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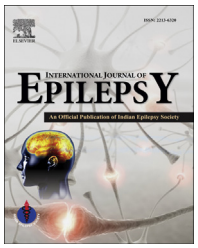

Original Article

Quality of life predictors in patients with epilepsy and cognitive disabilities

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ABSTRACT

Purpose: We aimed to assess the QOL and its predictors in Bulgarian patients with refractory epilepsy (RE) and cognitive problems.
Methods: We conducted a study based on questionnaires designed for people with intellectual disability (the stigma scale, the Glasgow Depression Scale, the Glasgow Anxiety Scale, the Glasgow Epilepsy Outcome Scale – GEOS-35) and a purposeful interview on clinical and social factors of 64 patients (50% men) with RE and cognitive problems.
Results: The mean total score of the GEOS-35 was 76 ± 2.34 (an indicator of low QOL). On univariate analysis, the GEOS-35 total score was associated with seizure frequency and severity, stigma, depression, and anxiety. On multivariate regression analysis predictors of the GEOS-35 total score were anxiety, seizure severity, and stigma $P < 0.001$ ($F = 14.66$). Regarding the GEOS-35 subscales, on multivariate regression analysis, we found that 1. Seizure severity, seizure type, and anxiety were predictors of "concerns about seizures" $P < 0.001$ ($F = 8.99$); 2. Anxiety was the only predictor of "concerns about treatment" $P < 0.001$ ($F = 7.98$); 3. Anxiety and seizure severity were predictors of "concerns about caring" $P < 0.001$ ($F = 12.12$); and 4. Seizure severity and stigma were predictors of "concerns about social impact" $P < 0.001$ ($F = 18.31$).
Conclusions: We have affirmed the low QOL in patients with RE and cognitive problems and its clinical and social determinants. The results from our study prove the necessity of a multidisciplinary approach for quality of life improvement in these patients.

1. Introduction

Quality of life assessment in patients with refractory epilepsy is a result of the refraction of the particular clinical and psycho-social features of the disease through the prism of individual and subjective concepts, relations, and experience. Generally, epilepsy has a great influence on all aspects of quality of life (physical, mental and social health), which is exercised directly – by affecting the physical and mental health, and indirectly – by introducing limitations and decreasing the opportunities for taking part in quality of life improving activities. Epilepsy is more prevalent in people with intellectual disabilities than the general population.[1,2]

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Previous studies have paid scant attention to the quality of life of people with epilepsy and cognitive problems.[2] Knowledge about the specific needs of these patients and the concerns of their families, which could improve skills training, social integration, and quality of life, is insufficient. No study of quality of life (QOL) and its predictors in patients with refractory epilepsy (RE) and cognitive problems has been performed in Bulgaria.

1.1. *Purpose of the study*

Assessment of the quality of life and its predictors in Bulgarian patients with cognitive problems and refractory epilepsy.

2. Patients and methods

The study was performed with the participation of a representative extract of 246 patients with epilepsy who attended the Clinic of Neurology at the University Hospital in Plovdiv, Bulgaria for a regular examination or in cases of unsatisfactory seizure control or adverse events from treatment.

All study procedures were performed after the approval of the Local Ethics Commission at the University of Medicine, Plovdiv. Every patient was introduced to the study design and an informed consent form was signed by the patient or the patient's guardian/caregiver before participation in the study procedures.

The study included 64 patients with RE and cognitive problems who fulfilled the inclusion criteria. We accepted epilepsy as refractory in cases in which adequate seizure control with atleast two potentially effective anti-epileptic drugs prescribed as mono- or polytherapy in maximal tolerated doses had not been achieved for a period of one year or three times longer period than the longest interictal period in the last year. We used the following inclusion criteria: a signed informed consent form; age between 18 and 65 years; a diagnosis of RE; cognitive impairment based on the Evaluation rapide des fonctions cognitives (ERFC)[3] with a score <47 in patients upto 60 years of age and primary education, or <46 in patients between 60 and 65 years of age and less than a primary education or illiteracy; lack of progressive somatic or neurological disease; lack of a simple or complex partial seizure in the last 4 h; and lack of generalised tonic-clonic seizures in the last 24 h. We defined mild cognitive impairment as cases with an ERFC score of 36–46/47, moderate cognitive impairment as cases with a score of 17–35, and severe cognitive impairment as cases with a score of less than 17.

We investigated the correlations between depression, anxiety, demographics (age and gender), degree of cognitive impairment, clinical findings (seizure frequency and severity, seizure type, type of epilepsy, aetiology of epilepsy, focal neurological deficit, and prescribed treatment), stigmatisation, social status (marital status, education, and occupation), and the quality of life. The data were collected by a trained health professional by means of a purposeful interview and examination of the patients' medical documentation.

With the help of their principal caregivers (carers who had participated in care decisions for atleast the preceding three months) 56 patients with mild to moderate intellectual disability completed the Glasgow Depression Scale for people with a Learning Disability (GDS-LD),[4] the Glasgow Anxiety Scale for people with Intellectual Disability (GAS-ID),[5] and the stigma scale.[6] A good reliability and high internal consistency was proven for all of these scales.[4–6]

The Liverpool Seizure Severity Scale (LSSS)[7] was fulfilled by 59 participants who had a seizure in the previous month. In cases with severe cognitive impairment, caregivers completed the LSSS and the carer supplement of the GDS-LD (GDS-CD).[4]

The Glasgow Epilepsy Outcome Scale (GEOS-35) was administered as a measure of health-related quality of life by assessment of clinical, social, and care concerns, as well as treatment outcomes. The scale integrates concerns expressed by clinicians and health practitioners, as well as family and staff carers. It comprises' four subscales: the 1st subscale – "concerns about seizures" (10 items), the 2nd subscale – "concerns about treatment" (nine items), the 3rd subscale – "concerns about caring' (eight items), and the 4th subscale – "concerns about social impact" (eight items). Every item is assessed according to a five-point scale: 0 = "never a concern", 1 = "occasionally a concern", 2 = "fairly often a concern", 3 = "often a concern", and 4 = "very often a concern". The reliability, internal consistency, and validity of the GEOS-35 for use with clinical populations having epilepsy and mental retardation has been demonstrated by Espie et al 2001.[1] In our study, the GEOS-35 was completed by the principal caregivers of all included patients. We accepted the obtained total scores of the scale (corresponding to health-related QOL) as very low (106–140), low (71–105), medium (36–70), and high (1–35).

Data were processed using STATA Version 10 (Stata Corp., College Station, TX, U.S.A.) and SPSS (Statistical Package for the Social Sciences), version 14.0 (SPSS Inc., Chicago, IL, U.S.A.). Results for the quantitative variables are expressed as the mean ± SE (standard error) and results for the qualitative variables are expressed as percentages. The indices of QOL were the principal outcomes. The associations of QOL with depression, anxiety, demographics, degree of cognitive impairment, stigmatisation, and clinical and social findings were tested by means of the χ^2 – Test and F – Test. Pearson's correlation coefficient (r) was used to determine correlations between the above mentioned characteristics. The complex influence of the significant clinical findings was determined by means of multivariate regression analysis. The level of significance was set at $P < 0.05$.

3. Results

Thirty-two (50%) of the participants in our study were men; the remaining 32 participants were women. Their mean age was 44.88 ± 1.84 years. The mean duration of epilepsy was 31.78 ± 1.60 years. The clinical findings, degree of cognitive impairment, depression, anxiety, stigma, and social characteristics of the participants with RE are shown in Table 1.

All study participants had been declared disabled, only two (3.13%) were occupied, and seven (10.94%) had retired on a pension.

The mean total score of the GEOS-35 was low (76 ± 2.34). The mean subscale scores were as follows: the 1st subscale ("concerns about seizures") – 21.11 ± 0.86 (corresponding to

Table 1 – Clinical findings, mental status, social characteristics, and stigma of patients with RE and cognitive problems.

Clinical findings and social characteristics	N	P (%)	SE
Type of epilepsy			
- Partial	33	51.56	6.13
- Generalised	31	48.44	6.13
Type of seizures			
1. Partial			
- Complex partial	2	3.12	–
- Partial with secondary generalisation	4	5.25	6.25
2. Generalised			
- Generalised tonic-clonic	22	34.38	5.98
3. Polymorphic	36	56.25	6.25
Aetiology of epilepsy			
- Idipathic	6	9.37	3.67
- Cryptogenic	36	56.25	6.25
- Symptomatic	22	34.38	5.98
Focal neurological deficit			
- Yes	38	59.37	3.93
- No	26	40.63	3.93
Cognitive impairment			
- Mild	21	32.81	5.92
- Moderate	35	54.69	6.27
- Severe	8	12.50	4.17
Recent seizure frequency			
- No seizures in recent years	5	7.81	3.38
- Low (1–11 seizures/year)	4	6.25	3.05
- High (per month, per week, or daily)	55	85.94	4.38
Seizure severity (LSSS score)			
- Mild (1–20)	3	5.08	–
- Moderate (21–40)	24	40.68	6.45
- Severe (41–60)	30	50.85	6.56
- Very severe (61–80)	2	3.39	–
Treatment:			
- Monotherapy	7	10.94	3.93
- Polytherapy	57	89.06	3.93
Depression (GDS-LD/GDS-CD score)			
- No	38	59.37	6.19
- Yes	26	40.63	6.19
Anxiety (GAS-ID score)			
- No	16	28.57	5.69
- Yes	40	71.43	5.69
Educational level			
- No education and specialised school	19	29.69	5.76
- Elementary	24	37.50	6.01
- Secondary and higher	21	32.81	5.92
Marital status			
- Not married	38	59.38	6.19
- Married	21	32.81	5.92
- Divorced	4	6.25	3.05
- Widowed	1	1.56	–
Stigma			
- None	6	10.72	4.17
- Mild	18	32.14	6.30
- Moderate	18	32.14	6.30
- Severe	14	25.00	5.84

often having concerns), the 2nd subscale ("concerns about treatment") – 16.56 ± 0.63 (corresponding to having concerns fairly often), the 3rd subscale ("concerns about caring") – 17.02 ± 0.66 (corresponding to often having concerns), and the 4th subscale ("concerns about social impact") – 21.09 ± 0.64 (corresponding to often having concerns).

Table 2 – Correlation of seizure frequency with the GEOS-35 total score in patients with RE and cognitive problems.

QOL (GEOS-35 total score)	Seizure frequency			Total
	No seizures in recent years	Low	High	
High N (p%)	1 (33.3%)	0 (0%)	2 (66.7%)	3 (100.0%)
Moderate N (p%)	2 (10.0%)	1 (5.0%)	17 (85.0%)	20 (100.0%)
Low N (p%)	2 (5.6%)	3 (8.3%)	31 (86.1%)	36 (100.0%)
Very low N (p%)	0 (0%)	0 (0%)	5 (100.0%)	5 (100.0%)
Total N (p%)	5 (7.8%)	4 (6.3%)	55 (85.9%)	64 (100.0%)

There was no association of the GEOS-35 total score with gender, age, epilepsy duration, degree of cognitive impairment, focal neurological deficit, seizure type, type of epilepsy, aetiology of epilepsy, therapy, marital status, educational level, and work occupation, $P > 0.05$.

We found that lower GEOS-35 total scores were associated with higher seizure frequency, $P < 0.05$ ($\chi^2 = 7.92$) – Table 2.

Greater seizure severity correlated with lower GEOS-35 total scores, $P < 0.01$ ($\chi^2 = 14.06$); $P < 0.001$ ($r = 0.51$) – Table 3.

Lower GEOS-35 total scores were associated with stigma and its severity, $P < 0.01$ ($\chi^2 = 10.65$); $P < 0.001$ ($r = 0.43$) – Table 4.

Lower GEOS-35 total scores were associated with depression, $P < 0.01$ ($\chi^2 = 7.82$); $P < 0.01$ ($r = 0.35$) – Table 5.

We discovered that lower GEOS-35 total scores were associated with anxiety, $P < 0.001$ ($\chi^2 = 18.18$); $P < 0.001$ ($r = 0.55$) – Table 6.

The multivariate regression analysis predictors of the GEOS-35 total score were anxiety, seizure severity, and stigma. They explained 47% of its variations, $P < 0.001$ ($F = 14.66$).

We obtained the following subscale results:

Seizure type was associated with "concerns about seizures", $P < 0.01$ ($\chi^2 = 10.64$). Of the patients who were often and very often concerned about seizures, 65.7% and 100%, respectively, had polymorphic seizures, $P < 0.01$ ($r = 0.36$).

Seizure frequency was associated with "concerns about seizures", $P < 0.001$ ($\chi^2 = 18.39$), and "concerns about social impact", $P < 0.05$ ($\chi^2 = 8.87$). Of the patients who were often and very often concerned about seizures, 91.4% and 100%, respectively, had high seizure frequencies, $P < 0.001$ ($r = 0.50$). Of the patients who were often and very often concerned about social impact, 90% and 85.7%, respectively, had high seizure frequencies, $P < 0.01$ ($r = 0.31$).

Seizure severity was associated with: "concerns about seizures", $P < 0.05$ ($\chi^2 =$ "concerns about treatment", $P < 0.05$ ($\chi^2 = 7.96$); and "concerns about social impact", $P < 0.01$ ($\chi^2 = 11.11$)). Of the patients who were often and very often concerned about seizures, 65.7% and 100%, respectively, were moderately and severely stigmatised, $P < 0.01$ ($r = 0.34$). Of the patients who were often concerned about treatment, 47.4% were moderately stigmatised and 36.8% were harshly stigmatised, $P < 0.05$ ($r = 0.30$). Of the patients who were very often concerned about social impact, 54.5% were moderately stigmatised and 45.5% were severely stigmatised, and only 12.5% and 13.9%, respectively, of the non-stigmatised participants were fairly often and often concerned about social impact, $P < 0.001$ ($r = 0.42$).

Anxiety was associated with: "concerns about seizures", $P < 0.05$ ($\chi^2 = 7.95$); "concerns about treatment", $P < 0.05$

Table 3 – Correlation of seizure severity with the GEOS-35 total score in patients with RE and cognitive problems.

GEOS-35 total score	Seizure severity (LSSS)				Total
	Mild	Moderate	Severe	Very severe	
High QOL N (p%)	2 (100.0%)	0 (0%)	0 (0%)	0 (0%)	2 (100.0%)
Moderate QOL N (p%)	1 (5.6%)	10 (55.6%)	7 (38.9%)	0 (0%)	18 (100.0%)
Low QOL N (p%)	0 (0%)	14 (41.2%)	19 (55.9%)	1 (2.9%)	34 (100.0%)
Very low QOL N (p%)	0 (0%)	0 (0%)	4 (80.0%)	1 (20.0%)	5 (100.0%)
Total N (p%)	3 (5.1%)	24 (40.7%)	30 (50.8%)	2 (3.4%)	59 (100.0%)

Table 4 – Correlation of stigma with the GEOS-35 total score in patients with RE and cognitive problems.

GEOS-35 total score	Stigma				Total
	No	Mild	Moderate	Severe	
High QOL N (p%)	0 (0%)	2 (100.0%)	0 (0%)	0 (0%)	2 (100.0%)
Moderate QOL N (p%)	5 (25.0%)	8 (40.0%)	3 (15.0%)	4 (20.0%)	20 (100.0%)
Low QOL N (p%)	1 (3.3%)	8 (26.7%)	14 (46.7%)	7 (23.3%)	30 (100.0%)
Very low QOL N (p%)	0 (0%)	0 (0%)	1 (25.0%)	3 (75%)	4 (100.0%)
Total N (p%)	6 (10.7%)	18 (32.1%)	18 (32.1%)	14 (25%)	56 (100.0%)

($\chi^2 = 7.49$); and "concerns about caring", $P < 0.01$ ($\chi^2 = 10.83$). Of patients who were fairly often, often, and very often concerned about seizures, 9 (52.9%), 26 (81.3%), and 4 (100%), respectively, had anxiety, $P < 0.01$ ($r = 0.38$). Of patients who were fairly often and often concerned about treatment, 66.7% and 89.5%, respectively, had anxiety, $P < 0.01$ ($r = 0.36$). Of patients who were fairly often, often, and very often concerned about caring, 50%, 89.3%, and 100%, respectively, had anxiety, $P < 0.01$ ($r = 0.41$).

On multivariate regression analysis, seizure severity, seizure type, and anxiety were found to be predictors of "concerns about seizures". They explained 36% of their variations, $P < 0.001$ ($F = 8.99$). Anxiety was the only predictor of "concerns about treatment" and explained 13% of their variations, $P < 0.001$ ($F = 7.98$). Both anxiety and seizure severity were proven to be predictors of "concerns about caring" and explained 33% of their variations, $P < 0.001$ ($F = 12.12$). Seizure severity and stigma were predictors of "concerns about social impact" and explained 42% of their variations, $P < 0.001$ ($F = 18.31$).

4. Discussion

There is need of a beyond-seizure-counts approach to people with epilepsy and cognitive problems to improve the psychosocial consequences of the disease. The ability to measure the QOL in people with intelligence deficits despite communication limitations has been confirmed by Ventegodt et al (2010).[8] Current knowledge is limited on the long-term effect of seizure disorders on mental health, QOL, and cognition in adults with intellectual disability.[9] Few studies have paid attention to the QOL of people with epilepsy and cognitive problems. To narrow this gap, our study aimed to assess the QOL of patients with RE and intellectual disability based on caregivers' concerns about seizures, treatment, caring, and social impact and to determine its predictors.

Sabaz et al (2001) discovered that the presence of intellectual disability independently depresses health-related QOL outcomes in children with RE.[10] Surprisingly, the results of a recent study by Endermann (2013) showed that health-related QOL did not seem to be strongly impaired in young adults with mild intellectual disabilities.[11] The mean total score of the GEOS-35 obtained in our study was 76 ± 2.34 (an indicator of a low QOL). A possible explanation of our results is that patients with mild, moderate, and severe intellectual disability were included in the study. Caregivers specified that concerns about treatment occurred fairly often, while concerns about seizures, caring, and social impact occurred often. These results indicate some confidence in the prescribed treatment, uncertainty in seizure type and caring, and a realisation that epilepsy and cognitive problems have negative influence on the social aspects of the QOL.

Table 5 – Correlation of depression with the GEOS-35 total score in patients with RE and cognitive problems.

GEOS-35 total score	Depression (GDS-LD/GDS-CD)		Total
	No	Yes	
High QOL N (p%)	3 (100.0%)	0 (0%)	2 (100.0%)
Moderate QOL N (p%)	15 (75.0%)	5 (25.0%)	20 (100.0%)
Low QOL N (p%)	19 (52.8%)	17 (47.2%)	36 (100.0%)
Very low QOL N (p%)	1 (20.0%)	4 (80.0%)	4 (100.0%)
Total N (p%)	38 (59.4%)	26 (40.6%)	64 (100.0%)

Table 6 – Correlation of anxiety with the GEOS-35 total score in patients with RE and cognitive problems.

GEOS-35 total score	Anxiety (GAS-ID)		Total
	No	Yes	
High QOL N (p%)	2 (100.0%)	0 (0%)	2 (100.0%)
Moderate QOL N (p%)	11 (55.0%)	9 (45.0%)	20 (100.0%)
Low QOL N (p%)	3 (10.0%)	27 (90.0%)	30 (100.0%)
Very low QOL N (p%)	0 (0%)	4 (100.0%)	4 (100.0%)
Total N (p%)	16 (28.6%)	40 (71.4%)	56 (100.0%)

On univariate analysis, the GEOS-35 total score correlated with seizure frequency and severity, stigma, depression, and anxiety. Seizure type, seizure frequency and severity, stigma, and anxiety were found to have an impact on some QOL aspects. Polymorphic seizures were associated with more frequent "concerns about seizures". Higher seizure frequency was associated with more frequent "concerns about seizures" and "concerns about social impact". A recent study by Endermann (2013) also found that seizure frequency affected only some health-related QOL variables.[11] Greater seizure severity was associated with more frequent "concerns about seizures", "concerns about caring", and "concerns about social impact" in our study participants. Stigma was associated with more frequent "concerns about seizures", "concerns about treatment", and "concerns about social impact". Anxiety was associated with more frequent "concerns about seizures", "concerns about treatment", and "concerns about caring". Endermann (2006) identified the current emotional state as the most influential predictor of all QOL measures in people with epilepsy and mild intellectual disabilities in residential care.[12] In another study, the same investigator found that psychological distress was the only predictor of all QOL measures in young adults with RE and mild intellectual disabilities.[11]

In a multivariate regression analysis of our study results, predictors of the GEOS-35 total score were anxiety, seizure severity, and stigma. Regarding the GEOS-35 subscales, multivariate regression analysis found that: 1. Seizure severity, seizure type, and anxiety were predictors of "concerns about seizures"; 2. Anxiety was the only predictor of "concerns about treatment"; 3. Anxiety and seizure severity were predictors of "concerns about caring"; and 4. Seizure severity and stigma were predictors of "concerns about social impact". We found no similar results in the literature.

5. Limitations

The first limitation might be the relatively small number of participants in the study, which is due to the difficulties regarding the cooperation of patients with cognitive problems and their caregivers. The participation of only those patients with access to the University Clinic of Neurology, who usually attended it for regular examination or in cases of unsatisfactory seizure control or adverse events from treatment, is also a limitation. These limitations do not devalue the results from the first Bulgarian study of the QOL in patients with epilepsy and cognitive problems. Further investigations of patients, with a variety of demographic, clinical, and social characteristics, are needed.

In **conclusion,** we have affirmed the low QOL in patients with RE and cognitive problems and its clinical and social determinants. Seizure frequency and severity, anxiety, and stigma proved to be the most influential predictors of the QOL in these people. The results from our study motivate a multidisciplinary approach for quality of life improvements in these patients.

Conflicts of interest

The author has none to declare.

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