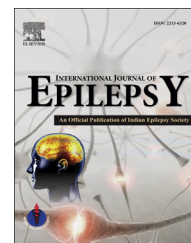


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## Original Article

# Study of quality of life in epilepsy patients with psychiatric co-morbidities using QOLIE-31



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## ABSTRACT

**Background:** Epilepsy is a neurological condition affecting both the sexes in all age groups and is associated with psychiatric co-morbid conditions. There is a paucity of available published data regarding psychiatric co-morbid conditions and quality of life in patients with Epilepsy (PWE) from developing countries.

**Methods:** We evaluated the quality of life in 80 PWE, 80 with asthma (asthma control subjects: AC) and 80 normal healthy patients (normal control subjects: NC) using the QOLIE-31 item inventory.

**Results:** Psychiatric co-morbid conditions are more common in PWE (32.50%) as compared to the AC (17.5%) and NC (7.5%). The quality of life in PWE was significantly lower when compared to control subjects and it was further low in the presence of co-morbid psychiatric disorders.

**Conclusion:** Co-morbid psychiatric disorders should be identified and documented in PWE and treating these disorders apart from the control of seizures may significantly improve their quality of life.

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## 1. Introduction

Though epilepsy is a neurological condition affecting the population universally, it has significant psychosocial impact which has seldom been documented and quantitated by a neurologist.

Despite an extensive literature indicating that patients living with epilepsy are more prone to develop psychiatric co-morbidities, it has continued to go unrecognized or untreated

in both children and adults with epilepsy.<sup>1</sup> An association between epilepsy and psychiatric co-morbidities has been known since antiquity, and it ranges from 20% to 50%, reaching 80% in selected populations, like individuals with temporal lobe epilepsy (TLE), and patients with medically intractable epilepsy who are candidates for surgical treatment, and these indices are far superior to those found in the general population (10–20%).<sup>2</sup> Verrotti et al have stated that Axis I disorders according to the DSM range from 19% to 62%,

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**Table 1 – Psychiatric co-morbid disorders found in patients with epilepsy (DSM-IV-TR).**

Anxiety
Anxiety NOS
Generalized anxiety disorder
Panic disorders
Agoraphobia, social phobia
Posttraumatic stress disorders
Depression (most common 30%)
Bipolar disorders (I, II, mixed, NOS)
Interictal and chronic psychoses
Personality disorders
Aggression and mental retardation

with rates of major depressive episodes from 32% to 48%.<sup>3</sup> Psychiatric co-morbid disorders found in patients with epilepsy are listed in Table 1.<sup>4</sup>

There is a bidirectional relationship among psychiatric illnesses, epilepsy, and suicidality; that is, not only can the epileptic disorder antedate onset psychiatric symptoms in a given patient but also the diagnosis of mood and behavioral disorders may be made before a first epileptic seizure.<sup>5</sup> Patients with epilepsy are therefore at greater risk of developing these psychiatric disorders, and patients with psychotic disorders, suicidality, and mood and attention deficit disorders have a significantly greater risk of developing epilepsy. This bidirectionality suggests that the structural and functional modifications of one disease increase the risk of the development of the other.<sup>2</sup> It is clear that the relationship between psychiatric disorders and epilepsy is complex and is not only a consequence of epilepsy.<sup>4</sup>

Quality of life (QOL) has been defined as ‘a composite measure of physical, mental and social wellbeing as perceived by each individual or by group of individuals that is to say, happiness, satisfaction and gratification as it is experienced in such life concerns as health, marriage, family work, financial situation, educational opportunities, self-esteem, creativity, belongingness and trust in others’.<sup>6</sup> QOL evaluation is a relatively new measure to evaluate the outcome of treatment for epilepsy. QOL is influenced by biological factors as well as cultural, social and religious beliefs and values. QOL is significantly affected in epilepsy patients by these co-morbid psychiatric disorders and stigma. Social support and treating them may improve outcomes independently.<sup>7–9</sup> Therefore it is important to document the incidence and the type of co-morbid psychiatric disorders in Indian patients, so that they can be addressed with specific remedial measures.

Epilepsy carries an enormous social stigma and people with epilepsy tend to have lower QOL.<sup>10</sup> They are prone to have poorer self-esteem, higher levels of anxiety, and depression. They are more likely to be underemployed or unemployed with lower rates of marriage and greater social isolation.<sup>11,12</sup>

Although there are numerous studies assessing the QOL of people with epilepsy from all over the world, similar studies from the developing countries, especially India are sparse.<sup>7,13–15</sup>

It is necessary to ascertain the magnitude of the problem as a part of the systematic approach to challenges in epilepsy management. Thus, we conducted the present study in order to assess the QOL in epilepsy in our region by QOLIE-31 inventory.<sup>9,16</sup>

## 2. Materials and methods

This was a cross-sectional hospital based case control study. Consecutive epilepsy patients aged  $\geq 18$  years attending the Neurology outpatient department at a tertiary care referral hospital. The patients were on regular antiepileptic drugs (AED) at least for the past one month. The study was conducted from March 2011 to March 2012. The study was approved by the institute's ethics committee. The patients who had undergone surgery or implant of Vagus nerve stimulator and those who did not give informed consent were excluded from the study.

The control subjects were either those having bronchial asthma (disease control subjects) attending the outpatient Department of Medicine or the healthy attenders accompanying the patients (healthy control subjects).

Written informed consent was taken from PWE and control subjects. A semi structured proforma was prepared to collect the socio-demographic details and clinical variables including gender, age, height, weight, location/address, marital status, socio economic status, education, occupation, family income, past history, family history, personal history, history of other illness/other drugs, age of onset of epilepsy, duration of epilepsy, frequency of seizures, AED therapy, psychotropics, AEDs used in the treatment of psychiatric disorders (on/off label)—mood stabilizers for bipolar disorders (phenytoin, carbamazepine, valproate, oxcarbazepine, lamotrigine, topiramate, and levetiracetam), and AEDs used for anxiety (benzodiazepines, pregabalin, gabapentin, and zonisamide).

The International League Against Epilepsy (ILAE) 1989 classification was used to classify the type of seizures. All the patients were administered MINI6.0<sup>17</sup> for evaluation of psychiatric co-morbid disorders and QOLIE-31 questionnaire<sup>9,16</sup> for the assessment of quality of life in epilepsy with or without co-morbid disorder.

[MINI is a brief structured interview for the major Axis 1 psychiatric disorders in DSM VI and ICD 10. QOLIE31 is a 31 item Quality of Life in Epilepsy Inventory developed with cross cultural translations comprised of subscales grouped into two subgroups: Emotional/Psychological effects (seizure worry, overall QOL, emotional well being, energy/fatigue subscales) and Medication/Social effects (medication effects, work driving social limits, cognition function subscales). Precoded numeric values to responses to some QOLIE-31 items are in a direction such that a higher number reflects a more favourable health state and some other items with a lower score reflects a more favourable state. To account for these differences in scoring procedure in QOLIE 31, first converts the raw precoded numeric values of items, to 0–100 point score, with higher scores reflecting a better quality of life. The investigator read aloud the questionnaire for all the patients surveyed and asked for responses. The overall scores can be derived by weighting and summing QOLIE 31scale scores].

The results were analyzed by using software SPSS version 20.0. Descriptive statistics – mean, SD and % were done. Other statistical methods used are Chi-square test (with Yates correction) or Fischer's exact test, Odds ratio with 95% confidence intervals (CI) for comparisons of binary outcomes. One

**Table 2 – Socio-demographic details of the three groups.**

Variable	Patients with epilepsy (PWE) (N = 80)	Disease control subjects (N = 80)	Healthy control subjects (N = 80)	ANOVA
Mean age $\pm$ SD in years	33.77 $\pm$ 11.4	39.53 $\pm$ 12.55	33.36 $\pm$ 10.25	
<b>Sex</b>				
Males (%)	53 (66.25%)	46 (57.5%)	60 (75%)	
Females (%)	27 (33.75%)	34 (42.5%)	20 (25%)	
<b>Education</b>				
High school and above	60 (75%)	32 (40%)	51 (63.75%)	F = 9.205, df = 2, p < 0.001
Middle school and below	20 (25%)	48 (60%)	29 (36.25%)	
<b>Occupation</b>				
Skilled worker and above	26 (32.5%)	29 (36.25%)	48 (60%)	F = 20236, df = 2, p = 0.109
Semiskilled worker and below	54 (67.5%)	51 (63.75%)	32 (40%)	
<b>Family income (In Indian rupees)</b>				
>4894	30 (37.5%)	17 (21.25%)	32 (40%)	F = 2.653, df = 2, p = 0.073
<4893	50 (62.5%)	63 (78.75%)	48 (60%)	
Income mean scores	4.613 (CI 4.284–4.94)	4.96 (CI 4.72–5.201)	4.53 (CI 4.275–4.80)	
<b>Socioeconomic status</b>				
Lower middle class and above	29 (36.25%)	21 (26.25%)	40 (50%)	F = 6.574, df = 2, p = 0.002
Upper lower class and below	51 (63.75%)	59 (73.75%)	40 (50%)	
Socioeconomic mean scores	3.59 (CI 3.38–3.78)	3.86 (CI 3.69–4.03)	3.40 (CI 3.24–3.56)	

Note: Socio-demographic profile was analyzed by Kuppuswamy socioeconomic status classification 2007.

way analysis of variance (ANOVA) with post hoc analysis was done for continuous outcomes between the three participant groups. We compared the Relative Risks (RR) and 95% confidence interval (CI) for socio-demographic and clinical variables between those with and without psychiatric co-morbidity.

### 3. Results

Eighty consecutive PWE attending the neurology outpatient department were enrolled for the study. A similar number of disease control subjects and healthy control subjects were administered with MINI 6.0 and QOLIE 31 questionnaire.

The total number of PWE having co-morbid psychiatric disorders in this study was 26/80 (32.50%) as against 14/80 (17.5%) in disease control subjects and 6/80 (7.5%) healthy control subjects.

The socio-demographic details of the three groups are listed in Table 2.

#### 3.1. Patients with epilepsy (PWE)

The age of onset of seizures was below 30 years in 65/80 (81.25%) PWE and those who had seizure onset after 30 years were 15/80 (18.75%). Duration of seizures was >5 years in 63/80 (78.75%) PWE and <5 years in 17/80 (21.25%). The average duration of seizures was 13.07  $\pm$  9.55 years. Frequency of seizures was  $\leq$  one per year was reported in 46/80 (57.5%) PWE and  $\geq$  two per year in 34 (42.5%) patients respectively. The recurrence of seizures within the previous 6 months and more than 6 months back was reported in 44/80 (55%) and in 36/80 (45%) PWE respectively. 16/80 (20%) of PWE had history of seizures in family members and 64/80 (80%) did not. There was no history of seizures in the control subjects.

Different types of seizures noted in PWEs were as follows: simple partial seizures in 4 (5%) patients, complex partial seizures (CPSs) in 2 (2.5%), generalized seizures in 49 (61.25%), generalized seizures and history of hot water epilepsy in 2 (2.5%), simple partial seizures with secondary generalization in 13 (16.25%), generalized seizures with myoclonic jerks (Juvenile myoclonic epilepsy) in 4 (5%), and CPSs with secondary generalization in 6 (7.5%) patients.

PWE who were on monotherapy were 45/80 (56.25%), 27 (33.75%) were on dual therapy and 8 (10%) were on polytherapy. Among PWE who were on monotherapy, 13/80 (16.25%) were on Phenytoin (DPH), 17/80 (21.15%) Phenobarbitone (PB), 10/80 (12.5%) Carbamazepine (CBZ), 4/80 (5%) Sodium Valproate (SV), 1 (1.25%) Levetiracetam (LEV). With this data, it was inferred that 40 patients were on one or more of the mood stabilizers (CBZ, SV, Oxcarbazepine, Lamotrigine, LEV) singly or in combination – 24 were on CBZ, 11 on SV, 3 on LEV and 1 each on Oxcarbazepine, and Lamotrigine respectively.

Fifty nine of the 80 PWE (73.75%) reported that they were taking AEDs regularly, 16/80 (20%) reported that they had occasionally missed the AEDs and 5/80 (6.25%) were missing their medications frequently. In PWE, 46/80 (57.5%) had good seizure control (no seizures in the past two years or one episode in the past one year), 15/80 (18.75%) had fair control of seizures (1–5 episodes in the past 1 year) and 19/80 (23.75%) had poor control ( $\geq$ 1 seizures per month).

#### 3.2. Psychiatric co-morbidities in PWE, disease controls and healthy control subjects

Among the total study population of 240 patients, 46 had psychiatric co-morbidities, and 9 had suicidal behaviors. The distribution of the psychiatric co-morbidities in the three groups are depicted in Table 3.

**Table 3 – Distribution of psychiatric co-morbidities among the groups.**

Psychiatric co-morbidities	Patients with epilepsy (PWE) (N = 80)	Disease control subjects (N = 80)	Healthy control subjects (N = 80)	Total (N = 240)
Major depressive disorder	21	12	3	36
Secondary co-morbidity				
Suicidality	09	—	—	09
Panic disorder	01	—	—	01
Alcohol dependent syndrome	01	—	—	01
Agoraphobia	01	—	—	01
Alcohol dependent syndrome	02	—	—	03
Generalized anxiety disorder	—	02	03	05
Psychotic disorders	02	—	—	02
Overall prevalence of psychiatric co-morbidity	26/80 (32.50%)	14/80 (17.5%)	6/80 (7.5%)	46/240 (19.16%)

### 3.3. Psychiatric co-morbidities in PWE

There were 26 PWE who had co-morbid psychiatric conditions. Among them 20/51 (39.21%) patients were from lower socioeconomic status and 6 out of 29 (20.68%) were from middle and upper socioeconomic status.

In PWE with psychiatric co-morbidities, major depressive disorder was found in 21 and 9 out of these 21 patients had co-morbid suicidal behavior. 17/65 (80.96%) PWE who had onset of seizures between 11 and 30 years of age were associated with major depressive disorder and 4/15 (19.04%) PWE who had onset of seizure after 30 years of age were associated with major depressive disorder. 18/63 (85.68%) PWE who had seizures > 5 years duration had depressive disorder and 3 out of 17 (14.62%) PWE who had seizures < 5 years duration had depressive disorder. 14/34 (66.64%) PWE who had frequency of seizure > 2 per year were associated with major depressive disorder and 7/46 (33.36%) who had no seizure or less than 1/year were associated with major depressive disorder.

In PWE who had history of seizure in family member/s, 8/16 (50%) had depressive disorder and 13/64 (20.03%) patients who did not have history of seizure in family were having depressive disorder. 18/44 (40.90%) who had seizure in the last 6 months had depressive disorder and 3/36 (8.33%) who had seizure 7 months or later had depressive disorder.

Major seizure types were primary generalized seizures and partial seizures with secondary generalization. 10/49 (20.40%) patients with generalized seizures had depressive disorder and 6/13 (46.15%) patients with partial seizures with secondary generalization had depressive disorder.

### 3.4. Antiepileptic medications

Three of the 13 PWE on DPH had major depressive disorder. 5/17 PWE on PB had major depressive disorder. 2/10 PWE on CBZ therapy had major depressive disorder. 5/13 PWE who were on DPH and PB had major depressive disorder. 1/8 PWE who were on PB and CBZ had major depressive disorder. 1/3 PWE who were on PB and SV had major depressive disorder. 4/8 PWE on poly therapy had depressive disorder (Table 4). Major depression was found to a lesser extent among the patients on mood stabilizers (CBZ, SV, Oxcarbazepine, Lamotrigine, LEV)

than those who were not, though the difference was not statistically significant.

Thirteen of the 59 PWE who were taking medications regularly had major depressive disorder. 6/16 PWE who had lapses some time in taking medication had major depressive disorder. 2/5 PWE who had frequent lapses in taking medications had major depressive disorder.

Seven of the 46 PWE who had good control of seizures had major depressive disorder, 6/15 PWE who had fair control of seizures had major depressive disorder and 8/19 PWE who had poor control of seizures had depressive disorder.

### 3.5. Systemic symptoms in PWE

Eleven PWEs had systemic illness, three had hypertension, three had diabetes mellitus, one was detected to be HIV-positive, one had an old stroke (left hemiparesis) and hypertension, one had left infantile hemiplegia, and two had old strokes (right hemiparesis). Four out of these eleven (36.36%) PWEs had depressive disorder, and 16/69 (23.18%) PWEs without systemic illness had depressive disorder.

### 3.6. Quality of life in epilepsy

The overall QOL, emotional well being, lack of energy/fatigability, cognitive function, social function and the overall scores in PWEs, disease control subjects and healthy control subjects are respectively depicted in Table 5.

### 3.7. Quality of life in PWE associated with psychiatric co-morbid disorders

QOLIE 31 scores for seizure worry, overall QOL, emotional well being, lack of energy/fatigue, cognition, medication effects, social function and the overall score among the PWEs associated with various co-morbidities viz., major depressive disorder, suicidality, panic disorder, agoraphobia, alcohol dependent syndrome and psychosis respectively are depicted in Table 6. The QOLIE 31 overall score was 78.13 in PWE, 88.81 in disease control subjects and 92.79 in healthy control subjects. It is noteworthy that QOLIE 31 scores were significantly lower in the PWEs in all domains ( $p < 0.05$ ) as compared to the control subjects.



**Table 4 – Antiepileptic medications and psychiatric co-morbidity.**

	PWE N = 80	MDD N = 21	Agoraphobia N = 1	Alcohol dependent syndrome N = 3	Psychosis N = 2	Total psy. co-morbid disorders
<b>Monotherapy</b>						
Phenytoin	13	3	1	2		6
Phenobarbitone	17	5				5
Carbamazepine	10	2			1	3
Sodium valproate	4					
Levetiracetam	1					
<b>Dual therapy</b>						
PHT + PBT	13	5				5
PBT + CBZ	8	1				1
PBT + SOD VAL	3	1				1
PBT + CLB	1					
CBZ + SOD VAL	1					
OCB + CLB	1					
<b>Polytherapy</b>						
PHT + PBT + OXC	1					
PHT + PBT + CBT	2	1				1
PHT + PBT + CBZ + CLB	1	1			1	2
PBT + CBZ + VAL	1	1				1
PBT + CBZ + LEV + CLB	1	1				1
CBZ + VAL + LEV	1					
VAL + LAM + OXC	1					

#### 4. Discussion

Epilepsy is a chronic and serious neurological disorder with multifaceted uncertainties and stigmatization which have significant negative role in the QOL of those afflicted by the disorder.<sup>13</sup>

The objective of our study was to assess the impact of the seizure frequency and severity and psychiatric co-morbidities on the QOL of PWE wherein we compared the PWEs with control subjects with healthy control subjects and control subjects with a chronic illness (asthma). There were few reasons for choosing the patients suffering from asthma as disease control subjects in our study: a) like epilepsy, asthma is a chronic disorder with exacerbations and remissions and is associated with psychiatric co-morbidities (DSM-IV depressive and anxiety disorders), b) as is true with epilepsy, few population-based longitudinal studies that have examined the chronology of the development of asthma and psychiatric disorders have reported the relationships to be bidirectional: early development of respiratory symptoms and asthma is associated with a greater risk of depressive and anxiety disorders, and early development of psychiatric disorders is

associated with a greater subsequent risk of asthma. Few larger population-based studies have observed elevated prevalence of most DSM-IV depressive and anxiety disorders in youths and adults with asthma relative to comparison subjects and the prevalence of meeting criteria for one or more DSM-IV depressive and anxiety disorders was twice as high in youths with asthma relative to comparison subjects (16.3% versus 8.6%) after controlling for socioeconomic status, other medical co-morbidity, and health risk behaviors.<sup>18–20</sup>

The results of our study reinforce those of earlier studies that revealed that psychiatric co-morbidity is common in people with epilepsy and that depression is the most common co-morbid disorder.<sup>21–25</sup> The rates of depression in PWE in this sample were four times more than that in age and sex matched healthy controls and double than those with bronchial asthma, reinforcing previous observations that depression in epilepsy is more than just a reaction to living with a chronic disorder<sup>26,27</sup> and is, partly, biologically driven.

Indian studies in this regard are far and few. Shetty et al have assessed QOL with QOLIE-89 instrument in 60 people with epilepsy and found that QOL was impaired in people with epilepsy with increased impairment in women, older patients, simple partial seizures, and those with recent seizure.<sup>13</sup>

**Table 5 – QOLIE 31 in patients with epilepsy, disease control subjects and normal control subjects (ANOVA).**

	Patients with epilepsy (PWE) (N = 80)	Disease control subjects (N = 80)	Healthy control subjects (N = 80)	Mean	Confidence interval	df	F	p value
Overall quality of life	73.84	74.53	79.18	75.85	74.01 ± 77.69	2	3.30	0.039
Emotional Well being	73.35	91.25	91.15	85.25	83.76 ± 86.73	2	130.9	<0.001
Lack of energy/fatigability	81.18	83.81	87.37	84.10	82.59 ± 85.59	2	5.82	0.003
Cognitive function	84.82	94.27	98.34	92.47	90.76 ± 94.19	2	25.57	<0.001
Social function	71.93	86.66	95.2	84.60	82.51 ± 86.68	2	40.76	<0.001
Overall Score	78.13	88.81	92.79	86.57	85.10 ± 88.04	2	62.12	<0.001

**Table 6 – Quality of Life in Epilepsy in PWE and psychiatric co-morbid disorders.**

QOLIE 31 item scale	PWE	MDD	Suicidality	Panic disorder	Agoraphobia	Alcohol dependent syndrome	Psychosis
	N = 80	N = 21	N = 9	N = 1	N = 1	N = 3	N = 2
Seizure worry (8%)	79.95	60.71	54.92	0	76.66	71.88	51.99
Overall quality (14%)	73.84	50.35	47.77	10	82.5	47.50	52.5
Emotional wellbeing (15%)	73.35	59.80	51.00	20	72	53.33	70
Lack of energy/fatigability (12%)	81.12	62.61	51.33	5	80	60.0	67.5
Cognition (27%)	84.82	64.85	59.93	30.83	90	56.01	53.33
Medication effects (3%)	88.19	75.26	72.21	61.1	88.90	75.93	61.1
Social function (21%)	71.93	53/33	50.55	30	56	50.0	49.5
Overall score	78.13	59.78	54.64	21.46	76.81	55.50	56.74

The percentages given in brackets of QOLIE 31 scales is the weightage given to each item and overall score is given by weighting and summing QOLIE 31 scales done according to QOLIE 31 scoring manual.

Thomas et al have observed that frequent seizures and polytherapy have significant association with QOL and have opined that QOL estimate is a useful outcome measure to assess epilepsy care from a patient's perspective. It is relatively easy to give out simple self-administered QOL instruments like QOLIE-31 even in busy epilepsy clinics in developing countries. The management of a person with epilepsy should focus on better control of seizures with appropriate use of AEDs, preferably monotherapy, which would improve quality of life.<sup>14</sup> Sinha et al have interviewed 204 epilepsy patients at Kolkata, India with the Bengali version of QOLIE 9. The mean of total QOLIE score was  $18.02 \pm 4.87$ , the range being 10–30. Multiple linear regression analysis revealed that workdays lost due to epilepsy in last three months, use of two or more antiepileptic drugs, higher frequency of seizure, and longer time gap between onset of seizure and consultation with neurologist were significant predictors for poorer quality of life score in the epilepsy patient.<sup>15</sup>

In the present study, psychiatric co-morbid conditions were more common in PWEs (32.50%) as compared with the disease control (17.5%) and healthy control (7.5%) subjects, reinforcing the previous studies that psychiatric co-morbidities are more common in PWE.<sup>7,12,22,24</sup>

The patients with epilepsy were lower in their average education level, less skilled in their occupation with low family income and living lower socioeconomic status compared to patients who are normal and similar findings were found in some studies.<sup>28,29</sup>

Longer duration of seizures, increased frequency of seizures, recent recurrence of seizures, anticonvulsant polypharmacy, poor compliance with medications, and family history of seizures were associated with increased psychiatric co-morbidity as has been concluded in our recently published paper.<sup>30</sup>

Herodes et al, reported lower scores with shorter duration of epilepsy with significant effects on energy, emotional wellbeing and bodily pain.<sup>31</sup> Duration of epilepsy, which might play an important role in QOL, was analyzed and it was found that patients with duration of more than 15 years had poor QOL. These patients had significant physical and emotional trauma which had limited their daily activities with poor attention/concentration with feeling of language dysfunction which was statistically significant. These patients also had

seizure worry, fatigability, memory disturbance and health discouragement. They were also worried about long-term side effects of antiepileptic drugs and had poor social support.<sup>31</sup>

Increased seizure frequency had major effect on the QOL in a study done by Herodes et al.<sup>31</sup> Guekht et al, reported that patients with frequent seizures had low social contact and feelings of stigmatization.<sup>32</sup> In the present study, although not statistically significant, there was a trend towards poor QOL with increased number of seizures. These patients had emotional and physical factors which had limited their daily activities. They also complained of poor social interaction, decreased energy level and feeling of social isolation.

Seizure related variables such as complex partial seizures, frequency of seizures, temporal proximity to seizures; poor drug compliance, anticonvulsant polypharmacy and a family history of psychiatric disorder have been identified previously as increasing the risk of developing psychiatric disorder<sup>22,33</sup> though not all previous reports have identified seizure frequency as contributory.<sup>21</sup>

Seizure severity could be accepted as an independent determinant of QOL. The seizure severity and its correlation with the QOL have been assessed by few scientists<sup>27,29</sup> and the results from those studies support our conclusion. Vickrey et al have confirmed that the seizure severity correlates with the overall score of QOLIE-89 ( $r = -0.424$ ,  $P < 0.01$ ).<sup>34</sup> Harden et al have also found that the seizure severity is associated with scores of the QOLIE-31 subscales: “social functioning” ( $r = -0.280$ ,  $P = 0.002$ ) and “overall QOL” ( $r = -0.210$ ,  $P = 0.023$ ) but in contrast to our results they have proved a correlation of the seizure severity with the subscales “seizure worry” ( $r = -0.265$ ,  $P = 0.004$ ) and “cognitive function” ( $r = -0.209$ ,  $P = 0.024$ ).<sup>35</sup> A possible explanation for some dissimilarities of study results is the usage of different seizure severity and QOL questionnaires.

In PWEs with good seizure control, only 7/46 (15.2%) had major depressive disorder compared with 13/34 (41.2%) PWEs with fair or poor seizure control. The PWEs who had seizures of 1–5 per year or >1/month were significantly associated with depressive disorder compared with the patients who had 1 or no seizure in the past 1 year. Increased seizure frequency is associated with increased psychiatric co-morbidities.<sup>33</sup> On the contrary, some studies have found that increased psychiatric co-morbidities are not associated with increased seizure frequency.<sup>36–38</sup>

The high seizure frequency has a negative impact on most social aspects, some aspects associated with epilepsy and the overall health and the increase in seizure frequency is associated with a decrease in the respective aspects of QOL. Therapy (mono- or polytherapy) was the only co-factor of seizure frequency for the subscale “overall health” scores. Special features of PWE mentality (to feel safer when on polytherapy) are a possible explanation about the poorer results of patients on monotherapy. Therefore, seizure frequency could be accepted as an independent determinant of QOL.<sup>13,14,24,27,28</sup>

The seizure frequency is among the factors with the most frequently studied the impact on the QOL. Lots of investigators have supported the statement that the higher seizure frequency has a negative influence on the QOL.<sup>4,5,7–10,12,16,21–23</sup> In the scientific literature, there is no agreement whether the clinical factors (seizure frequency most often cited) or the psychic factors (depression most often cited) are the main predictors of the QOL of people with epilepsy. Some investigators have accepted the seizure frequency as a very significant QOL predictor. Djibuti et al have proven its impact on the QOLIE-31 subscales “seizure worry”, “overall QOL”, “emotional well being”, “energy/fatigue”, “cognitive function”, and “social function”.<sup>39</sup> Guekht et al have found a significant but rather weak correlation with all QOLIE-31 subscales and have confirmed that seizure frequency is the most significant parameter related to QOL.<sup>32</sup> According to the study results of Tracy et al the seizure control has a weak correlation with the overall score of QOLIE-31 and the scores of the subscales “seizure worry”, “medication effects”, “social function”, and “overall QOL”.<sup>40</sup> In contrast to these scientists Gilliam has not found a correlation between the seizure frequency and the subscales of QOLIE-89.<sup>41</sup> A possible explanation for dissimilarities of various study results is the different study design, inclusion criteria and QOL questionnaires.

In recent years, numerous studies have proved improved QOL with monotherapy.<sup>42,43</sup> This may be partly due to reduced adverse effects commonly associated with polytherapy. The QOL was evaluated in relation to number of drugs in the present study and was found that patients on polytherapy had lower QOL scores compared to patients on single drug. This difference between mono and polytherapy scores did not show any statistical significance, but it showed definite trend towards good QOL in patients on monotherapy. Patients with polytherapy had poor health perception, limitation of social interaction and work, had low energy level with seizure worry, and health discouragement. This finding is in agreement with previous study which showed polytherapy is associated with poor QOL.<sup>44</sup>

The QOL of PWE by QOLIE 31 criteria in different domains like overall quality of life, emotional well being, lack of energy/fatigue levels, cognitive functioning and overall quality of life was significantly low when compared to control subjects. In some studies the QOL was poor in PWE compared with control subjects.<sup>7</sup>

The QOL of PWE associated with psychiatric co-morbidities was significantly lower when compared with PWE without psychiatric co-morbidities. In some studies, PWE with psychiatric co-morbid disorders were associated with poor QOLIE 31 scores.<sup>7,23,45</sup> The results are consistent and strengthen the evidence of poor QOL in PWE and psychiatric co-morbidities. The QOL was lower in PWE when compared to control

subjects probably because of social and psychological sequelae of seizures and epilepsy and adverse medication effects are persistent.<sup>16,41</sup>

In a study by Jacob & Tharyan,<sup>7</sup> PWEs rated their QOL significantly lower than those with asthma and age and sex matched controls as assessed by the generic WHOQOL-BREF scale. Those with psychiatric co-morbidity reported significantly lower scores on all domains of the generic scale and this association was also evident in those with epilepsy using the epilepsy-specific QOLIE 31 inventory. This association between lower quality of life in those with psychiatric co-morbidity does not seem specific only to epilepsy as those with psychiatric co-morbidity in all three groups had significantly quality of life lower scores; this perception of poorer quality of life may also be related to the negative cognitive appraisal common in depression.<sup>40</sup> However, this also confirms previous observations that attest to poorer quality of life in those people with epilepsy and psychiatric co-morbidity<sup>21,40</sup> and a higher suicidal rate in them compared to those people with epilepsy that were free of psychiatric disorder.<sup>21</sup>

The limitations of the present study include but are not limited to a) the cross-sectional design b) the sample size, which is too small to address the psychiatric pathologies beyond depression or to do any regression analyses c) the different groups which are not matched for sex and age d) the absence of neuroimaging and functional neuroimaging, which would have assisted in defining any focal basis to the psychiatric pathologies and e) the absence of neuroimaging, functional neuroimaging, video-EEGs, and even routine EEGs, which would have assisted in differentiating focal onset of seizures that rapidly generalized. However, these limitations do not devalue the results from our study.

To conclude, it is not just adequate control of seizures but also recognizing the psychiatric co-morbid disorder and its management will help the patient living with epilepsy to lead a better quality of life. Patients with epilepsy are more likely to have psychiatric co-morbid disorders compared with the other patients with chronic illness or with the healthy subjects. They are less educated, less skilled, earning low and living a lower socioeconomic status. QOL in epilepsy is low in PWE compared to the control subjects and with associated psychiatric co-morbid conditions it further declines.

It is of immense clinical importance to identify the co-morbid psychiatric disorders in PWEs as the treatment of these disorders apart from good seizure control may significantly improve their quality of life. Control of seizure, anti-epileptic drug monotherapy, and educating people regarding epilepsy will help to improve QOL in patients with epilepsy.

## Conflicts of interest

All authors have none to declare.

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