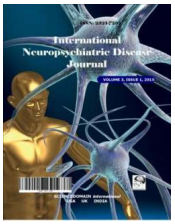

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Socio-demographic and Clinical Predictors of Co-morbid Psychiatric Disorders in Patients with Epilepsy

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Authors' contributions

This work was carried out in collaboration between all authors. All authors participated in and take responsibility for all aspects of the study. Author MAH read and approved the final manuscript.

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ABSTRACT

Background: Association between epilepsy and psychiatry has a long history that required a comprehensive care of patients with epilepsy. This would include special attention to the psychological and social consequences besides the control of seizures.
Aim: This study aimed at identifying the frequency of psychiatric disorders and its effects on the quality of life in patients with epilepsy as well as studying different variables crucial in the development of concomitant psychopathology.
Materials and Methods: This cross-sectional study was carried on 140 patients with epilepsy, 100 healthy controls. All subjects were subjected to assessment using SCID1, SCID11, Quality Of Life in Epilepsy, EEG monitoring.
Results: 72 patients (51.4%) had psychiatric illness, significantly lower quality of life (t= 2.087, p 0.041). predictors for psychiatric disturbances were young age of epilepsy onset (Beta=.741 for depression, .368 for anxiety disorders), long duration of epilepsy (Beta=.263, Beta=.400 for anxiety,

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personality disorders), frequency, severity of epilepsy (Beta=1.076, .410, .975 for depressive, anxiety, personality disorders respectively). Temporal lobe epilepsy predicted personality disorders (Beta= -.471) while extra temporal epilepsy was associated with depression and anxiety disorders (Beta= .827, Beta=.900 respectively).

Conclusions: This work raises the importance of proper history taking and mental state examination along with identification of high-risk groups who are more prone to psychiatric comorbidity.

Keywords: Epilepsy; depression; personality disorder; quality of life; comorbidity.

1. INTRODUCTION

Epilepsy is one of the commonest neurological diseases. The prevalence of epilepsy all over the world is estimated to vary from 0.5 to 1.5% among different populations [1]. It is characterized by a tendency to recurrent epileptic seizures. Epileptic seizures are the clinical correlates of paroxysmal events generated by an enduring condition of hyper-excitability and hyper-synchrony of brain electrical activity. However, the clinical spectrum of epilepsy encompasses many neurobehavioral co morbidities [2]. Epilepsy and neurobehavioral conditions might share some physio-pathologic, genetic, and environmental mechanisms [3].

The close association between epilepsy and psychiatry has a long history. The relationship between them and reciprocal influence had been identified in several studies [4]. However, the traditional approach to epilepsy care was focusing on the seizures and their treatment while ignoring the presence of comorbid psychiatric symptoms and disorders [5]. Recognition of their negative impact on the quality of life of epileptic patients recently has increased the need for their early identification with a careful psychiatric history or, as well as detection for the presence of psychiatric symptoms with objective scales [6].

Furthermore, careful detection of risk factors for the development of psychiatric symptoms is very important in the early detection, and proper management and choice of antiepileptic drugs as some are known to have positive or negative psychotropic effects [7].

The underlying pathophysiologic mechanisms of interictal, ictal and postictal psychiatric disorders are different. The interictal might represent worries about the occurrence of seizures and their possible consequences while the postictal are directly related to epileptic discharges [8]

In this study, we were interested in the frequency of different psychiatric disorders among patients with epilepsy and their effect on the quality of life. We also examined epilepsy patients with comorbid psychiatric diseases to identify different variables crucial in the development of concomitant psychopathology.

2. SUBJECTS AND METHODS

The present Study focused on inter-ictal psychiatric disorders. Enrolled in this cross-sectional study, a convenience sample, comprising 140 epileptic patients, attended neurology outpatient clinic in Mansoura University Hospitals. The control group comprised 100 age and sex matched healthy subjects were selected from hospital employees in Mansoura University Hospitals, with no personal or family history of epilepsy, who agreed to join the study. Written informed consent was obtained from them to join the study after ethical approval and in accordance with the Helsinki Declaration of 1975, as revised in 2000.

2.1 Inclusion Criteria

Diagnosis and categorization of epilepsy were done according to 2010 International League Against Epilepsy (ILAE) Commission revision, confirmed by inter-ictal EEG. Controlled or uncontrolled patients were also identified.

2.2 Exclusion Criteria

- History of clinical seizure for at least one week (*ie. interictally*) before the inclusion in the study, as anxiety and depression present in most cases of ictal and postictal disappeared within 2–3 days [9].
- History of status epilepticus for at least 6 months before the onset of the study.
- Revealed CNS side effects from their antiepileptic medication at the time of

examination that might affect their psychological evaluation.
- Past history of any psychiatric illness.
- History of substance or alcohol abuse.
- History of head trauma, other chronic or systemic diseases.
- Mini-Mental State Examination (MMSE) patients with score <24.

2.3 Research Design

- Interictal electroencephalogram (EEG) was done for all patients to confirm the diagnosis as well as categorization of epilepsy type if possible.
- All subjects were subjected to initial assessment in comparison to control for detection of the presence of associated psychiatric disorders using:

  - Structured Clinical Interview for DSM-IV (SCIDI) [10], divided into six modules, for the diagnoses of psychiatric disorders at the Axis I Diagnostic and Statistical Manual, fourth edition (DSM-IV) [11].
  - Structured Clinical Interview for DSM-III-R personality disorders (SCID-II) for assessment of the Axis II personality disorders [12].
  - The Quality of Life in Epilepsy 31(QOLIE-31) [13] was applied only to the patient group. It consists of seven dimensions: seizure worry, the overall quality of life, emotional well-being, energy/fatigue, medication effects, social function, cognitive function and overall score. The scores vary from 1 to 100, with a higher score indicating a better quality of life. The mean application time for the test was about 10 minutes.

After the initial assessment, patients were classified into two groups; those without (75 patients) psychiatric disorder and with psychiatric (65 patients) disorder in addition. Both groups were compared for the social and demographic variables. Predictors of psychiatric comorbidity were investigated.

2.4 Statistical Analysis

The data were coded and entered into a computer using Statistical Package for Social Sciences (SPSS) version 15.0 (Chicago, IL, USA). Results for normally distributed data were presented as means with standard deviation (SD) while number and percentage for non-normally distributions. Normally distributed continuous variables were compared using t-test. The categorical variables were compared using chi-square and Fisher's exact test. All statistical tests were two-sided, with a p-value of <0.05 taken to indicate statistical significance. Linear stepwise regression analysis test was used for prediction.

3. RESULTS

As shown in Table 1, there were no statistically significant differences between the patient (140 patients) and the control groups (100 persons) in reference to age, gender, educational level, employment status, and marital status. The clinical characteristics of the epileptic patients demonstrated the mean duration of illness of (14.2±6.4) years, 61.4% of the patients have active epilepsy, and 69.3% are maintained on two antiepileptic drugs, while 21.4% on more than 2 drugs.

Active epilepsy implies a seizure in the preceding year. Seizure remission (remittent epilepsy) implies no seizures in the preceding year.

Depression: major depression, dysthymia, and depression not-otherwise specified (NOS); *anxiety disorders:* Generalized anxiety disorder, obsessive compulsive disorder (OCD) and Panic disorder; *mixed anxiety depression; psychosis;* and *personality disorders:* cluster A, B, and C - namely avoidant, dependent, and obsessive- were prevalently higher in epileptic patient than in control group p= .002, .001, .001, .005 respectively (Table 2).

In persons with epilepsy, psychiatric co-morbidity was significantly higher in those with high age, males, married, employed, controlled seizures, abnormal EEG, and those without history of hospital admission (p= .028, .015, .035, .004, .001, .001, .004 respectively). In contrary it was significantly lower in those with divorce, active uncontrolled seizures, history of hospital admission, abnormal temporal EEG activity (p= .005, .031, .020, .024 respectively, while it was not significantly affected by duration of illness, female gender, level of education, unmarried, non-employed, number of antiepileptic drugs and those with normal EEG (p= .659, .239, .414, .134, .138, .782, .061 respectively) (Table 3).

In (Table 4), Significant lower scores at all parameters as well as the overall quality of life

were detected among epileptic patients with psychiatric disturbances (t= 2.087; p= .041).

Investigating the predictors of psychiatric disorders in epileptics showed positive associations between all comorbid psychiatric disorders and seizure frequency: severity (Beta= 1.076, Beta= .410, Beta= .975), temporal lobe epilepsy (Beta= .827, Beta= .900, Beta= -.471 respectively). Significant associations were found between the late age of onset and depression (Beta=.741), early age in anxiety (beta= -.368). Personality disorders (cluster C) was significantly correlated with duration of illness (Beta= .400), quality of life (Beta= .278) (Table 5).

Table 1. Sociodemographic and clinical characteristics in patients and control groups

	Patients (140) No (%)	Control (100) No (%)	T	P
Age in years	28.7±8.6	29.3±7.9	-.523	.602
Sex				
Male	72 (51.4%)	52 (52%)	3.226	.072
Female	68 (48.6%)	48 (48%)	3.448	.063
Education				
<12 years	96 (68.6%)	71 (71%)	3.743	.053
>12 years	44(31.4%)	29 (29%)	3.082	.079
Employment				
Non-employed	77 (55%)	56 (56%)	3.316	.069
Employed	63 (45%)	44 (44%)	3.374	.066
Marital status				
Single	64 (45.7%)	44 (44%)	3.704	.054
Married	44 (31.4%)	30 (30%)	2.649	.104
Divorced	32 (32.9%)	26 (26%)	.621	.431
Duration of illness in years	14.2±6.4			
Seizure activity				
Remittent	54 (38.6%)			
Active	86 (61.4%)			
Medication				
Single drug	13 (9.3%)			
2 drugs	97 (69.3%)			
>2 drugs	30 (21.4%)			

Table 2. Prevalence of psychiatric disorders

	Patients (n=140) No (%)	Control (n=100) No (%)	P
Depressive illness (total)	27 (19.3%)	2 (2%)	
Major depressive disorder	5	1	**.002**
Dysthymia	9	1	
Depression NOS	13	0	
Anxiety disorders (total)	24 (17.1%)	4 (4%)	
Generalized anxiety disorder	5	2	**.001**
Obsessive Compulsive	12	1	
Panic disorder	7	1	
Mixed anxiety and depression	18 (12.9%)	3 (3%)	**.001**
Psychosis	2 (1.4%)	0	
Personality disorders			
Cluster A (paranoid, schizoid, schizotypal)	1	0	
Cluster B (borderline, antisocial, histrionic, narcissistic)	0	1	**.005**
Cluster C (dependent, avoidant, obsessive, passive aggressive)	18 (12.9%)	2 (2%)	
Total	72 (51.4%)	12 (12%)	**P= .001****

Table 3. Relationship between psychiatric disturbances and clinical and demographic variables

	No psychiatric disorder (n=75)	Positive psychiatric disorders (n=65)	t/ x^2	Significance
Age	29.4±9.3	27.5±8.2	2.246	.028*
Duration of illness in years	13.8±6.8	14±7.4	-.444	.659
Sex				
Male	44 (58.7%)	24 (36.9%)	5.882	.015*
Female	31 (41.3%)	41 (63.1%)	1.389	.239
Education				
<12 y	52 (69.3%)	44 (67.7%)	.667	.414
>12 y	23(30.7%)	21 (32.3%)	.091	.763
Marital status				
Single	38 (50.7%)	26 (40%)	2.250	.134
Married	29 (38.7%)	15 (23%)	4.455	.035*
Divorced	8 (11.6%)	24 (37%)	8.000	.005**
Employment				
Non-employed	32 (42.7%)	45 (69.2%)	2.195	.138
Employed	43 (57.3%)	20 (30.8%)	8.397	.004**
Medications (antiepileptics)				
1 drug	7 (9.3%)	6 (9.2%)	.077	.782
2 drugs	53 (70.7%)	44 (67.7%)	.835	.361
>2 drugs	15 (21%)	15 (23.1%)		
Seizure activity				
Remittent	42 (56%)	12 (18.5%)	16.667	.001**
Active	33 (44%)	53 (81.5%)	4.651	.031*
Past history of admission				
Yes	18 (24%)	35 (53.8%)	5.261	.020*
No	57 (76%)	30 (46.2%)	8.379	.004**
EEG				
Normal	16 (21.3%)	7 (10.8%)	3.522	.061
Temporal	29 (38.7%)	49 (75.4%)	5.128	.024*
Extratemporal	30 (41%)	9 (13.8%)	11.308	.001**

**Significant p<.05 **highly significant p<.01*

Table 4. Quality of life in epileptic patients with and without psychiatric disturbances

	No psychiatric disturbances	Positive psychiatric disorders	T	P
Seizure worry	40.8±6.9	38.7±3.3	2.101	.040*
Emotional wellbeing	56.6±8.2	41.3±6.1	11.811	.001**
Energy/fatigue	41.4±6.9	39.3±3.8	2.246	.028*
Cognitive functioning	40.9±5.8	39.4±5	2.166	.034*
Medical effects	54.2±8.7	49.7±10	2.522	.014*
Social functioning	49.7±2.6	40.7±6.2	5.159	.001**
Overall quality of life	41.8±5.5	39.6±6.4	2.087	.041*

**Significant p<.05 **highly significant p<.01*

4. DISCUSSION

In the present study, a high prevalence of psychiatric disorders was detected among patients with epilepsy. The main psychiatric diagnoses noted were depressive disorders, anxiety disorders, and personality disorders. Our results agree with the literature as most reports show that depressive disorders are the most frequent psychiatric comorbidity in patients with epilepsy [6,14,15] followed by anxiety disorders [16,17]. This may be attributed to unpredictability of seizure that result in helplessness and excessive fear of future seizure. In consistency with most of the previous studies by [18-21]. High frequency of the cluster C personality disorders; avoidant, dependent, and obsessive was found in this study. This

corresponds with the clinical impression of (Swinkels et al. [21]), that epileptic patients are frequently seen as anxious, unstable, and introvert people, who avoid personal contact because of uncertainty.

An association was present between depression and anxiety disorders (12.9%). Studies with adults and children suffering from epilepsy have shown a high prevalence of this comorbidity in association with epilepsy, sometimes up to 70% [17,22]. Interestingly, the association of personality disorder with anxiety and depression was not significant. This result agreed with the results of [23,24], who suggests that the elevated prevalence for personality disorder in epileptic patients cannot be attributed to the high prevalence of anxiety and mood disorders which usually found in epilepsy.

Regarding the demographic differences, epilepsy group with comorbid psychiatric disturbances consisted of more single persons and persons with a lower education and a higher degree of unemployment; factors which are inversely related to the risks of psychiatric disorders. Being more single may be due to hypo-sexuality and decreased libido that are common in epilepsy together with social isolation and dependence that limit marriage opportunity. However, the associated neurological and cognitive impairment can lead to lower educational level and subsequent unemployment specifically with recurrent or poorly controlled seizure [15,25].

There was significant association between family history of the psychiatric disorders and the development of depression, which was supported by the study of Tedrus et al. [26], while was not confirmed in comorbid anxiety or personality disorders. This may be interpreted by the self-underreporting of family history due to the usual fear of stigma in our culture. Furthermore, the comorbidity with psychiatric disorders may be more complex and multifaceted than suggested by genetic factor alone.

Psychiatric comorbidity showed a significant effect on the QoL, similar to the results of previous studies [27,28]. Also supported by a study made in Iran, the Gulf, near East [29] which considered the presence of psychiatric co-morbidity as a strong independent predictor of low scores in the QOLIE-31. However, in some studies, the presence of psychiatric disorders especially depression plays an important role in the patient's judgment about his/her QoL [30]. Another important factor linked to both depression and anxiety is the perceived stigma [31]. This is critical because high rates perceived stigma itself are present in about half of patients with epilepsy [32].

Table 5. Predictors of psychiatric disorders

	Depression	**Anxiety**	**Personality**
Age	R square=.998 Beta=.741 p=.007	R square=.979 Beta=-.368 p=.001	R square=.997
Sex		Beta=.263 p=.006	
Duration			Beta=.400 p=.010
Family history	Beta=.583 p=.007		
Marital status			
Education			
Frequency	Beta=1.076 p=.006	Beta=.410 p=.011	Beta=.975 p=.034
Medications			
Employment			
Type of epilepsy	Beta=.827 p=.014	Beta=.900 p=.038	Beta=-.453 p=.030
Past history of admission			
Quality of life			Beta=.278 p=.041

Predictors: Depression, Anxiety, Personality

Similar to previous studies [21,33], the prevalence of anxiety disorders were significantly higher among patients with early onset epilepsy. As young age of epilepsy onset is usually associated with poor seizure control and an underlying brain lesion as well as mixed electroencephalograph patterns that all predict future psychiatric morbidity and impaired social functioning together with fearfulness of future seizure and unpredictability.

A positive association between the long duration of epilepsy and the PD was detected which support the result of a previous work about the influence of epilepsy upon the development of maladaptive personality traits in epileptic patients [34].

As was presented in a previous study [35], a positive relationship exists between the presence of psychiatric disturbances and the severity of epilepsy as indicated by high frequency of seizure. Patients with severe epilepsy often use more anti-epileptic medication. It is likely that in these patients the need for control is usually high (because seizures mean a loss of control). Therefore, they are probably more prone to develop social and psychological consequences for everyday life, low self-esteem and interpersonal relationships problems, factors that increase the liability of psychiatric comorbidity [21].

Apart from personality disorders, patients with partial epilepsy were significantly associated with depression and anxiety more than those with generalized epilepsy which agree with many studies [36-38]. Another evidence was that depression, anxiety, and partial epilepsy may share some biological and structural mechanisms related to limbic system dysfunctions [39,40].

Finally, epilepsy is not only a disease entity, but commonly has psychiatric co-morbidity. Psychiatric disorders are usually unrecognized and untreated in large number of patients with epilepsy so the management remains incomplete leading to poor quality of life and risk of adverse consequences like noncompliance to therapy, suicide, and many psychosocial troubles. The importance of proper history taking and mental state examination along with identification of high-risk group who are more prone to psychiatric comorbidity means more accurate evaluation and repeated follow up.

5. LIMITATIONS AND FUTURE DIRECTIONS

The focus of this study was mainly on outpatients sample (who are more or less have controlled seizures). Further studies include in addition admitted epileptic patients will provide more chance for comparative analysis and understanding. The study was cross-sectional, and therefore, couldn't show the causal relationships. A longitudinal study would be better to confirm the causal relationship among variables. Considering these limitations, the findings may be biased and may be difficult to generalize in other patient populations except after more in-depth studies considering these preliminary results. Designing simple, short, screening tool to address this problem is very important. Nowadays, short structured diagnostic interview such as The Mini-International Neuropsychiatric Interview (M.I.N.I.) could be suggested for early detection of these cases [41].

6. CONCLUSION

Identification of high-risk epileptic patients with psychiatric comorbidity is very important.

Epileptic patients with comorbid psychiatric disorders have poor quality of life.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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