CAREGIVER BURDEN IN EPILEPSY IN GREECE

I. Karakis,[1] A. Tsiakiri,[2] C. Piperidou[2]
[1] Department of Neurology, Emory University School of Medicine, Atlanta, GA, USA
[2] Department of Neurology, Democritus University of Thrace, Alexandroupolis, Greece

Abstract

Aim: Due to its chronicity and unpredictability, epilepsy confers significant burden to its bearers and their loved ones, affecting their quality of life (QOL). Contrary to persons with epilepsy (PWE), little is known about caregiver burden (CB) and QOL in Greece and worldwide. Here we attempt to identify the magnitude of epilepsy burden to Greek caregivers, explore factors associated with it and compare it with that from an international PWE-caregivers cohort. Methods: Patients were recruited from the outpatient epilepsy clinic in the university hospital of Alexandroupolis and from the epilepsy monitoring unit of two academic hospitals in Boston. 49 Greek and 126 American PWE and their 31 Greek and 48 American caregivers, respectively, completed questionnaires providing demographic, disease-related, psychiatric, cognitive, sleep, QOL and burden information. Results: Compared to the American patients, Greek patients were more commonly unemployed, of lower educational attainment and with lower neuropsychological scores. Their disease was overall under better control with fewer antiepileptic drugs (AED). They exhibited lower indices of depression, anxiety and sleepiness. Greek caregivers were often parents or siblings as opposed to spouses in the US cohort; they also had lower educational attainment and spent, on average, more time for patient care. Overall, patient QOL appeared worse in the US vs the Greek population while CB did not differ significantly between the two cohorts. On regression analysis for the combined cohort, the number of AED and the time allocated to patient care were associated with higher CB. The latter attained statistical significance for the US cohort and approximated statistical significance for the Greek cohort independently. Conclusion: In a selected PWE-caregiver Greek cohort attending the outpatient epilepsy clinic, we identified modest degree of CB, comparable to a US cohort and to what is reported in the literature for other chronic neurological conditions. Time allocated to patient care emerged as the most consistent factor associated with that burden.

Key words: Caregiver, Burden, Epilepsy, Quality of life, SF36v2, Zarit Burden Interview, Greece

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Introduction:

Epilepsy is a chronic, unpredictable and frequently disabling neurologic disorder that poses numerous challenges and consequences at multiple levels. It imposes a significant toll to the patient in terms of personal suffering, to the family for daily assistance and to the society as a whole with regards to the morbidity and its socioeconomic repercussions. Yet, contrary to other chronic medical and neurological conditions, much of the literature on epilepsy burden and the impact on quality of life focuses on the patient as the "client" and fails to see the family as a "co-client", particularly for adult PWE[1].

Rather than a mere clinical disorder, epilepsy is also a social label of an "undesired differentness"[2]. It has been a culturally devalued condition across the world and throughout history[3]. The study of cross-cultural differences in QOL in PWE not only offers insights on the commonalities of their psychosocial hardships but also reveals culture-specific predictors of psychosocial well-being, with potential tailored to each culture's therapeutic ramifications[4]. Comparing the results of studies derived from single countries is suboptimal given the variability of study sample selection, the differences of the psychosocial parameters examined and the heterogeneity of the methodology applied[5]. On the other hand, direct cross-cultural comparisons assessing the same parameters with common study design and procedures allow for more robust inferences[5].

Hitherto, there is a scarcity of cross-cultural studies in the field of epilepsy. In particular, Dodrill et al reported significantly more emotional difficulties, problems relating to accepting and coping with the diagnosis of epilepsy and overall psychosocial functioning in people in the US compared to Canada, Finland and former East Germany[6]. Similarly, Collins et al identified poorer general physical health, emotional well-being, life fulfillment and increased level of worries in the US PWE compared to the UK and New Zealand[4]. A more extensive study across a large number of European countries (France, Germany, Italy, Holland, Spain, Sweden, Switzerland and the UK) also reported marked cross-cultural differences, with perceived impact of epilepsy and stigma being the poorest in France and consistently better in Spain and Holland, controlling for socio-demographic and disease characteristics[5]. Three factors, namely seizure frequency, seizure type and employment status, showed consistent associations with the various measures of QOL[5]. Focusing on levels of knowledge about epilepsy, Doughty et al highlighted significant differences across various European countries[7]. In a large study of >5000 patients living in 15 European countries, seizure frequency was unanimously a key factor influencing patients' perception of the impact on health status and stigma, but even patients with infrequent seizures had a fairly compromised QOL compared to those who were seizure-free, emphasizing the need for attention to the psychological aspects of the disease[8]. Similarly, data collected from 3,889 people with epilepsy from 10 countries in the Middle East highlighted the poorer QOL of PWE, particularly for physical and social functioning, energy and vitality, compared to patients without epilepsy[9].

The above studies provide useful insight into psychological issues in epilepsy across countries from a patient perspective. However, the literature is void of cross-cultural studies focusing on the caregiver. Culture shapes one's perspective of family responsibilities and may therefore influence the perception and reaction of CB among people of different ethnicities[10]. In this explorative, cross-sectional study, we attempt to address this need. We attempt to ascertain the burden of epilepsy to the caregivers in Greece compared with those in the USA, provide potential explanations for any discrepancies, analyze clinical repercussions of these findings and pave the path for similar research endeavors on a larger scale.

Methods:

i. Participants

This is a cross-sectional study conducted between September 2009 and June 2011 at Democritus University of Thrace (DUT), Massachusetts General Hospital (MGH) and Boston University Medical Center (BUMC). At DUT, PWE with their accompanying caregivers were recruited at the outpatient epilepsy clinic, while at MGH and BUMC, recruitment for both patients and caregivers occurred in the Epilepsy Monitoring Unit (EMU). In all locations, patients were asked to participate by completing a series of questionnaires and underwent bed-side cognitive evaluations. Patients who were unable to speak the local language or unable to read and write due to cognitive impairment were excluded. Caregivers who accompanied them were also asked to complete questionnaires. Caregiver was defined as the family member who was primarily responsible for providing every-day care for the patient. Only patients with clinically established epilepsy were included in the analysis, while patients with non-epileptic seizures, mixed disorders or unclear diagnoses were excluded along with their caregivers. Consent for participation was obtained from all eligible available caregivers. That recruitment process yielded 49 Greek and 126 American PWE and their 31 Greek and 48 American caregivers, respectively. The study was approved by the institutional review boards.

ii. Questionnaires and procedures

A detailed analysis of the questionnaires and procedures has been described elsewhere[1,11,12]. In brief, participating patients completed questionnaires providing demographic (age, gender, race, religion, employment, education, living situation and marital status) and epilepsy related (age of epilepsy onset, epilepsy duration in years, average number of seizures per month in the past year, number of AED, self-reported compliance) information. The information collected was cross-validated with medical records review.

Cognitive evaluation was performed by a neurologist or neuropsychologist via administration of the Montreal Cognitive Assessment (MoCA) test[13]. Anxiety and depression levels were measured using the Beck anxiety[14] and Beck depression[15] inventory, respectively. Both have been extensively used previously in epilepsy research[16]. Sleep quality was assessed by completing the Epworth sleepiness scale[17]. While not specific to patients with epilepsy, it has been previously widely used to assess sleep impairment in a host of diseases including epilepsy[18]. QOL was evaluated by completing the QOLIE-31 instrument. QOLIE-31 is one of the most commonly applied QOL instruments in epilepsy with good reliability and validity[19]. The 31-item self-administered questionnaire has seven subscales: seizure worry, overall QOL, emotional well-being, energy/fatigue, cognitive function, medication effects and social functioning. A score ranging from 1-100 is obtained from each subscale with higher scores indicating better QOL.

Caregivers accompanying the patients also completed questionnaires providing demographic information (age, gender, race, religion, employment, education, marital status, cohabitation and time spent for patient care in hours per week). Time spent for patient was loosely defined as the time devoted to everyday activities where caregiver participation was indispensable, including AED provision, outpatient and emergency department visits and driving for any patient-related activity. Given the lack of a disease specific questionnaire to assess their burden, the Zarit caregiver burden inventory was used. This is a 22-item inventory derived from the original 29-item inventory[20]. It is the most widely used standardized, validated scale to assess caregiver burden, administered previously in various neurological disorders, including epilepsy[21,22]. The 22 items evaluate the effect of disease on the caregiver's QOL, psychological suffering, financial difficulty, shame, guilt and difficulty in social and family relationships. Scores range from 0 to 88 with higher scores indicating higher burden (<20: little or no burden, 21-40: mild to moderate burden, 41-60: moderate to severe burden, 61-88: severe burden). Caregiver health-related QOL was assessed by administering the second version of the SF-36 generic questionnaire (SF36v2)[23], available only for the US caregivers. This is a generic QOL instrument that assesses eight health concepts. Scores standardized to norms and weighted averages are used to create a physical component summary (PCS) and a mental component summary (MCS) composed by the first and last four of the aforementioned health concepts, respectively. All health dimension scores are standardized to normal by employing a linear transformation of data originally scored on a 0-100 scale. Norm-based scores have a mean of 50 and a standard deviation of 10 in the general US population. Therefore, any score <50 for any health dimension and component scale falls below the general population mean and each point represents 1/10th of a standard deviation. This allows direct comparison among different populations[23] and has established precedence in epilepsy caregiver research.

Various paraclinical (e.g. laboratory, electroencephalographic and radiological) data were collected as part of standard of care. Routine AED levels were drawn at the time of the encounter. For patients on more than one AED, they were deemed to be above, within or below the antiepileptic drug reference range of their regimen depending on the serum level of the majority of drugs in their regimen. EEG data were derived from the initial recording during the completion of the questionnaires at the EMU or from historical EEG records at the outpatient clinic. They were incorporated into the clinical impression for the purposes of epilepsy type classification (partial with or without secondary generalization and primary generalized), epilepsy location (uni-temporal right or left, bi-temporal, extratemporal right or left, multilobar or idiopathic generalized epilepsy) and etiology (symptomatic, cryptogenic or idiopathic). Radiological data included findings of the patient's last brain magnetic resonance imaging (normal, mesial temporal sclerosis, diffuse atrophy, vascular, developmental or other abnormality).

Analysis

Summary scores were created for all the aforementioned variables, and descriptive statistics were used. Comparison of the two cohorts of patients and two cohorts of caregivers was done using t-test or their non parametric equivalent for continuous variables and Chi-square for categorical variables. Univariate associations between the Zarit burden score as the outcome of interest and the various patient and caregiver related predictors were explored by using Pearson correlation for continuous variables and one-way ANOVA for categorical variables. Statistical significance was set at 0.05. Those variables identified as statistically significant in the univariate analysis were subsequently fitted in a multivariate linear regression model in order to conduct an adjusted evaluation of associated factors of caregiver burden both for the combined cohort as well as for each cohort independently. Statistical analysis was performed in SAS 9.3 (North Carolina).

Results:

Patient demographics are detailed in table 1. The mean age of patients in both cohorts was 38 years. Compared to the American patients, Greek patients were more commonly unemployed, of lower educational attainment and with lower neuropsychological scores. Their disease was overall under better control with fewer antiepileptic drugs (AED). They exhibited lower indices of depression, anxiety and sleepiness.

Caregiver demographics are detailed in table 2. Greek caregivers were often parents or siblings as opposed to spouses in the US cohort; they also had lower educational attainment and on average spent more time for patient care.

As illustrated in table 3, patient QOL appeared worse in the US vs the Greek cohort in most QOL domains such as energy/fatigue, cognitive functioning, medication effects, social functioning, including the overall score. Most of the remaining domains such as seizure worry and overall quality of life approximated but did not attain statistical significance.

Caregiver QOL scores were only available in the US cohort, demonstrating lower QOL scores in the mental compared to the physical component of the scale applied. CB scores fell on the border zone of the mild-moderate range for both cohorts of caregivers and did not differ statistically (table 4).

On regression analysis for the combined cohort, number of AED and time allocated to patient care were associated with higher caregiver burden. Time allocated to patient care attained statistical significance for the US cohort (in addition to patient number of AED, patient cognitive testing scores, patient overall QOL scores and caregiver education) and approximated statistical significance for the Greek cohort independently (table 5).

Discussion:

To summarize our findings, in a selected PWE-caregiver Greek cohort attending the outpatient epilepsy clinic, we identified modest degree of CB, comparable to a US cohort and to what is reported in the literature for other chronic neurological conditions. Time allocated to patient care emerged as the most consistent factor associated with that burden.

Table 1. Patient characteristics

	US Patients N=126	Greek Patients N=49	P value
Demographic characteristics			
Age (mean±SD)	38.20±13.48	37.65±16.46	0.82
Gender (n, %female)	74 (58.73%)	23 (46.94%)	0.15
Race (n, % caucasian)	103 (83.74%)	49 (100%)	0.0027
Religion (n,% Christian)	75 (75%)	39 (79.59%)	0.53
Employment (n, %employed)	68 (55.74%)	10 (20.41%)	<0.0001
Education (n, % some college and beyond)	85 (75.89%)	9 (18.37%)	<0.0001
Living situation (n, %living with family or others)	101 (85.59%)	45 (91.84%)	0.26
Marital status (n, %married)	51 (40.78%)	22 (44.90%)	0.59
Epilepsy characteristics			
Age of onset of epilepsy (mean±SD)	23.84±16.42	23.34±13.96	0.85
Duration of epilepsy (mean±SD)	14.80±13.54	14.65±12.92	0.95
Number of seizures per month (median, IQR)	3 (7)	0.5 (1)	<0.0001
Number of AED (median, IQR)	2 (2)	2 (1)	0.0029
Compliance (n, % compliant)	95 (77.87%)	46 (95.83%)	0.0079
Paraclinical characteristics			
EEG Posterior Dominant Rhythm (mean±SD)	9.40±1.13	9.03±1.04	0.20
EEG findings			0.39
Slowing	21 (16.94%)	4 (28.57%)	
Interictal spikes	46 (37.10%)	3 (21.43%)	
Normal	57 (45.97%)	7 (50%)	
MRI Findings (n, %abnormal)	83 (69.17%)	17 (35.42%)	<0.0001
Neuropsychological and sleep characteristics			
Montreal Cognitive Assessment Score (MoCA) (mean±SD)	25 .31±3.49	22.18±5.73	0.0007
Beck Depression Inventory (mean±SD)	13.25±12.09	8.38±7.51	0.0018
Beck Anxiety Inventory (mean±SD)	15.64±13.34	7.34±6.62	0.0002
Epworth Sleepiness Scale (mean±SD)	8.71±4.58	6.10±3.62	0.0014
Sleep disordered questionnaire for sleep apnea (SDQ-SA)	24.31±7.63	N/A	N/A

*SD=standard deviation, IQR=inter-quartile range, AED=antiepileptic drugs, EMU=epilepsy monitoring unit, EEG=electroencephalogram, TLE=temporal lobe epilepsy, IGE=idiopathic generalized epilepsy, MRI=magnetic resonance imaging ,QOLIE-31= Quality of Life 31 questionnaire

Past studies have explored psychosocial issues in patients with epilepsy in Greece. In particular, in a multi-center study performed in 223 patients attending the outpatient epilepsy clinic, Piperidou et al identified disease specific factors (seizure frequency, disease duration, polypharmacy and benzodiazepine use) as independent determinants of patient QOL[24]. The same group of investigators validated the presence of sleep disturbance, particularly insomnia, in PWE and its negative impact on their QOL[25]. Kimiskidis et al have corroborated the association between epilepsy and psychiatric comorbidities in Greek PWE and investigated demographic and disease-related variables which constitute risk factors for their emergence[26]. Finally, focusing on children with epilepsy and their families, Serdari et al demonstrated that

Table 2. Caregiver characteristics

	US Caregivers N=48	Greek Caregivers N=31	P value
Age (mean±SD)	46.18±13.20	48.45±9.08	0.36
Gender (n, %female)	33 (68.75%)	15 (48.39%)	0.07
Race (n, % caucasian)	45 (93.75%)	31 (100%)	0.15
Religion (n,% Christian)	36 (75%)	21 (67.74%)	0.48
Relationship to patient (n, %)			
Spouse/partner	28 (58.34%)	9 (29.30%)	0.01
Parent/sibling	18 (37.50%)	16 (51.62%)	
Other	2 (4.17%)	6 (19.35%)	
Employment (n, %employed)	34 (70.83%)	16 (51.61%)	0.08
Education (n, % some college and beyond)	39 (81.25%)	6 (19.35%)	<0.0001
Marital status (n, %married)	38 (79.17%)	25 (83.33%)	0.64
Cohabitation with patient (n, %)	43 (89.58%)	25 (80.65%)	0.26
Time spent for patient care (hours) per week (median/IQR)	4.5 (10)	7 (9)	0.04

*SD=standard deviation, SF36v2=short form 36 health survey version 2

Table 3. QOL scores and subscores for US vs Greek patients

	US Patients N=126	Greek Patients N=49	P value
Quality of life characteristics (QOLIE-31)			
Seizure worry	43.36±27.93	51.84±29.91	0.08
Overall quality of life	57.90±21.62	64.89±23.84	0.06
Emotional Wellbeing	61.03±21.31	60.81±21.98	0.95
Energy/Fatigue	43.02±22.69	63.43±21.49	<0.0001
Cognitive Functioning	50.54±25.64	67.15±22.91	0.0001
Medication Effects	44.35±28.28	63.08±26.39	0.0001
Social Functioning	46.87±28.40	56.23±28.10	0.05
Overall Score	51.31+18.29	61.71±19.23	0.0013

Table 4. QOL and burden scores of USA vs Greek caregivers

	US Caregivers N=48	Greek Caregivers N=31	P value
Quality of life characteristics (SF36v2)			
Physical Component Scale (PCS) (mean±SD)	53.91±8.86	N/A	N/A
Mental Component Scale (MCS) (mean±SD)	45.51±11.31	N/A	N/A
Burden characteristics			
Zarit Burden Inventory (mean±SD)	20.02±14.47	19.12±10.90	0.77

Table 5. Determinant of caregiver burden

Variable	Parameter Estimate	Standard Error	P-Value
US patients			
Number of AED	5.14	2.03	0.01
Patient MoCA	-0.78	0.38	0.05
QOLIE-31 overall score	-0.22	0.09	0.02
Caregiver education	-11.76	3.98	0.005
Time spent for patient care	0.15	0.08	0.06
Greek patients			
Time spent for patient care	0.29	0.11	0.07
Combined US and Greek patients			
Number of AED	4.83	1.67	0.0054
Time spent for patient care	10.20	0.05	0.0001

better knowledge of the disease resulted in fewer missed school days and that the majority of children did not discuss their disease with their peers[27].

Somewhat in line with these prior studies, we demonstrated the toll that epilepsy takes on the life of its bearers, with approximately only 20% of our patients being highly educated and employed and less than half of them being married. Compared to the US cohort, Greek patients were more impacted in those social domains, despite suffering from an overall better controlled disease. Yet, the impact on their sleep, psychiatric state and most QOL subscales, including the overall score, appeared less pronounced. Interestingly, the poorer QOL of PWE in USA compared to PWE in Europe has been a consistent finding in prior studies, regardless of methodology[4,6].

CB and QOL has attracted research interest in Greece for other chronic medical (e.g. cancer[28-30] and chronic breathlessness[31]), mental (e.g. schizophrenia[32,33] and neurological (e.g. multiple sclerosis[34,35]) conditions. Studies focusing on epilepsy are glaringly absent.

In our study, we identified a modest degree of CB in Greek families living with epilepsy. This burden appears comparable with other chronic neurological disorders where similar burden scales were used[1]. It also appears comparable with that of the US cohort, despite the fact that the US patients were more severely afflicted by the disease clinically and psychologically. This finding may account for differences in caregivers' demographics, since the US caregivers belonged to higher socioeconomic status and thus may have had more resources to provide care, partially suggested by the increased amount of time spent for patient care in the Greek population. That parameter of time approximated statistical significance as the primary predictor of burden in the Greek cohort. When all patient-caregiver pairs were combined, the number of AED also played a significant predictive role. For the US cohort, patient cognitive status and QOL as well as caregiver education emerged as important determinants. This variability in the associations may indeed hail from frank differences between the two countries in the ways PWE and their caregivers perceive their disease and cope with it or may be merely an outcome of the heterogeneity of the study populations and the study methodology.

Incorporating patient and caregiver findings together, one may identify a number of possible explanations for these cross-cultural differences. As stated in prior cross-cultural studies in epilepsy, differences may be a reflection of contrasts of personal outlook and expectations, societal perspectives and tendencies towards concealment or disclosure of diagnosis, local differences in availability and accessibility to health and social care, legal and statutory limitations posed by the government on the level of activity (e.g. driving) and social integration (e.g. education, employment) of PWE or just merely artifacts of the applied study design[36]. It may be that a combination of the aforementioned explanations or even additional overlooked factors account for our findings.

There are certain advantages to our study. We focused on cross-cultural, adult patient-caregiver interactions, where the literature is sparse. Participants could complete the surveys independently, they had well-defined disease characteristics and cross-reference with medical records provided an additional checkpoint for accuracy. Numerous patient- and caregiver-related factors were taken into account when assessing CB.

Yet, reader should be cautioned about certain limitations. Albeit widely-used, the self-reporting nature of this study bears a risk of recall bias. Despite the careful translation of our burden questionnaire, no cross-cultural validation was performed. Along similar lines, caregiver QOL questionnaire was not available for our Greek cohort. The modest sample size of caregiver participants may have underpowered our study for the detection of additional associations. The recruitment in academic settings raises questions about the generalizability of the results to the community. Despite the extensive evaluation of patient-associated factors, caregiver-related aspects that may have been associated with their burden may have been overlooked. The cross-sectional design prevented longitudinal inferences and associations from being explored. Finally, the absence of a non-epilepsy patient-caregiver control group limited our ability to directly compare our findings with other chronic neurologic or medical disorders in which caregivers also play a significant role.

The potential limitations notwithstanding, the results of the present study show preliminary cross-cultural similarities and differences in the impact of epilepsy both to the patient as well as to the caregiver. Similar to prior research on PWE[4,5], country of residence appears to play a significant role in the impact of the disease to the caregiver, highlighting the importance of social context in both cases. It also emphasizes the complexity of cross-cultural investigations. Future research should aim to confirm or refute these preliminary findings, at a larger scale and across more countries and settings, including, ideally, control groups from other chronic medical conditions, validated and disease specific caregiver-focused questionnaires and a longitudinal design. In the interim, health care professionals are encouraged to inquire not only the patients but also their caregivers about their feelings and need for education and support, beyond the traditional reliance of medical tests and clinical outcomes[37].

Conclusion:

In a selected cohort of person with epilepsy attending an outpatient epilepsy clinic in Greece, we identified modest degree of caregiver burden, comparable to that of a US cohort. We also demonstrated cross-cultural similarities and differences in the predictors of this burden. The findings presented herewith reinforce the importance of acknowledging the caregiver as a key stakeholder and, at times, a hidden patient in epilepsy, both from a clinical as well as from a research perspective. These results also emphasize the challenges and need for further cross-national investigation of psychosocial repercussions in epilepsy.

Disclosures:

None of the authors has any conflict of interest to disclose related to this unfunded project.

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