



# Quality of Life in Patients with Drug Resistant Epilepsy

## *İlacı Dirençli Epilepsi Hastalarında Yaşam Kalitesi*

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### Abstract

**Objective:** Quality of life (QOL) is considered the main outcome in epilepsy trials, but in developing countries such as India, data available regarding QOL in drug-resistant epilepsy (DRE) are scarce. The present study was designed to assess the QOL in patients with DRE and to identify the impact of various demographic and clinical factors affecting QOL.

**Materials and Methods:** Data regarding demographic and clinical factors were collected among 50 patients with DRE at PGIMS, Rohtak. QOL was measured using the QOL in epilepsy-31 (QOLIE-31) questionnaire. Multiple regression analysis was used to determine which variables were associated with QOLIE-31 total and multi-item scores.

**Results:** Among the 50 patients who were enrolled, the mean age was  $28.48 \pm 11.66$  years; 36% were females; 44% were unmarried; majority received primary and secondary education and belonged to upper lower socioeconomic status. Of the 50 patients, 30% had focal and 70% had generalized seizures, out of which 68% were uncontrolled seizures. The total QOLIE-31 score was  $39.29 \pm 7.43$ . Lower QOLIE-31 scores were strongly associated with higher seizure frequency, lower socioeconomic status, and marital status. Of all these variables, seizure frequency and marital status independently influenced the total score. Seizure frequency negatively correlated with all domains of QOL, but this was significant for energy/fatigue and social functioning.

**Conclusion:** High seizure frequency, marital status, and socioeconomic status are factors that had a significant influence on QOL.

**Keywords:** Drug-resistant epilepsy, quality of life, QOLIE-31

### Öz

**Amaç:** Epilepsi çalışmalarında yaşam kalitesi (YK) ana sonlanım olarak kabul edilir, ancak Hindistan gibi gelişmekte olan ülkelerde ilacı dirençli epilepside (İDE) YK ile ilgili veriler azdır. Bu çalışma, İDE hastalarında YK'yi değerlendirmek ve YK'yi etkileyen çeşitli demografik ve klinik faktörlerin etkisini tanımlamak için tasarlanmıştır.

**Gereç ve Yöntem:** PGIMS, Rohtak'ta İDE'li 50 hastanın demografik ve klinik özellik verileri toplandı. YK, "Epilepsili hastalarda yaşam kalitesi ölçeği (QOLIE-31)" kullanılarak değerlendirildi. Hangi değişkenlerin toplam QOLIE-31 ve çoklu madde puanları ile ilişkili olduğunu belirlemek için çoklu regresyon analizi kullanıldı.

**Bulgular:** Çalışmaya dahil edilen 50 hastanın yaş ortalaması  $28,48 \pm 11,66$  yıl idi. Hastaların %36'sı kadın, %44'ü evlenmemiş, çoğunluğu ilk ve orta eğitim mezunu ve daha düşük sosyoekonomik statüye sahipti. Elli hastanın %30'u focal, %70'i jeneralize nöbete sahipti, %68'inin nöbetleri kontrol altında değildi. Toplam QOLIE-31 skoru  $39,29 \pm 7,43$  idi. Düşük QOLIE-31 skoru yüksek nöbet sıklığı, düşük sosyoekonomik statü ve medeni durum ile güçlü bir şekilde ilişkiliydi. Tüm bu değişkenler arasında nöbet sıklığı ve medeni durum toplam skoru bağımsız olarak etkiledi. Nöbet sıklığı tüm YK bileşenleri ile negatif korelasyon gösterdi, ancak bu, enerji/yorgunluk ve sosyal işlevsellik için önemliydi.

**Sonuç:** Yüksek nöbet sıklığı, medeni durum ve sosyoekonomik statü YK üzerinde anlamlı etkiye sahip faktörlerdir.

**Anahtar Kelimeler:** İlacı dirençli epilepsi, yaşam kalitesi, QOLIE-31

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## Introduction

Epilepsy is a frequent neurologic disorder affecting approximately 50 million people across the globe (1). Anti-epileptic drugs are the mainstay of therapy with the majority of patients showing a response to this treatment. However, approximately 20-40% patients do not respond and they represent resistant epilepsy (2), which according to the International League Against Epilepsy (ILAE), is defined as the failure of adequate trials of two tolerated, appropriately chosen and administered anti-seizure drugs (whether as monotherapy or in combination) to achieve seizure freedom (3).

Epilepsy, in particular, drug-resistant epilepsy (DRE), is life-altering condition and significantly hampers the psychosocial wellbeing of affected individuals. The impact of epilepsy cannot be understood merely through seizure episodes, it is determined by the reciprocity of various psychosocial factors as psychiatric and medical comorbidities. The underlying etiology and conditions to which the patient is made vulnerable, the direct effect of seizures, and adverse effect of anti-seizure drugs are the factors responsible for these medical comorbidities. DRE affects cognitive well-being and patients with DRE often experience concentrating difficulties (4).

Psychopathological disorders such as depression and anxiety are also commonly observed (5). Epilepsy affects social functioning, causes family problems, prevents people from finding suitable employment, and diminishes their standard of living (6). People with DRE often suffer from social stigmas associated with the disease (7,8).

All of these factors have a great influence on impaired quality of life (QoL).

The purposes of addressing QoL include improving patient care, differentiating and assessing the suitable treatment options, and evaluating the distribution of healthcare resources. Thus, an integral approach consisting of physical, social, psychological, and emotional assessments is required in assessing QoL in individuals with DRE. These areas go further on the assessment of seizure frequency and severity, and adverse effects of medications, i.e., towards an understanding of the impact of epilepsy on daily life. In our country, the studies on QoL in patients with DRE are very limited. Therefore, the present study was conducted to assess the QoL in patients with DRE and various variables having significant association with it.

## Material and Methods

This study recruited 50 adult patients DRE as per the ILAE criteria at PGIMS, Rohtak. All participants were fully informed about the aim of research and written informed consent was obtained from them. All study subjects were subjected to detailed investigations and clinical examinations. The study was approved by the ethics committee of the Pt B D Sharma University of Health Sciences (E-002769). Patients with non-epileptiform seizures, lack of compliance with treatment, history of substance or alcohol abuse, significant cognitive dysfunction, any antedating psychiatric condition before the start of seizures were excluded from the study.

We employed the QoL in epilepsy-31 (QOLIE-31) questionnaire as the main data collection tool. The QOLIE-31 inventory

consists of 31 items. It includes the subscales that appeared to be the most important from reports by patients with epilepsy. The questionnaire comprises seven different scales: Seizure Worry (five items), Emotional Well-Being (five items), Energy/Fatigue (four items), Social Function (five items), Cognitive Function (six items), Medication Effects (three items), an Overall QoL (two items). In addition, there is one single item covering overall health. The scale is scored from 0 to 100. High scores reflect that the QoL is high (9).

### Statistical Analysis

Categorical variables are presented as number and percentage and continuous variables are presented as mean  $\pm$  standard deviation and median. The normality of the data was tested using the Kolmogorov-Smirnov test. If normality was rejected, the non-parametric test was used. Quantitative variables were compared using the independent t-test between the two groups and analysis of variance (ANOVA) between more than two groups. The Spearman rank correlation coefficient was used to assess the association of various parameters with each other. A p value of <0.05 was considered statistically significant. Analysis was performed using the Statistical Package for the Social Sciences version 21.0 software package.

## Results

The mean age of the patients was 28.48 $\pm$ 11.66 years, 36% were females, most of them were housewives, and 56% were unmarried (Table 1). The majority were educated up to primary school and none was post graduate because most of the population

Table 1. Participants characteristics and quality of life in epilepsy-31

Baseline characteristics			
Scale	Level	Mean $\pm$ SD	P value
Age	$\leq$ 20 (n=17)	41.24 $\pm$ 5.69	0.602
	21-30 (n=18)	38.03 $\pm$ 9.2	
	31-40 (n=9)	38.07 $\pm$ 7.55	
	>40 (n=6)	39.36 $\pm$ 6.13	
Sex	Female (n=18)	41.43 $\pm$ 6.26	0.128
	Male (n=32)	38.08 $\pm$ 7.86	
Marital status	Married (n=22)	42.71 $\pm$ 4.63	0.003
	Unmarried (n=28)	36.6 $\pm$ 8.13	
Educational status	Primary (n=34)	37.8 $\pm$ 8.03	0.102
	Secondary (n=12)	41.94 $\pm$ 4.91	
	Graduate (n=4)	44.06 $\pm$ 4.71	
Socio-economic status	Lower (n=3)	32.07 $\pm$ 7.03	<0.0001
	Lower middle (n=11)	43.18 $\pm$ 3.95	
	Upper lower (n=25)	41.46 $\pm$ 6.4	
	Upper middle (n=1)	36.06 $\pm$ 0	

SD: Standard deviation

resided in rural areas. Almost half belonged to the upper lower class, followed by the lower class of Kuppuswamy socioeconomic status scale 2018. Most of the patients were students, followed by laborers and farmers. Focal seizures constituted 30% of the total. Uncontrolled seizures were present in 68% of patients. The mean QOLIE-31 score was  $39.29 \pm 7.43$ . The clinical and demographic factors affected the total QOLIE-31 score and also the sub-scores, as given in Table 2 (Figure 1). QoL was affected by the age of seizure onset, sex, education, type of seizure, control of seizure, and duration of seizure, but the association was not significant. There was a significant association between socioeconomic status, marital status, and seizure frequency with QoL.

Seizure frequency was negatively correlated with the total QoL score with a correlation coefficient of  $-0.365$  ( $p=0.009$ ), energy/fatigue ( $r=-0.306$ ) and social function ( $r=-0.307$ ), which was significant (Table 3). Seizure frequency was negatively correlated with other domain sub scores of QOLIE-31, but the correlation was not significant ( $p>0.05$ ).

On performing univariate linear regression, seizure frequency, marital status, and socio-economic status were the significant factors affecting the total QoL score (Table 4).

After adjusting for confounding factors, both seizure frequency and marital status independently affected the total score according to multivariate linear regression (Table 5) (Figure 2).

### Discussion

Epilepsy is a common chronic neurologic disorder. Seizures occur episodically, but they worsen social functioning and emotional well-being, and also affect financial status. Thus, the overall assessment of QoL is of crucial importance. The evaluation of QoL is a novel measure to assess the outcome of epilepsy and to design appropriate interventions. In the present study, seizure frequency was the most important factor that determined the QoL. Apart from this, socioeconomic status and marital status also affected QoL. Age of seizure onset, sex, duration of seizures, and seizure types had no significant association.

Cramer et al. (10) reported that the total QOLIE-31 score in patients with epilepsy varied from 40 to 60 points. However, it was low  $-39.29 \pm 7.43$  in the present study and compared with other studies conducted in different countries (11,12). The difference can be attributed to factors such as the availability of healthcare services, difference in cultures, lack of knowledge, and financial status, leading to non-adherence to treatment. This result validates the elaboration of solutions for improving the psychosocial healthcare services for countries with patients with epilepsy with low QoL.

High seizure frequency had a significant influence on all domains of QoL in this study. This is in line with the results of various studies

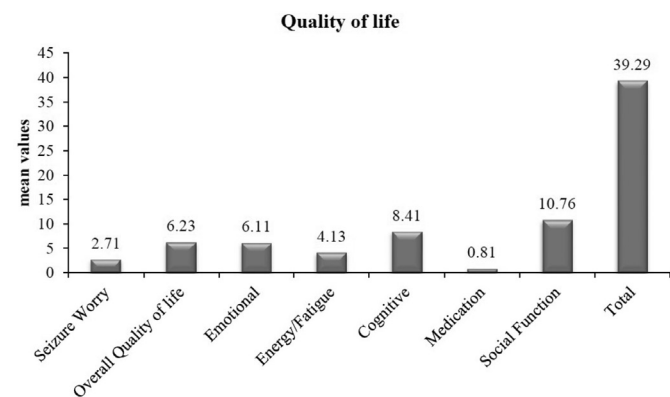


Figure 1. Quality of life with various factors

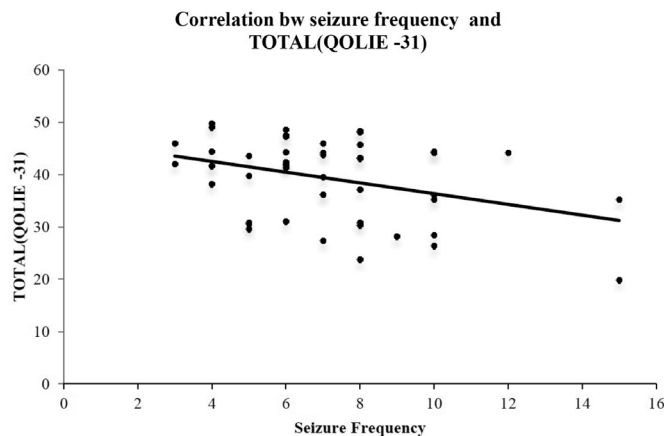


Figure 2. Correlation of seizure frequency with quality of life QOLIE-31: Quality of life in epilepsy-31

Quality of life	Mean ± SD	Median	Minimum-maximum	Inter quartile range
Seizure worry	2.71±2.66	1.97	0-14.4	1.250-3.300
Overall quality of life	6.23±1.05	6.3	3.5-9.4	6.300-7
Emotional	6.11±1.99	6	3-10.8	4.800-7.200
Energy/fatigue	4.13±1.29	4.5	0.6-7.2	3-4.800
Cognitive	8.41±3.01	9.45	1.12-13.42	5.400-10.900
Medication	0.81±0.43	0.83	0-2.33	0.490-0.990
Social function	10.76±1.77	11.13	5.25-14.28	10.080-12.180
Total	39.29±7.43	41.89	19.79-49.7	35.260-44.260

SD: Standard deviation

**Table 3. Correlation of total scores of quality of life in epilepsy-31 and other baseline characteristics**

	<b>Correlation coefficient</b>	<b>P value</b>
Age at seizure onset (Years)	-0.01	0.9463
Age (Years)	-0.144	0.317
Last episode	0.147	0.31
Seizure duration (Years)	-0.027	0.855
Seizure frequency	-0.365	0.009

Analyzed using Spearman rank correlation

that proved seizure frequency to be a significant inverse predictor of QoL among different domains. In a study conducted by Guekht et al. (13) a significant association between QoL and seizure frequency, along with a significant but rather weak association between frequency of seizures and almost all subscales of QoL was noted. We revealed significant dependence between frequency of seizures and subscales of QoL: energy/fatigue and social functioning. High seizure frequency, by limiting usual daily activities, leads to impairment of physical, social, and emotional functioning, and finally to general deterioration of one's QoL. Although seizure frequency was also negatively correlated with other subscales as Seizure Worry, Overall QoL, Cognitive Functioning, Medication Effects, and Emotional Well-being, the correlation was not significant.

**Table 4. Univariate linear regression to find out significant factors affecting total score of quality of life**

	<b>Unstandardized coefficients</b>		<b>Standardized coefficients</b>	<b>P value</b>	<b>95.0% Confidence interval for B</b>	
	<b>B</b>	<b>Standard error</b>	<b>Beta</b>		<b>Lower bound</b>	<b>Upper bound</b>
Seizure frequency (no. of seizures/year)	-1.024	0.377	-0.365	0.009	-1.782	-0.266
Age (Years)	-0.067	0.092	-0.105	0.469	-0.251	0.117
Sex (Male taking female as reference)	-3.348	2.160	-0.218	0.128	-7.690	0.994
Marital Status (Unmarried)	-6.108	1.950	-0.412	0.003	-10.029	-2.187
Age at seizure onset	-0.061	0.096	-0.091	0.530	-0.255	0.133
Seizure type (focal taking GT-CS as reference)	-2.247	2.295	-0.140	0.332	-6.862	2.368
Seizure duration (Years)	-0.028	0.138	-0.029	0.841	-0.305	0.249
Controlled/uncontrolled (U Taking C as Ref)	-2.820	2.241	-0.179	0.214	-7.325	1.685
Last episode (Months)	0.219	0.157	0.198	0.168	-0.096	0.534
<b>Education (primary as reference)</b>						
Secondary	4.139	2.475	0.244	0.102	-0.849	9.127
Graduate	6.267	4.125	0.245	0.137	-2.100	14.633
<b>Socio economic status (lower class as reference)</b>						
Lower middle	11.107	2.397	0.703	0.0001	6.137	16.078
Upper lower	9.394	2.265	0.569	0.0002	4.801	13.988
Upper middle	3.990	7.318	0.155	0.596	-11.955	19.935
<b>Timing of seizure (day as reference)</b>						
Both	-0.622	2.747	-0.038	0.822	-6.193	4.950
Nocturnal	0.431	2.561	0.028	0.867	-4.758	5.620

GT-CS: Generalized tonic-clonic seizures

**Table 5. Multivariate linear regression to determine significant factors affecting total quality of life score**

	<b>Unstandardized coefficients</b>		<b>Standardized coefficients</b>	<b>P value</b>	<b>95.0% Confidence interval for B</b>	
	<b>B</b>	<b>Standard error</b>	<b>Beta</b>		<b>Lower bound</b>	<b>Upper bound</b>
Seizure frequency (no. of seizures/year)	-1.722	0.478	-0.665	0.005	-2.787	-0.657
Marital status (Married)	-11.719	4.692	-0.461	0.032	-22.173	-1.265

Marital status had a significant influence on all domains of QoL in the present study. These findings were consistent with the results of the study conducted by Singh et al. (14) which showed that the mean QOLIE-9 total scores were 16.66, 19.74, 20.13, and 24.00 in married, widowed, unmarried, and separated individuals, respectively. The differences in the means were statistically significant in ANOVA ( $p=0.002$ ). This implies that marriage confers a benefit to QoL (14). The marital relationship is an important constituent of family and provides social support and satisfaction, and failure to maintain marriage goes against social norms. Married individuals report positive features with better physical and psychological health (15). The spouse is mostly the caregiver of the patient and poor social integration in epilepsy can lead to inappropriate social behavior and exclusion (16). Patients with DRE seek supportive relationships to improve their QOL.

The majority of patients in the present study were from the upper lower class (50%), followed by the lower (26%) and lower middle class (22%). In the present study, it was seen that the association of QoL with socio-economic status was significant, and also the mean total score values increased with increased educational level, but the increase was not significant. Similar results were reported by Choi-Kwon et al. (17) Villanueva et al. (18) showed that the educational level of patients with drug-responsive epilepsy was higher than that of patients with DRE. In comparison to general population statistics, the members of the present group with continuing seizures experienced more unemployment, and lived more than others with high deprivation.

People with epilepsy frequently report diminished acculturation, lack of self-compliance, feeling condemned, reduced financial potential, and diminished aspiration (19,20). Though attitudes towards people with epilepsy have improved, stigmatization continues to negatively impact their psychological well-being and QoL, influencing their marital relationships, employability, and self-image. Thus, initiatives to improve the access of psychological services may help to alleviate the discrepancy against those who are socio-economically disadvantaged.

#### Study Limitations

The present study was associated with certain limitations. The small sample size was the major limitation. Therefore, in the future, more such studies that target the public understanding of epilepsy are required so that special programs can be established.

#### Conclusion

In the present study, the QOLIE-31 total score in DRE was  $39.29 \pm 7.43$ . Seizure frequency and marital status were independent variables affecting the total QoL score. An association of QoL with socioeconomic status was also seen. The management of epilepsy should focus more on psychosocial problems and medical comorbidities, initiate appropriate interventions for improving societal stigma, social functioning, and emotional status. The social consequences of seizures are more difficult to control than seizures themselves.

#### Ethics

**Ethics Committee Approval:** Our study approved by ethical committee of Pt B D Sharma university of health Sciences Rohtak (Haryana) INDIA (Decision no: E-002769).

**Informed Consent:** informed consent was taken from all study subjects

**Peer-review:** Externally and internally peer-reviewed.

#### Authorship Contributions

Surgical and Medical Practices: D.J., A.B., Concept: H.K.A., Design: H.K.A., D.J. Data Collection or Processing: A.B., Analysis or Interpretation: D.J., H.K.A., Literature Search: A.B., D.J., Writing: A.B., D.J., H.K.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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