bosak** *2015,* [20] and **Viguera** *2018,* [21] on the contrary in a single study **Wenyan** found that every 1-year increment of age, the odds of developing depression were decreased by 3.8%. [22] also, females were significantly associated with depression this finding is consistent with **Alsaadi** *2015* [5] *and* **Yildirim** *2018* [23] who revealed that females gender tend to be associated with depression while **Zhao Liu** when evaluated gender Differences in PWE in relation to anxiety and depression did not establish any difference between females and males although gender discrepancy has been stated in the general population for depressive and anxiety disorders but not in PWE. [24]

In our study, five antiepileptic drugs have been used by patients for treating epilepsy (Na valproate, Carbamazepine, Ox-Carbamazepine, Levitiracetam, and Lamotrigine). We couldn't find any significant correlation with psychiatric comorbiddities although polytherapy of anti-epileptic drugs and drug-resistant epilepsy was established by **Hamed** [18] and **Scott** [6] to be related to depression but we did not obtain any significant risk for both comorbidities. **Hamed** also explainned this relationnship by shared characteristics of antiepileptic medication side effects and symptoms of depression and anxiety, [18] **but Ho** [25] found drug-resistant epilepsy and clonazepam use were positively associated with risk of depression in PWE but not in Valproate, carbamazepine, and lamotrigine uses which may be explained by their mood-stabilizing effects therefor, mood stabilizing anti-epileptic could be considered when treating older or female epileptic.

Yang in a meta-analysis (2020) study risk factors of depression in PWE, and enrolled 51 cross-sectional studies, and also, estimated that older age (OR: 1.02, 95% CI: 1.00–1.04; $p = 0.019$), female gender (OR: 1.58, 95% CI: 1.30–1.93; $p < 0.001$) are statistically associated with depression. Also, **Yang** reported other risk factors for depression as being employed, poor antiepileptic drug adherence, poly-therapy, psychiatric stigma and long epilepsy duration. [26]

Our study has some limitations. Firstly, the sample size was small. Therefore, the patients might not represent the whole population of PWE, so a larger sample size will lead to more potent results. Secondly, patients were from tertiary hospitals; therefore patients may have a more severe form of epileptic seizures than those from the primary care centers, so further studies could overcome these drawbacks and could identify the relationship between depression and anxiety in one hand and specific types and syndromes of epilepsy.

Conclusion

The extent of depression and anxiety disorders was reasonably high among people with epilepsy. Early identification and management of depression and anxiety among people with epilepsy, and modulation of probable risk factors as possible might inflect the magnitude of the problem, and Screening for these comorbidities should be a practice in all neurology clinics when assessing PWE.

List of abbreviations

(DSM-5)	Diagnostic and Statistical Manual of Mental Disorders
(GAD-7)	Generalized AnxietyDisorder 7-Item scale
(NDDI-E)	Neurological Disorders Depr-ession Inventory for Epilepsy
(PWE)	Patients with epilepsy

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