www.jmscr.igmpublication.org
Impact Factor (SJIF): 6.379
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v6i9.36

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Research Article

Epilepsy correlates of depression and anxiety in patients with idiopathic epilepsy

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Abstract
Background and aim of the study: *Psychological disorders especially depression and anxiety occurs more commonly in epileptic patients than non-epileptics. We aim in this study to determine frequency and factors implicated in the development of depression and anxiety in patients with epilepsy.*
Patients and Methods: *A total of 100 consecutive patients with epilepsy attending outpatient clinic and epilepsy clinic at Sohag university hospital were included in this study.*
Results: *Depression was present in 71 patients (71%) and was significantly higher in females; younger age at onset of epilepsy; longer duration of epilepsy; patients on poly therapy; patients with uncontrolled seizures and patients with epileptic discharges on EEG. anxiety was present 70 patients (70%) and was significantly higher in females; younger age at onset of epilepsy; longer duration of epilepsy; patients with uncontrolled seizures and patients with epileptic discharges on EEG.*
Conclusion: *Screening for depression and anxiety in patients with epilepsy is mandatory especially in females; younger age at onset of epilepsy; longer duration of epilepsy; patients on polytherapy; patients with uncontrolled seizures and patients with epileptic discharges on EEG.*

Introduction

Psychological disorders especially depression and anxiety occurs more commonly in epileptic patients than non-epileptics.[1, 2] Despite this, anxiety and depressive disorders often remain unrecognized and untreated. This because most doctors tend to pay more attention for the patient's seizures and treatment. Also, few studies explained the possible mechanisms of depression and anxiety in epilepsy.[3] So, it is vitally important that doctor treating patients with epilepsy is able to recognize the symptoms of anxiety and depression.

The lifetime prevalence of depression in patients with epilepsy varies from 8 to 48% depending on the methodology of each study.[4,5] Depression lowers quality of life significantly and can directly increase seizure frequency through the mechanism of sleep deprivation and incompliance on antiepileptic medication. Also, some antiepileptic medications may worsen symptoms of depression. Failure to recognize depression or inadequate treatment can lead to suicide.[6]

Anxiety disorders may actually be more common and more disabling than depression in patients with epilepsy but they receive less attention than depressive disorders.[7]The prevalence of anxiety

disorders in patients with epilepsy is estimated to be twice than non-epileptics.[8] Anxiety can be seizure related or interictal. Fear is a common manifestation of partial seizures originating in the temporal lobe. Lack of proper diagnosis and treatment of anxiety disorders may lower the quality of life in patients with epilepsy.[7]

Aim of the study

To determine frequency and factors implicated in the development of depression and anxiety in patients with epilepsy.

Methods

The study was a cross-sectional study carried on 100 consecutive patients with epilepsy attending outpatient clinic and epilepsy clinic at Sohag university hospital in the period from September 2016 to December 2017. The study included patients who had a definite diagnosis of epilepsy for at least one year duration. Patients with secondary (symptomatic) epilepsy; mental retardation; learning disabilities; significant medical disorder; psychotic disorders; drug addiction; behavioral disorders or other evident abnormalities that could compromise cooperation and the ability to respond the questionnaires have been excluded. Also patients with Montreal cognitive assessment (MOCA) below 26 were excluded. We obtained a written informed consent from the participants after receiving a complete description of the study.

All subjects included in the study were subjected to the following: 1) complete physical and neurologic examination.2) electroencephalogram (EEG): All spontaneous EEGs were recorded in a resting awake condition with eyes closed. The EEG data were acquired by a computer-based system (Nihon Kohden Neurofax, SN:00429) from 16 electrode locations according to the 10/20 system) : Fp1, Fp2, F7, F3, F4, F8, T3, C3, C4, T4, T5, P3, P4, T6, O1, and O2 and interpretation done with bipolar montage.3) Brain imaging (CT brain or MRI brain) to exclude organic causes. 4) Routine laboratory investigations.5) Assessment of epilepsy was done by direct interview and questionnaire with the patient including the following information about: type of epilepsy according to the criteria of The International League Against Epilepsy (ILAE) 2010, frequency was divided to four grades (<1/year, ≥1/year, <1/month, ≥1/month, <1/week, ≥1/week)[9], medications, predisposing factors, family history of epilepsy, hospital admission , investigations, history of febrile convulsions.6) Assessment of depression by using the Arabic version of BECK DEPRESSION INVENTORY with 21-question multiple-choice self-report inventory. Score 0-10 for cases with no depression; 11-20 for mild depression; 21-30 for moderate depression and 31-63 for severe depression. 7) Assessment of anxiety by using the Arabic version of Taylor's Manifest Anxiety Scale with 50 true or false questions. Score from 0 to 16 indicate no anxiety, Score from 17 to 20 indicate mild anxiety, Score from 21 to 26 indicate moderate anxiety, Score from 27 to 29 indicate sever anxiety and Score from 30 to 50 indicate very sever anxiety.

Statistical Analysis

Data was analyzed using STATA intercooled version 12.1. Quantitative data was represented as mean, standard deviation, median and range. Data was analyzed using student t-test to compare means of two groups. When the data was not normally distributed Mann-Whitney test was used. Qualitative data was presented as number and percentage and compared using either Chi square test or fisher exact test. Graphs were produced by using Excel program. P value was considered significant if it was less than 0.05.

Results

Study population: The study was carried on 100 epileptic patients. The mean ± SD for patient's age was 24.7±8.20. Female patients were 59 represented (59.00%) while male patients were 41 represented (41.00%).

Epilepsy related data: Focal seizures occurred in 74 patients (74%), generalized occurred in 25 patients (25%) and unclassified seizures in one

patient (1%). The mean age of patient's onset of epilepsy was 16.26±8.88. The mean duration of epilepsy was 8.39±5.33 .According to the number of antiepileptic drugs used for epilepsy treatment, 3 patients (3%) use no antiepileptic drugs, 50 patients (50%) used monotherapy for treatment and 47 patients (47%) used polytherapy for treatment .The frequency of seizures in our patients was as the following: There were 19 patients (19%) had (< 1 seizure per year) , 17 patients (17 %) had (≥ 1 seizure per year ,< 1 seizure per month), 44 patients (44%) had (≥ 1 seizure per month, < 1seizure per week) and 20 patients (20%) had (≥ 1 seizure per week). According to previous history of febrile convulsions, 89 patients (89%) had no previous history of febrile convulsions and only 11 patients (11%) had previous history of febrile convulsions. According to family history of epilepsy, 82 patients (82%) had no family history of epilepsy while 18 patients (18%) had positive family history of epilepsy. Inter – ictal EEG findings in patients were as follow : Normal in 41 patients (41%) ,51patients (51%) had focal epileptic EEG including 27 patients (27 %) had left focal and 24 patients (24 %) had right focal while generalized epileptic EEG in 8 patients (8%). Table (1)

Table (1): Sociodemographic and epilepsy related data

Variables	Summary statistics
Age	
Mean ± SD	24.7±8.20
Median (range)	24.5 (12-50)
Gender	
Female	59 (59.00%)
Male	41 (41.00%)
Family history epilepsy	
No	82 (82.00%)
Yes	18 (18.00%)
Epilepsy type	
Focal	74 (74.00%)
Generalized	25 (25.00%)
Unclassified	1 (1.00%)
Age at onset of epilepsy	
Mean ± SD	16.26±8.89
Median (range)	15 (1-43)
Epilepsy duration	
Mean ± SD	8.39±5.33
Median (range)	8 (1-25)
Type of therapy	
No therapy	3 (3.00%)
Monotherapy	50 (50.00%)
Poly therapy	47 (47.00%)
Frequency of epilepsy	
< 1/year	19 (19.00%)
≥ 1/year, < 1/month	44 (44.00%)
≥ 1/month, < 1/week	20 (20.00%)
≥ 1/week	17 (17.00%)
History of febrile convulsions	
No	89 (89.00%)
Yes	11 (11.00%)
EEG finding	
Normal	41 (41.00%)
Epilepsy	59 (59.00%)

Depression related data: Depression was present in 71 patients (71%). Depression was severe in 19 patients (19%), moderate in 38 (38%) and mild in 14 patients (14%) as shown in figure (1). Depression was significantly higher in females; younger age at onset of epilepsy; longer duration of epilepsy; patients on polytherapy; patients with uncontrolled seizures and patients with epileptic discharges on EEG. Table (2)

Anxiety related data: anxiety was present 70 patients (70%); 5 patients (5%) had severe anxiety, 32 (32%) had moderate anxiety and 33 patients (33%) had mild anxiety as shown in figure (2). Anxiety was significantly higher in females; younger age at onset of epilepsy; longer duration of epilepsy; patients with uncontrolled seizures and patients with epileptic discharges on EEG. Table (2)

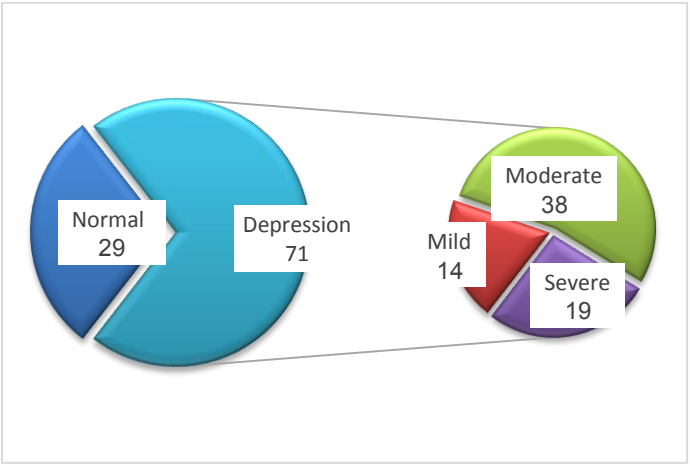

Figure (1): Prevalence of depression among studied populations

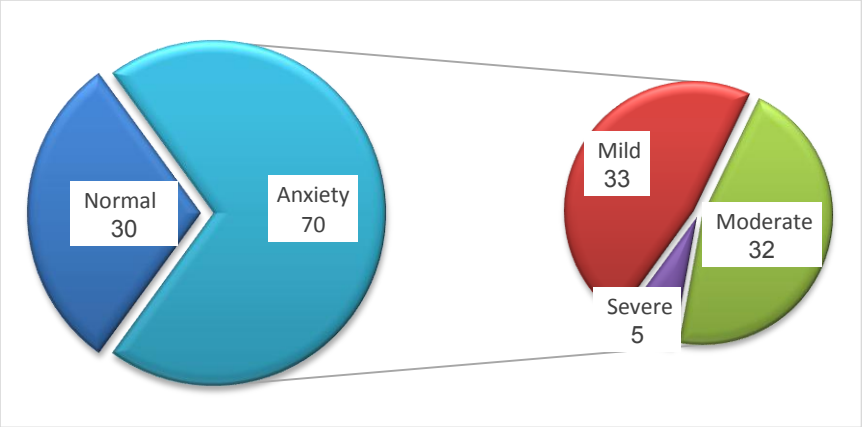

Figure (2): Prevalence of anxiety among studied populations

Table (2): Epilepsy characteristics in people with epilepsy suffering from depression and anxiety

Variables	No anxiety N=49	Anxiety N=47	P value	No depression N=51	Depression N=45	P value
Age						
Mean ± SD	25.83±7.47	24.21±8.51	0.25	26.03±7.37	24.15±8.51	0.19
Median (range)	25 (14-40)	23 (12-50)		25 (15-40)	24 (12-50)	
Gender						
Female	9 (30.00%)	50 (71.43%)	<0.000	8 (27.59%)	51 (71.83%)	<0.0001
Male	21 (70.00%)	20 (28.57%)	1	21 (72.41%)	20 (28.17%)	
Family history epilepsy						
No	24 (80.00%)	58 (82.86%)	0.73	23 (79.31%)	59 (83.10%)	0.66
Yes	6 (20.00%)	12 (17.14%)		6 (20.69%)	12 (16.90%)	
Epilepsy type						
Focal	18 (60.00%)	56 (80.00%)	0.06	18 (62.07%)	56 (78.87%)	0.10
Generalized	11 (36.7%)	14 (20.00%)		10 (34.48%)	15 (21.31%)	
Unclassified	1 (3.33%)	0		1 (3.45%)	0	
Age at onset of epilepsy						
Mean ± SD	21.37±8.42	14.07±8.20		21.55±8.41	14.09±8.19	
Median (range)	20.5 (9-35)	12.5 (1-43)	0.0001	21 (9-35)	12 (1-43)	0.0001
Epilepsy duration						
Mean ± SD	4.4±3.23	10.1±5.15	<0.000	4.44±3.30	10.00±5.17	<0.0001
Median (range)	4 (1-15)	9.5 (1-25)	1	4 (1-15)	9 (1-25)	
Type of therapy						
No therapy	1 (3.33%)	2 (2.86%)	0.3	1 (3.45%)	2 (2.82%)	0.01
Monotherapy	21 (70.00%)	29 (41.43%)		21 (72.41%)	29 (40.85%)	
Poly therapy	8 (26.67%)	39 (55.71%)		7 (24.14%)	40 (56.34%)	
Frequency of epilepsy						
< 1/year	11 (36.67%)	8 (11.43%)		10 (34.48%)	9 (12.68%)	
≥ 1/year, < 1/month	7 (23.33%)	37 (52.86%)	0.002	6 (20.69%)	38 (53.52%)	0.005
≥ 1/month, < 1/week	4 (13.33%)	16 (22.86%)		5 (17.24%)	15 (21.13%)	
≥ 1/week	8 (26.67%)	9 (12.86%)		8 (27.59%)	9 (12.68%)	
History of febrile convulsions						
No	28 (93.33%)	61 (87.14%)	0.37	27 (93.10%)	62 (87.32%)	0.40
Yes	2 (6.67%)	9 (12.86%)		2 (6.90%)	9 (12.68%)	
EEG finding						
Normal	19 (63.33%)	22 (31.43%)	0.003	19 (65.52%)	22 (30.99%)	0.001
Epilepsy	11 (36.67%)	48 (68.57%)		10 (34.48%)	49 (69.01%)	

Discussion

Our study found that patients with epilepsy have high frequency of depression (71%) and anxiety (70%). This was much higher than reported in previous studies.[3,10,11] This may be due to differences in methodology and questionnaires used in each study. Also, no accurate data about the prevalence of anxiety and depression in developing and middle east countries.

Depression and anxiety were higher in female patients with epilepsy than male patients. These results were in agreement with most studies.[3,4,6,10] This may be explained by more frequent incidence of mood disorders and anxiety disorders in females in general.

Our study found that depression and anxiety were more common in uncontrolled epilepsy as they were more patients with frequent seizures and patients on polytherapy. These results were similar to those reported in some studies.[6,12,13,14] Kindling phenomenon which occurs in epilepsy is associated with decrease in the activity of some neurotransmitters as serotonin, nor epinephrine dopamine and γ-Aminobutyric acid (GABA). The activity of these neurotransmitters also decreases in patients with anxiety and depression suggesting a common pathophysiologic mechanism. Also, higher stigmatization of epilepsy was present in patients with uncontrolled seizures which may be another participant in causing anxiety and depression.

In our study, anxiety and depression were more frequent in patients with younger age at onset of epilepsy and patients with longer epilepsy duration. These results were similar to those reported by Cusher et al., 2008 [15] while other studies[16-19] reported no significant difference regarding the age at onset of epilepsy or epilepsy duration. Our explanation is longer duration of epilepsy especially in young age was associated with changes in amygdala; hippocampus and neurotransmitters (as mentioned above). So, these pathophysiological changes need more time to develop explaining why anxiety and depression are more common with longer epilepsy duration.

Epilepsy type whether focal or generalized wasn't reported to be a risk factor for development of anxiety or depression in patients with epilepsy and this was in agreement with several studies.[15,16,18,19] However, some studies [20,21] found that patients with temporal lobe seizures, especially on left side, had higher level of anxiety while other studies [22, 23] found that left hemisphere lesions had higher reports of depression than those with right hemisphere lesions. In our opinion that all those results are inconclusive because most these studies depend on clinical seizure semiology only in localization of epileptic focus which is mostly inaccurate and may give false results. For example, it is difficult to differentiate frontal from temporal lobe seizures in some cases.

Conclusions and Recommendations

Our study found higher prevalence of anxiety and depression in patients with epilepsy than reported in most studies. Screening for depression and anxiety in patients with epilepsy is mandatory especially in females; younger age at onset of epilepsy; longer duration of epilepsy; patients on polytherapy; patients with uncontrolled seizures and patients with epileptic discharges on EEG.

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