

# The Impact of Affective State on Quality of Life in Focal Epilepsy in Turkey

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ABSTRACT

**Context:** Seizures and accompanying situations including social, medical, and psychiatric problems threaten the quality of life (QOL) in patients with epilepsy. The World Health Organization defines health is a state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity.

**Aims:** This study examines the prevalence of both depression and anxiety symptoms and also impact of the affective state on QOL in patients with focal epilepsy in Turkey. **Settings and Design:** One hundred and five patients with focal epilepsy over 18 years old were included in this study. The patients were classified into four groups according to the presence of AS and seizure control.

**Subjects and Methods:** Patients' affective symptoms (AS) and QOL were examined using the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and QOL in Epilepsy Inventory-31 (QOLIE-31). **Statistical Analysis Used:** We used descriptive statistics, Chi-square test, independent samples *t*-test, one-way analysis of variance, Mann-Whitney U-test, Kruskal-Wallis H-test, and also Pearson's and Spearman's correlation test for correlations. **Results:** There were positive correlations between total QOLIE-31 score and epilepsy surgery, employment, and seizure freedom, whereas negative correlations were found with antiepileptic drug use, anxiety, and depression. Statistically significant differences were found in QOLIE-31 totals and subscores between Groups 3 and 4 ( $P < 0.05$ ). **Conclusions:** The presence of AS has a negative impact on QOL in patients with focal epilepsy. Physicians should be aware that psychiatric comorbidities in epilepsy have a severe impact and epilepsy treatment requires comprehensive management.

**KEYWORDS:** Affective state, anxiety, depression, epilepsy, quality of life, Quality of Life in Epilepsy Inventory-31

## INTRODUCTION

Epilepsy is a widespread neurologic disorder, a prevalence of about 1% in Turkey, severely influencing community health.<sup>[1-3]</sup> It threatens drastically the quality of life (QOL) in epilepsy patients because of accompanying situations including social, medical, and psychiatric problems along with seizures.

The exact aim of epilepsy treatment is still the cessation of seizures; however, the World Health Organization defines health is a state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity.<sup>[4]</sup>

This study aims to assess the occurrence of depression and anxiety symptoms, the impact of affective

symptoms (AS), and also the sociodemographic and clinical factors affecting QOL in patients with focal epilepsy in Turkey.

## SUBJECTS AND METHODS

### Subject and data collection

The retrospective study was carried out in keeping with the 1964 Helsinki Declaration and its later adjustments. Written agreement form was approved from all

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**How to cite this article:** Taskiran E, Matur Z, Gül G, Bebek N, Baykan B, Gökyigit A, et al. The impact of affective state on quality of life in focal epilepsy in Turkey. J Neurosci Rural Pract 2019;10:267-72.

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| <b>Quick Response Code:</b><br> | <b>Website:</b><br>www.ruralneuropractice.com |
|  | <b>DOI:</b><br>10.4103/jnpr.jnpr_324_18       |

participants by e-mail or post. One hundred and five adult patients (48 males, mean age  $35.9 \pm 9.7$ ) with focal epilepsy who were followed up by our epilepsy outpatient clinic were included in the study. Those with psychiatric and mental disorders that could interfere with their capacity to respond to questions were excluded from the study.

Patients' AS and QOL, sociodemographic circumstances, and clinical factors related to the disease that may impact on patients' QOL were investigated. Data were collected from patient charts and surveys. Questionnaires were performed by face-to-face or telephone interviews. Survey of a patient lasted about 40 min.

The patients were categorized into four groups, considering AS and seizure control: Group 1 with good seizure control and no AS (38 patients), Group 2 with good seizure control and AS (6 patients), Group 3 with poor seizure control and no AS (30 patients), and Group 4 with poor seizure control and AS (31 patients).

We investigated age, gender, marital status, education, working status, and income level among the sociodemographic factors. Marital status was ascertained as married or single. Education up to high school was categorized as low-degree education. Working status was stated as working, homemaker, retired, student, and unemployed. Income level was based on the patient's individual earned income.

We assessed clinical features consisting of seizure type and frequency, age at onset of epilepsy, epilepsy duration, antiepileptic drug (AED) treatment, and presence of epilepsy surgery, history of febrile seizure, presence of magnetic resonance imaging (MRI) abnormality, and any psychiatric comorbidity that was diagnosed and under treatment by a psychiatrist. The patients, who did not have seizures for at least 1 year, were accepted as having good seizure control. The patients were divided into three classes according to their AED usage as follows: no drug, monotherapy, and polytherapy.

## Questionnaires

### *Quality of Life in Epilepsy Inventory-31*

We used Turkish version of QOL in Epilepsy Inventory-31 (QOLIE-31),<sup>[5]</sup> which is an extensively embraced epilepsy-specific QOL screening tool and a shortened version of QOLIE-89.<sup>[6]</sup> QOLIE-31 has seven subscales comprising overall QOL, seizure worry, emotional well-being, energy/fatigue, cognitive effects, medication effects, and social functioning; higher QOLIE-31 scores signify better QOL.<sup>[7]</sup> The overall Cronbach's alpha value of Turkish version of QOLIE-31 was 0.91.<sup>[5]</sup> All scores were computed in line with the QOLIE-31 scoring form.

### *Beck Anxiety Inventory and Beck Depression Inventory*

The Beck Anxiety Inventory (BAI) having 21 items describing common symptoms of anxiety measures severity of anxiety, scaling normal (0–21), mild disruption (22–26), moderate disruption (27–31), and severe disruption (32–63).<sup>[8]</sup> The Beck Depression Inventory (BDI) measures the severity of depression, having cutoff points of 0–15 for normal; 16–19 for mild depression; 20–23 for moderate disruption; and 24–63 for severe disruption. Participants with BAI scores above 21 points or BDI scores above 15 points were considered to have AS. Cronbach's  $\alpha$  range of the Turkish version of BDI and BAI is 0.74 and 0.93, respectively.<sup>[8,9]</sup>

## Data analysis

We used IBM SPSS (Version 22.0. Armonk, NY: IBM Corp.) to perform the statistics. Categorical variables were presented as a count with percentage while continuous variables as means with standard deviations and ranges. In multiple group comparisons, Chi-square test was used to compare frequency distributions and one-way analysis of variance (ANOVA) to compare means in normal variables, Kruskal–Wallis H-test in nonnormal variables. When found a statistically significant difference, independent sample *t*-test for normal variable and Mann–Whitney U-test for nonnormal variable were used for pair-wise comparisons after Bonferroni correction. Correlations between the clinical and demographic data and overall QOLIE-31 scores were evaluated with Pearson's correlation test in normal variable and Spearman's correlation test in nonnormal variable.

## RESULTS

One hundred and five patients were included in this analysis. Detailed sociodemographic and clinical data of all patients are presented in Tables 1 and 2. The mean age of the patients was  $35.9 \pm 9.7$  (range, 18–71 years) years. Of the 105 patients, 57 (54%) patients were women and 55 (49%) patients were married. Forty-eight (46%) patients had high-level education, 37 (35%) patients were employed, and 44 (42%) patients had income. The mean onset age of the epilepsy was  $14.7 \pm 11.8$  years (range, 0.5–47 years) and the mean duration of epilepsy was  $20.6 \pm 10.3$  years (range, 3–50 years). Forty-three (41%) patients had a febrile seizure. Focal seizures with deterioration in consciousness or awareness, as defined in the new classification, were the most commonly presented seizure type among all patients.<sup>[10]</sup> In addition, 51 (49%) patients had focal seizures and 48 (46%) had several other types of seizure. Ninety (86%) patients had a lesion in their MRI, 59 (66%) with mesial temporal sclerosis. Seventy-four (70.5%)

patients underwent epilepsy surgery, and the mean surgery age was  $30.2 \pm 8.1$  years (range, 16–60 years). Epilepsy surgery was more frequent in Group 1 (97%) and Group 2 (83%) (Pearson  $\chi^2$ ,  $P < 0.001$ ). Forty-four (42%) of all patients and 42 (57%) of the 74 patients who underwent surgery had good seizure control. Twenty-seven patients (26%) had four or more

seizures per month (10 from Group 3 and 17 from Group 4) [Table 2]. AEDs were discontinued for at least 1 year in 12 patients (11 from Group 1 and 1 from Group 2) [Table 2], 11 of whom had undergone epilepsy surgery. The percentage of patients without AED usage was the highest in Group 1 (29%). Sixty-seven patients (64%) were on polytherapy medication.

**Table 1: Sociodemographic features of the group**

|                        | Group 1 (n=38)    | Group 2 (n=6)    | Group 3 (n=30)    | Group 4 (n=31)   | Total (n=105)    |
|------------------------|-------------------|------------------|-------------------|------------------|------------------|
| Age                    |                   |                  |                   |                  |                  |
| Mean±SD (range), years | 38.8±10.6 (20-71) | 37.7±8.6 (28-50) | 34.1±10.3 (18-57) | 36.1±8.5 (19-58) | 35.9±9.7 (18-71) |
| Sex                    |                   |                  |                   |                  |                  |
| Female                 | 22                | 5                | 13                | 17               | 57               |
| Male                   | 16                | 1                | 17                | 14               | 48               |
| Marital status         |                   |                  |                   |                  |                  |
| Married                | 23                | 2                | 11                | 15               | 51               |
| Single                 | 15                | 4                | 19                | 16               | 54               |
| Education              |                   |                  |                   |                  |                  |
| Low                    | 16                | 3                | 16                | 22               | 57               |
| High*                  | 22                | 3                | 14                | 9                | 48               |
| Occupation             |                   |                  |                   |                  |                  |
| Working                | 18                | 2                | 9                 | 8                | 37               |
| Homemaker              | 11                | 1                | 4                 | 5                | 21               |
| Retired                | 2                 | 0                | 2                 | 3                | 7                |
| Student                | 0                 | 0                | 3                 | 1                | 4                |
| Unemployed             | 7                 | 3                | 12                | 14               | 36               |
| Income earning         | 20                | 2                | 11                | 11               | 44               |

\*High means high school and above. n: Number of patients, SD: Standard deviation

**Table 2: Clinical features**

|                              | Group 1 (n=38)   | Group 2 (n=6)    | Group 3 (n=30)     | Group 4 (n=31)   | Total (n=105)      |
|------------------------------|------------------|------------------|--------------------|------------------|--------------------|
| Onset age of epilepsy        |                  |                  |                    |                  |                    |
| Mean±SD (range), years       | 14.8±11.5 (1-47) | 13.0±6.4 (5-23)  | 12.6±13.1 (0.5-46) | 16.7±11.7 (1-41) | 14.7±11.8 (0.5-47) |
| Epilepsy duration            |                  |                  |                    |                  |                    |
| Mean±SD (range), years       | 21.3±10.2 (3-42) | 22.2±2.9 (18-26) | 21.1±11.7 (3-50)   | 19.0±10.1 (3-47) | 20.6±10.3 (3-50)   |
| Seizure type                 |                  |                  |                    |                  |                    |
| GTC                          | 2                | 0                | 0                  | 1                | 3                  |
| Focal                        | 21               | 5                | 15                 | 13               | 54                 |
| More than one type           | 15               | 1                | 15                 | 17               | 48                 |
| Seizure frequency            |                  |                  |                    |                  |                    |
| >4/months                    | 0                | 0                | 10                 | 17               | 27                 |
| ≤4/months->12/year           | 0                | 0                | 14                 | 8                | 22                 |
| ≤12/year                     | 0                | 0                | 6                  | 6                | 12                 |
| Seizure free at least 1 year | 38               | 6                | 0                  | 0                | 44                 |
| Epilepsy surgery             | 37               | 5                | 14                 | 18               | 74                 |
| Mean age of surgery          |                  |                  |                    |                  |                    |
| Mean±SD (years), range       | 29.6±7.4 (19-60) | 28.4±7.8 (23-42) | 30.5±11.4 (16-55)  | 29.6±7.4 (17-45) | 30.2±8.1 (16-60)   |
| Drug treatment               |                  |                  |                    |                  |                    |
| No drugs                     | 11               | 1                | 0                  | 0                | 12                 |
| Monotherapy                  | 15               | 4                | 4                  | 3                | 26                 |
| Polytherapy                  | 12               | 1                | 26                 | 28               | 67                 |
| Psychiatric comorbidity      | 10               | 4                | 9                  | 12               | 35                 |

n: Number of patients, SD: Standard deviation, GTC: Generalized tonic-clonic

Of 105 patients, 37 patients (35%) showed ASs (anxiety and/or depression) in the measurement of BAI and BDI. BAI revealed anxiety in 30 patients (29%) and depression was seen in 35 (33%) after the BDI. Thirty-five patients (33%) had a psychiatric comorbidity at the time of the survey and were on psychiatric drugs and 12 of those (34%) who were on psychiatric drugs had still ASs detected with BDI and BAI.

The mean total score of QOLIE-31 was  $57.2 \pm 27.2$  (range, 6–100). There were statistically significant differences in all of the subscores and total scores of QOLIE-31 between groups (ANOVA,  $P < 0.001$ ). *Post hoc* comparisons with Bonferroni correction showed statistically significant differences in all of the subscores and total scores of QOLIE-31 between Groups 3 and 4 ( $P < 0.05$ ), and also between Group 1 and the other three groups ( $P \leq 0.001$ ). In addition, those who have ASs with or without good seizure control showed lower subtotal and total QOLIE scores [Table 3]. A total of 39 (86.7%) patients with higher QOLIE scores had epilepsy surgery but only 6 (13.3%) patients without surgery ( $P = 0.001$ ).

The determinants that correlated QOL positively and negatively are shown in Table 4. Epilepsy surgery, seizure freedom, and employment positively affected QOL; however, AS and AED usage had negative effects on QOL.

## DISCUSSION

The frequency of depression and anxiety in our cohort was 33% and 29%, respectively. We found that the total QOLIE-31 score had positive correlations with epilepsy surgery, employment, and seizure freedom; however, negative correlations with AED usage, anxiety, and depression.

Prior studies have established the frequency of depression in resistant and well-controlled epilepsy was higher than healthy population, ranging from 20% to 55% and from 3% to 9%, respectively.<sup>[11]</sup> A prospective study

accomplished in the epilepsy clinic of a tertiary hospital in Turkey determined the frequency of depression and anxiety as 42% and 64.4%, respectively.<sup>[12]</sup> In this study, 37 patients (35%) showed ASs (anxiety and/or depression) in the measurement of BAI and BDI, while the frequency of depression and anxiety symptoms in our cohort was 33% and 29%, respectively. The frequency of depression and anxiety in this study is in the same range as reported in other literature.

Psychiatric comorbidities or ASs in patients with focal epilepsy are still an important challenge in epilepsy treatment for healthy life and good QOL. Patients with ASs (with or without good seizure control) showed lower total scores and subscores of QOLIE in our analysis. This suggests that we need to adopt a holistic perspective and treat patients with epilepsy. With that in mind, ASs should be considered during diagnosis and follow-up period of epilepsy.

Most of the previous studies related to QOL in patients with epilepsy suggested that the greatest significant determinant of QOL was seizure freedom.<sup>[13,14]</sup> However, there are also reports addressing depression is one of the most important factors affecting QOL in epilepsy.<sup>[15-17]</sup> Park *et al.* reported that the most intensive predictor of QOL was AS, after that seizure control and MRI abnormality. This study has also noted that patients with drug-resistant epilepsy without AS had significantly better QOL than patients with well-controlled epilepsy with AS.<sup>[18]</sup> QOL was negatively affected by the presence of AS in our cohort. In patients with AS, total and subscores of QOL were lower than others [Table 3]. Consistent with their results, our findings demonstrate that the presence of AS has an impact independent of seizure frequency on QOL because even with good seizure control, all patients with AS scored lower across all QOL subscales than individuals without AS in our analysis.

Among the subscores of QOLIE-31, the lowest score was for medication effect and seizure worry. Which

**Table 3: Subscores and total scores of Quality of Life in Epilepsy Inventory-31**

| Scores               | Group 1   | Group 2   | Group 3   | Group 4   | Total     | P*     | P**    |
|----------------------|-----------|-----------|-----------|-----------|-----------|--------|--------|
| Seizure worry        | 6.8±1.9   | 3.3±2.8   | 3.8±1.9   | 1.8±1.4   | 4.2±2.8   | <0.001 | <0.001 |
| Overall QOL          | 11.1±2.6  | 6.5±3.8   | 8.1±2.7   | 5.5±2.4   | 8.3±3.5   | <0.001 | 0.001  |
| Emotional well-being | 12.3±2.0  | 5.9±4.7   | 9.7±2.2   | 5.7±2.5   | 9.2±3.7   | <0.001 | <0.001 |
| Energy fatigue       | 9.6±1.9   | 5.5±2.7   | 7.5±1.8   | 3.9±2.0   | 7.1±3.0   | <0.001 | <0.001 |
| Cognitive            | 22.7±5.0  | 10.0±8.7  | 15.6±7.5  | 7.1±4.6   | 15.3±8.7  | <0.001 | <0.001 |
| Medication effect    | 2.5±0.7   | 1.2±1.0   | 1.4±1.1   | 0.8±0.5   | 1.6±1.1   | <0.01  | <0.01  |
| Social function      | 18.0±3.5  | 6.1±7.5   | 10.9±4.8  | 4.7±3.2   | 11.3±6.9  | <0.001 | 0.040  |
| Total QOLIE          | 82.9±14.4 | 38.5±29.8 | 57.1±18.3 | 29.5±12.0 | 57.2±27.0 | <0.001 | <0.001 |

\*Differences between all groups (ANOVA,  $P < 0.05$ ), \*\*Differences between Group 4 and Group 3 (ANOVA, *post hoc* comparisons with Bonferroni correction,  $P < 0.05$ ). QOL: Quality of life, QOLIE: QOL in Epilepsy Inventory, ANOVA: Analysis of variance

**Table 4: Variables and correlation with overall Quality of Life in Epilepsy Inventory-31 score**

|                                     | <i>P</i> | <i>r/f***</i> |
|-------------------------------------|----------|---------------|
| Age                                 | 0.681    | 0.041         |
| Male sex                            | 0.972    | 0.003         |
| Age at epilepsy onset               | 0.510    | -0.066        |
| Duration of epilepsy                | 0.191    | 0.131         |
| Being single                        | 0.291    | -0.104        |
| High education                      | 0.061    | 0.184         |
| Employment                          | 0.016    | 0.235         |
| Presence of income earning          | 0.187    | 0.130         |
| History of febrile seizure          | 0.446    | 0.081         |
| Presence of MRI lesion              | 0.133    | -0.151        |
| Presence of multiple seizure types  | 0.961    | -0.005        |
| Epilepsy surgery                    | <0.001   | 0.350         |
| Antiepileptic drug usage            | <0.001   | -0.475        |
| Presence of psychiatric comorbidity | 0.133    | -0.148        |
| Presence of depression*             | <0.001   | -0.601        |
| Presence of anxiety**               | <0.001   | -0.740        |
| Seizure freedom                     | <0.001   | 0.605         |

\*Detected with BDI, \*\*BAI, \*\*\**r* for continuous variables and *f* for nominal variables. MRI: Magnetic resonance imaging, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory

subscores scores have more impact on QOL is not clear in the literature. One study showed that the lower QOL scores were in the energy/fatigue and emotional well-being subscores for patients with depressive symptoms.<sup>[19]</sup> Whereas Gaus *et al.* and Jacoby *et al.* stated that the effects of medication and seizure worry contributed the most toward affective state in QOL.<sup>[20,21]</sup> This discrepancy may be related with sociocultural aspects of life such as the level of treatment adherence, perceived stigma, and the level of social support, which shows that many factors may affect QOL subscores in patients with epilepsy.

It was suggested that polytherapy affects QOL negatively in patients with epilepsy, and patients on polytherapy have lower QOL scores than those on monotherapy in literature.<sup>[22,23]</sup> There was a negative correlation between drug use and QOL, while seizure freedom was found as a favorable factor affecting QOL in our study. The total and medication effect subscores of QOLIE-31 were the lowest in Group 4, which consisted of patients with poor seizure control and AS, as well as the highest polytherapy rate [Table 4]. Eleven of 12 patients using no drug had higher QOLIE scores. Only one of those was well-educated patient had lower score. This patient was women and single. She had gone epilepsy surgery and became seizure free but had effective symptom.

There was a positive correlation between total QOLIE-31 score and epilepsy surgery in our study. Epilepsy surgery is currently posited as one of the most

important factors on QOL. Aydemir *et al.* showed that QOL of patients underwent temporal lobe epilepsy surgery was improved, and the postsurgery group had higher scores on all subscales of 36-Item Short Form Health Survey.<sup>[24]</sup> In this study, 86.7% of the patients with higher QOLIE scores had epilepsy surgery but only 13.3% of patients without surgery. The patients who underwent epilepsy surgery usually showed a significant improvement of QOL with a marked lessening in seizure frequency. This improvement was prominent in patients becoming seizure free for at least 1 year and using fewer AEDs after surgery [Table 1]. All of the 34 patients who underwent epilepsy surgery in Group 1 became seizure free and showed the highest QOL scores. In addition, this group was better than others in the evaluation of all subscores of QOLIE-31 (e.g., seizure worry, social function, medication effect, and energy fatigue), which may be related with lower seizure frequency and fewer AED usage. This clearly shows the beneficial effects of epilepsy surgery are correlated with improved QOL in line with literature.<sup>[25,26]</sup>

Being unemployment affected QOL negatively in our study. Thirty-six (34%) of our patients were unemployed. The highest ratio of unemployment was in Group 4 (14/30) who, unsurprisingly, had the lowest QOL scores. In the literature, however, the relationship between employment status and QOL is controversial. Some studies reported that employment status was one of the main factors affecting QOL,<sup>[23,27,28]</sup> whereas other stated that socioeconomic status did not predict QOL.<sup>[22]</sup>

Although the duration of epilepsy,<sup>[14,22]</sup> MRI abnormality,<sup>[18]</sup> and seizure type (14) were previously found to be among factors that variously affected QOL in the literature, we could not determine the correlation of QOL with these three factors in our study. Our study also did not determine any correlation between marital status and QOL, epilepsy onset age, sex, and level of education. However, the highest rate of marriage was found in Group 1. The presence of AS and bad seizure control affect the family stabilities, marriage rates, and also social life according to this analysis [Table 1]. The patients and their relatives as well as the whole community should be informed about unnecessary stigma because a good marriage can have a positive effect on epilepsy control.

We had some limitations in this study. One was that we carried out this study through telephone conversations and based on self-reports. The other was the lower number of patients with good seizure control and AS in Group 2.

## CONCLUSION

In short, our findings suggest that the presence of AS has an impact on QOL, independent of seizure frequency.

Physicians should be aware of the severe impact that psychiatric comorbidities have on patients with epilepsy. Consideration and treatment of AS in these patients is just as important as seizure frequency for improving the QOL patients with epilepsy. The patients with epilepsy should be treated with the holistic perspective with the aim of establishing a healthy life. One additional thing to note is that our study showed that of the 35 patients (33%) with a psychiatric comorbidity who were treated with psychiatric drugs, 12 (34%) still had ASs on their BDI and BAI tests. Our management strategies in patients with epilepsy who have ASs need to be meticulously reviewed.

### Acknowledgment

The authors would like to thank Dr. Tara Stewart for providing language help.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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