

## Comorbidity of Psychiatric Disorders in Epileptic Patients A descriptive Study

Saadoun Dawood Ahmed Al-Jiboori

Department of Medicine, College of Medicine, Kirkuk University

### Abstract:

**Background:** Epilepsy is a chronic disorder characterized by seizures, or paroxysmal brain dysfunction due to excessive neuronal discharge. Psychiatric and cognitive disturbances are relatively common in epilepsy, especially in refractory epilepsy.

**Aim of study:** The aim of the study is to detect the psychiatric disorders and their frequency in epileptic patients.

**Patients and Methods:** This descriptive study consisted of 104 patients with idiopathic epilepsy; 60 males and 44 female, aged between 17-68 years, who were attending either private clinics or the Psychiatric Unit at Azadi Teaching Hospital, Kirkuk, between December 2012 and January 2014. Diagnoses of comorbid psychiatric disorders were done according to Diagnostic and Statistical Manual of Mental Disorders.

**Results:** The most frequent psychiatric disorders were anxiety disorders (59.64%) followed by sexual dysfunction in males (50%).

**Conclusion:** This study reveals that those patients with epilepsy are at high risk of comorbidity of psychiatric disorders.

**Key words:** Comorbidity, Psychiatric disorders, Epilepsy.

### Introduction:

Comorbidity is a condition in clinical practice where several diseases coexist in the same patient at the same time<sup>(1)</sup>.

Epilepsy is a chronic disorder characterized by seizures or paroxysmal brain dysfunction due to excessive neuronal discharge. Psychiatric and cognitive disturbances are relatively common in epilepsy, especially in refractory epilepsy<sup>(1,2,3)</sup>. Epileptic disorders were initially thought to be psychiatric ailments where the body of the person was possessed by demons signifying their total control of human body and their psyche by causing involuntary convulsive events<sup>(4)</sup>. A modern view of epilepsy and mental illness evolved, it states that people with epilepsy are normal mentally, but it is the brain damage and the site that lesion that leads to an association between epilepsy and mental illness<sup>(5)</sup>.

Patients with epilepsy have a high prevalence of psychiatric comorbid disorders. Many of these comorbidities have a significant impact on the medical management and quality of life of these patients<sup>(2)</sup>. The most common psychiatric conditions in epilepsy in adults were depression, anxiety, and psychoses<sup>(6-8)</sup>.

Schmitz et al. found that multiple interacting biologic and psychosocial factors determine the risk for development of either schizophreniform psychoses or major depression in patients with epilepsy and concluded that behavioral disorders in epilepsy had multiple risk factors and multifactorial etiology<sup>(9)</sup>.

One of the variables linking depression and epilepsy is a family history of depression. A greater frequency of depression has been found in patients

with seizures originating in limbic structures; also, a frontal lobe dysfunction has been associated with depression. The quality of life is often suboptimal for patients with epilepsy, and this may adversely affect mood<sup>(10-14)</sup>. Increased financial stress, life stressors, and poor adjustment to seizures are predictive of increased depression<sup>(15)</sup>. Depression in epilepsy may also result from iatrogenic causes (pharmacologic and surgical)<sup>(16)</sup>.

Patients with epilepsy may have abnormal personalities. This may be attributed to many biological variables, for example, head injury following recurrent seizures, or the prescription of long-term anticonvulsant drugs, which may lead to behavioral change. In addition, it may relate to psychosocial variables, such as stigmatization and a low expectancy of achievement by the family or the teachers. Description of traits specific to the 'epileptic personality' include the adjectives 'pedantic', 'circumstantial', 'adhesive', or 'viscous'<sup>(17)</sup>.

In a systemic review, Clancy et al. found that up to (6%) of individuals with epilepsy have a comorbid psychotic illness and those patients have an almost eight fold increased risk of psychosis. The prevalence rate of psychosis is higher in temporal lobe epilepsy (7%)<sup>(18)</sup>.

Psychiatric and behavioral changes are common among individuals with epilepsy. The primary clinical problem in this area is the lack of early recognition and diagnosis. In many cases, patients simply do not spontaneously report the problems. In other cases, the clinician and nurse fail to inquire about the patient's mental health<sup>(19)</sup>. Chronic psychiatric symptoms are sometimes even misinterpreted as "a normal reaction" to

having epilepsy<sup>(20)</sup>. Certain psychiatric patients, especially the elderly, will often deny feelings of depression or sadness when questioned about their mental state<sup>(19)</sup>. Similarly many physicians are too quick to deny that antiepileptics may contribute to behavioral problems especially to the subtler types of cognitive or school performance problems<sup>(19)</sup>. The aim of this study is to detect the psychiatric disorders and their frequency in epileptic patients.

### **Methods:**

This descriptive study consisted of (104) patients with idiopathic epilepsy; (60) males and (44) females, aged between (17-68) years, who were attending either private clinics or the psychiatric unit at Azadi Teaching Hospital, Kirkuk, between December 2012 and January 2014. Cases satisfying the following criteria comprised the sample of the study. The criteria were: no evidence of pervasive developmental disorders, Alzheimer's dementia or mental subnormality, without any other somatic or neurological comorbidities. Clinical diagnosis of idiopathic epilepsy corroborated by abnormal Electroencephalography (EEG), no history of psychiatric disorders preceding the onset of epilepsy, the duration of epilepsy for more than 12 months and patients had to be seizure-free for the last 72 hours (to exclude ictal and post ictal symptoms) before entering the study. All patients were examined neurologically and psychiatrically, by the author and a specifically designed data sheet was developed. Data sheet included information about sex, age, marital status, education level, and mental state examination. Diagnosis of any comorbid psychiatric disorders was done

according to the Diagnostic and Statistical Manual of mental disorders, 4th Text Revised (DSMIV-TR) <sup>(21)</sup>. All Patients were interviewed to acquire information to fill the data sheet after they gave verbal consent to participate in this study. Descriptive statistical analysis was done, including, mean  $\pm$  standard deviation (SD), frequency and percentage using the SPSS software package version 16.

### **Results:**

A total of (104) patients were reviewed of them 64(61.5%) were male patients and 40(38.5%) were females. The mean age of the patients was (38.25) years (standard deviation; SD=13.17). The sociodemographic characteristics of the patients are shown in (Table 1). The

majority of the patients were married (71.2%). The majority of our patients were graduates of intermediate and secondary schools (62.5%).

Table 2 shows the frequency of psychiatric disorders. The anxiety disorders were the most frequent (59.64%), followed by sexual dysfunction which was identified in half of the males and 30.8% of the total sample. Other psychiatric disorders were, in descending order: depression (11.5%), personality disorders (5.8%) and psychosis (2.8%). The drugs that were prescribed for the patients are shown in (Table 3). Carbamazepine was the most commonly used medication followed by Valproic acid and both of them in combination, respectively.

**Table (1):** Sociodemographic characteristics of study patients.

Variables	No.	%
<b>Sex</b>		
Male	64	61.5
Female	40	38.5
<b>Marital state</b>		
Single	30	28.8
Married	74	71.2
<b>Age (years)</b>		
17-29	32	30.8
30-42	36	34.6
43-55	22	21.1
56-68	14	13.5
<b>Education level</b>		
Illiterate and primary schools	19	18.3
Intermediate and secondary schools	65	62.5
Institutions and Universities	20	19.2
<b>Employment</b>		
Students	14	13.5
Employed	39	37.5
Unemployed	51	49

**Table (2):** Frequency of psychiatric disorders.

Psychiatric Disorders	Frequency	%
Anxiety disorders	62	59.64
Sexual dysfunctions: Erectile dysfunction; Hyposexuality and Orgasmic dysfunction	32 (male patients)	(50%) of male (30.8% of the total)
Depression	12	11.5
Personality disorders: Dependent (3); Avoidant (2); Obsessional (1).	6	5.8
Psychoses	3	2.8

**Table (3):** Antiepileptic medications which were consumed by patients.

	Antiepileptic medications
1.	Carbamazepine only
2.	Valproac acid only
3.	Carbamazepine with valproac acid
4.	Carbazepine , valproac acid and clonazepam
5.	Clonazepam only
6.	Lamatrogen only

## **Discussion:**

The most frequent psychiatric disorders were anxiety disorders (59.64%). Symptoms of anxiety may result from or exacerbated by psychological, neurobiological factors, epileptic related factors, age of the patients and the medication related factors. Psychological factors include responses to the unpredictability of seizures, restrictions of normal activities, fear of death and feeling of poor control over seizures<sup>(22)</sup>. This results in lower self-esteem, stigmatization, and social rejection<sup>(5, 23, 24)</sup>. Neurobiological factors result from epileptic activity in certain areas of the brain which directly cause paroxysmal anxiety, usually in the form of panic<sup>(25)</sup>. The amygdala seems to be a particularly important structure for the production of anxiety symptoms and epileptic discharges in temporal lobe epilepsy<sup>(26)</sup>. Neurotransmitter systems are also suggested to be related with anxiety

disorders and epilepsy. The role of GABA receptors and neurotransmitters including serotonin, dopamine and noradrenaline in both epilepsy and anxiety disorders indicate another pathophysiological similarity between the two disorders<sup>(27)</sup>.

Epilepsy related factors, higher seizures frequency has been found to be associated with anxiety disorders in some adult studies<sup>(28)</sup>.

Age as a factor, the age of the patient and the duration of the epilepsy were examined as associated factors for anxiety disorders in epilepsy. In adult patients, first onset epilepsy in late life is shown to be linked with higher levels of anxiety<sup>(29)</sup>.

The medication related factor, most of the previous studies have demonstrated that AntiEpileptic Drug (AED) polytherapy is associated with increased risk of anxiety disorders<sup>(30)</sup>. This increased risk can occur as a side

effect of the AEDs or as a function of complications related to AEDs withdrawal<sup>(31)</sup>. In addition, the situation in Iraq in the last decades, in which the Iraqi patients were exposed to many daily types of trauma (explosion, homicide, kidnapping, migration and displacement, and an explosive laden cars)<sup>(32)</sup>.

Sexual dysfunctions were seen in half of the epileptic male patients. The result is similar to other studies<sup>(33, 34)</sup>. There are several potential causes of sexual dysfunction, including; neurological, endocrine, psychiatric, psychological disorders iatrogenic (due to antiepileptic medications as shown in (Table 3), and cognitive effects<sup>(35)</sup>.

Depressive disorders were identified in about one tenth of the patients (11.5%), this prevalence is less than frequency that was seen in another study<sup>(36)</sup>. Multiple factors are implicated in the development of depression in epilepsy including clinical (seizure frequency, seizure type or foci, epilepsy duration, age at onset, antiepileptic drugs) and psychosocial ones (life stressors, employment, marital status, quality of life)<sup>(2)</sup>.

The explanation for this result, first, in our sample, there was no family history of psychiatric illness, particularly depression, and, the second, might be due to the medications which were used (Table 3) that are acting as an anti-depressive.

Personality disorders were identified in 5.8% of the patients, this prevalence is less than the frequency in another study<sup>(37)</sup>. The difference might be due to the clinical characteristic of the cases in each study. In the earlier study there was higher percentage of personality disorders where many of the patients had refractory epilepsy. Other causes

which might increase the risk of personality disorders among epileptic patients includes seizure frequency (number of seizure episodes per month), duration of illness, age, age at onset, and site of epileptic discharge<sup>(36)</sup>. Psychoses disorders were observed with similar frequency (2.8%) to another study<sup>(38)</sup>. A history of febrile seizures progressing to epilepsy has been associated with a 3-fold increased risk of developing schizophrenia<sup>(39)</sup>. An association has been drawn between psychosis and Temporal Lobe Epilepsy (TLE)<sup>(40)</sup>, and in particular, left TLE, but this remains uncertain and controversial. And psychosis has been reported in association with generalized epilepsy as well as other focal epilepsies, most notably frontal lobe epilepsy<sup>(41)</sup>.

### **Conclusions:**

The present study shows that patients with epilepsy are at higher risk of comorbidity of psychiatric disorders. Management of epileptic patients must include a team of psychiatrists in addition to neurophysiologist and neurologists to ensure optimal care for the patients.

### **References:**

- [1]. Feinstein AR. The pre-therapeutic classification of comorbidity in chronic disease. *J Chronic Dis* 1973; 23:455-469.
- [2]. Titlic M, Basic S, Hajnsek S, Lusic I. Comorbidity psychiatric disorders in epilepsy: a review of literature. *Bratisl Lek Listy*. 2009; 110(2):105-109.
- [3]. Price BH, Adams RD, Coyle JT. Neurology and psychiatry: closing the great divide. *Neurology*. Jan 11 2000; 54(1) 8-14 [Medline].
- [4]. D Hill. Historical Review. In: Reynolds and M Trimble, editors, *Churchill and Livingstone* 1981, Edinburgh 1-10

- [5]. P Fenwick. 1981. EEG Studies. In E Reynolds and M Trimble, editors, Churchill and Livingstone 1981, Edinburgh 145-184
- [6]. Gaitatzis A, Carroll K, Majeed A et al. The Epidemiology of the comorbid of epilepsy in the general population. *Epilepsia* 2004; 45(12): 1613-1622.
- [7]. Kobau R, Gilliam F, Thurman DJ. Prevalence of self-reported epilepsy or seizure disorder and its associations with self-reported depression and anxiety: results from the 2004 Health Styles Survey. *Epilepsia*. Nov 2006; 47(11): 1915-21. [Medline].
- [8]. Barry J, Lembke A, Gisbert PA, et al. Affective disorders in epilepsy. In: Ettinger AB, Kanner AM, eds. *Psychiatric issues in Epilepsy: A practical Guide to Diagnosis and Treatment*. Philadelphia, PA: Lippincott Williams & Williams; 2007:203-247.
- [9]. Schmitz EB, Robertson MM, Trimble MR. Depression and schizophrenia in epilepsy: social and biological risk factors. *Epilepsy Res*. May 1999; 35(1): 59-68.
- [10]. Kanner AM, Balabanov A. Depression and epilepsy: how closely related are they? *Neurology*. Apr 23 2002; 58(8 Suppl 5): S27-39.
- [11]. Harden CL, Goldstein MA. Mood disorders in patients with epilepsy: epidemiology and management. *CNS Drugs*. 2002; 16(5): 291-302. [Medline].
- [12]. Baker GA, Smith DF, Dewey M, Jacoby A, Chadwick DW. The initial development of Health-related quality of life model as an outcome measure in epilepsy. *Epilepsy Res*. Sep 1993; 16(1):65-81. [Medline].
- [13]. Hermann BP. Quality of life in epilepsy. *J Epilepsy*. 1992; 5:153-165
- [14]. Perrine K, Hermann BP, Meador KJ, Vickrey BG, Cramer JA, Hays RD, et al. The relationship of neuropsychological functioning to quality of life in epilepsy. *Arch Neurol*. Oct 1995; 52(10):997-1003. [Medline].
- [15]. Dodrill CB. Behavioral effects of antiepileptic drugs. *Adv Neurol*. 1991; 55:213-24. [Medline].
- [16]. McConnell H, Duncan, D. Treatment of psychiatric comorbidity in epilepsy. In: McConnell H, Duncan, Snyder P, eds. *Psychiatric Comorbidity in Epilepsy*. Washington, DC: American Psychiatric Press: 1998:245.
- [17]. JS Duncan, SD Shorvon, DR Fish. *Clinical Epilepsy*. Churchill Livingstone. London. 1995. page 326.
- [18]. Clancy et al. The prevalence of psychosis in epilepsy; a systematic review and meta-analysis. *BMC Psychiatry* 2014, 14:75
- [19]. Devinsky O. *Psychiatric and Behavior Disorders in Epileptic Patients*. *Advanced Studies in Medicine*; Vol.3 (7B). July 2003
- [20]. Devinsky O, Kanner AM, Ettinger AB. Forward: therapy for cognitive and Behavioral Disorder in Epilepsy. *Epilepsy Behav*. 2002; 3 (suppl): S1
- [21]. American Psychiatric Association (APA): *Diagnostic and Statistical Manual of mental disorders, 4th Text Revised (DSM-IVTR)*. American Psychiatric Press, Washington, DC, 2000.
- [22]. Couldridge, L.; Kendall, S. & March, A. (2001). A systematic overview-a decade of research: the information and counseling needs of people with epilepsy. *Seizure*, 10, 8, 605-14.
- [23]. De Souza, Salgado PC. A psychological view of anxiety and depression in epilepsy. *Epilepsy Behav*. Feb 2006; 8(1):232-8. [Medline].
- [24]. Vazquez B, Devinsk O. Epilepsy and anxiety. *Epilepsy Behav*. 2003; 4(suppl4): 520-525.
- [25]. Trimble, M.R. & Van, Elst, L.T. (2003). The amygdala and psychopathology studies in epilepsy. *Ann NY AcadSci*, 985,461-8.
- [26]. Cendes, F.; Andermann, F. & Gloor, P. et al. (1994). Relationship between atrophy of the amygdala and ictal fear in temporal lobe epilepsy. *Brain*, 117, 4, 739-46.

- [27]. Charney, D.S. (2003). Neuroanatomical circuits modulating fear and anxiety behaviors. *Acta Psychiatrica Scand*, (Suppl.417), 38-50.
- [28]. Garcia-Morales, I.; De la Peña Mayor, P. & Kanner, A. M. (2008). Psychiatric comorbidities in epilepsy: identification and treatment. *Neurologist*, Nov, 14(6 Suppl 1), 15-25.
- [29]. Smaldone M, Sukkarieh T, Reda A, Khan A. Epilepsy and erectile dysfunction; a review. *Seizure* 2004; 13: 453-459.
- [30]. Baker, G.A.; Jacoby, A.; Buck, D.; Brooks, J; Potts, P. & Chadwick, D.W. (2001). The quality of life of older people with epilepsy: findings from a UK community study. *Seizure*, 10, 2, 92-9.
- [31]. Mula, M.; Pini, S. & Cassano, G.B. (2007). The role of anticonvulsant drugs in anxiety disorders: a critical review of the evidence. *J Clin Psychopharmacol*, 27, 263-72.
- [32]. Al-Yassen A. Q., Salih A.I. Prevalence of Post-Traumatic Stress Disorder among Basrah Medical Students. *The Medical Journal of Basrah University*, 2010; Vol.28 (2)
- [33]. Williams, J.; Steel, C. & Sharp, G.B. et al. (2003). Anxiety in children with epilepsy. *Epilepsy Behav*, 4, 729-32.
- [34]. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its Medical and Psychological Correlates: results of the Massachusetts Male Aging Study. *J Urol*. 1994; 151:54-61.
- [35]. Lambert MV. Seizures, Hormones, and Sexuality. *Seizure* 2001; 10: 319-40.
- [36]. Todorova K, Arnaudova M. Depressive Disorder in Epilepsy. *J of IMAB*; Issue: Vol. 16, book 3, 2010/ 57.
- [37]. Lopez-Rodriguez F., et al. Personality Disorders among Medically Refractory Epileptic Patients. *J Neuropsychiatry Clin Neurosci* 1999; 11: 464-469.
- [38]. Vuilleumier P, Jallon P. [Epilepsy and Psychiatric Disorders: Epidemiological data]. *Rev Neurol (Paris)*. May 1998; 154(4): 306-17 [Medline].
- [39]. Vestergaard M, Pedersen CB, Christensen J, Madsen KM, Olsen J, Mortensen PB. Febrile seizures and risk of schizophrenia. *Schizophr Res*. 2005; 73: 343-349.
- [40]. Kanemoto K, Tsuji T, Kawasaki J. Re-examination of interictal psychoses based on DSM IV psychosis classification and international epilepsy classification. *Epilepsia*. 2001; 42: 98-103.
- [41]. Kanemoto K, Tadokoro Y, Oshima T. Psychotic illness in patients with epilepsy. *Ther Adv Neurol Disord*. 2012; 5: 321-334.