Epilepsy & Behavior 93 (2019) 43–48

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

# Impact of epilepsy and antiepileptic drugs on health and quality of life in Indian children

Divya Nagabushana [*,1], Praveen-Kumar S., Jagadish B. Agadi

*Department of Neurology, Bangalore Medical College and Research Institute, Fort, K.R. Road, Bengaluru, Karnataka 560002, India*

ARTICLE INFO

*Article history:*
Received 5 November 2018
Revised 18 January 2019
Accepted 18 January 2019
Available online 1 March 2019

*Keywords:*
Quality of life
Children with epilepsy
Antiepileptic drugs
Indian
Prospective study
QOLCE scale

ABSTRACT

*Background and objectives:* Epilepsy affects the physical, cognitive, emotional, social wellbeing, and thereby the overall quality of life (QOL). Epilepsy is the most prevalent neurological disorder in the pediatric age group with a prevalence of 3.13 to 3.73 per 1000 in India. It is imperative for the primary caregiver to look beyond seizure control for improving wellbeing of children with epilepsy (CWE). Hence, there is a need to understand the predictors of QOL in Indian CWE. The objective of this study was to assess the impact of epilepsy and antiepileptic medications on the child's development, health, scholastic performance, and QOL and to identify the predictors of QOL.
*Methods:* This study was a cross-sectional hospital-based prospective study with sociodemographic, clinical data collected from 110 children (age 4–18 years). Seizure severity was assessed with the Hague Seizure Severity Scale, and adverse effects of antiepileptic drugs (AEDs) were assessed using the Adverse Event Profile Scale. The QOL was measured employing the Quality of Life in Children with Epilepsy (QOLCE) questionnaire.
*Results:* The mean total QOLCE score was 72.6 ± 13.6. Among the subscale scores, memory had the highest mean of 86.5, and the lowest mean was observed for QOL item (40.4). There was no significant association of the total QOLCE score with any of the sociodemographic variables such as gender, place, socioeconomic status, paternal/maternal education, or family type. Children with more severe seizures had significantly lower energy and QOL subscale scores and greater depression and anxiety. Prolonged duration of epilepsy, frequent seizures, and recent seizures had a significant negative correlation with the mean total QOLCE score. Children with epilepsy who are on multiple AEDs, prolonged duration of AED intake, or poor adherence to AEDs have significantly lower total QOLCE score. Children manifesting adverse effects to AEDs had significantly lower overall QOL affecting all domains.
*Conclusion:* Overall QOL in CWE is most compromised by polytherapy, poor adherence to medication, adverse effects of AEDs, hospitalization, and presence of developmental delay.

## 1. Introduction

Epilepsy is the most prevalent neurological disorder in the pediatric age group with a reported prevalence of 0.5 to 0.62% in children among developed countries and a prevalence of 3.13 to 3.73 per 1000 in India [1–3]. The burden of epilepsy is significant in India with 10 million individuals with epilepsy. Children with epilepsy (CWE) face several challenges. The impact of epilepsy on a child and family is multifold with medical, psychological, educational, personal, economic, and social ramifications [4].

The impact depends on several factors: severity of epilepsy; neurological dysfunction; complexity of clinical management and side effects of antiepileptic drugs (AEDs); family environment; perception of the disorder by the child, family, and society; sociocultural beliefs, stigma; restrictions in the activities as well as innate coping abilities of the child and family; the level of healthcare and social support, and the extent of resources available to deal with the epilepsy [5–9]. Also, CWE frequently exhibit comorbidities such as attention-deficit/hyperactivity disorder (ADHD), learning disabilities, depression, and anxiety that impede developmental progress and affect emotional health [10–15]. The scholastic performance is affected by the illness as well as by the AEDs [16]. Cognition, working memory, processing speed, attention, executive function, and language are also known to be affected in epilepsy, either because of disease or because of the adverse effects of the AEDs [17–20].

Health-related quality of life (QOL) (HRQOL) is a multidimensional concept that covers physical, emotional, mental, social, and behavioral components of wellbeing and functioning as perceived by patients [21]. The International League against Epilepsy (ILAE) Commission on Epidemiology states that HRQOL is the "broadest and most important outcome of any chronic health condition." Assessment of the control of epilepsy by only monitoring the seizure frequency and severity and

---

[*] Corresponding author.
*E-mail address:* divya.nagabushana@gmail.com (D. Nagabushana).

[1] Present Address: Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS), Hosur Road, Bengaluru, Karnataka, India 560029.

https://doi.org/10.1016/j.yebeh.2019.01.021
1525-5050/

screening for adverse effects of AEDs is inadequate for evaluation of the overall health of CWE.

Studies have revealed that the QOL in CWE is affected by various factors such as age of onset of seizure, seizure type, frequency, and severity, adverse effects of drugs as well as family socioeconomic status, social stigma, parental anxiety and presence of other comorbidities [22–26]. There have only been limited studies in India that have cast light on this issue. The social stigma, prejudice associated with epilepsy, and poor awareness of the disease in India can impact the development of the child at this vulnerable age and affect the overall health. It is imperative for the primary caregiver to look beyond seizure control for improving wellbeing of CWE. Hence, there is a need to better understand the predictors of QOL in Indian CWE. This will help clinicians to incorporate measures to improve the overall QOL rather than simply controlling seizures with medications. The present study was conducted to assess the impact of epilepsy and antiepileptic medications on a child's development, health, scholastic performance, and QOL and to identify the predictors of QOL.

## 2. Methods

### 2.1. Study participants

This study was a hospital-based prospective study carried out at the tertiary government hospital attached to the Bangalore Medical College and Research Institute, Bengaluru catering to patients predominantly from the state of Karnataka, India from January 2016 to July 2017. One hundred ten children and adolescents with epilepsy aged 4 to 18 years were recruited. The sample size was calculated with margin of error of 4 at 95% confidence interval with *P*-value of 0.05 and power of 80%. The standard deviation of the QOL score observed in a previous study by Aggarwal et al. was used for estimation of the sample size, which was determined to be 110 [27]. The study participants were consecutive patients attending the out-patient clinic or admitted in the ward of the neurology department. Children with active epilepsy (defined as a child currently being treated for epilepsy or whose most recent seizure occurred within the past two years) were included in the study. Classification of the type of seizure was done as per the ILAE classification of seizures [28]. Children were enrolled after obtaining surrogate consent from parent or responsible guardian. Children with severe intellectual disability, progressive neurodegenerative disorder, or with chronic medical disorders, such as, asthma, diabetes, congenital heart disease, and chronic kidney disease, were excluded. The intellectual ability was assessed by the primary investigator based on the age appropriate scholastic achievement. The intelligence quotient (IQ) of children with poor scholastic performance was also assessed by a clinical psychologist, in order to avoid inclusion of children with severe intellectual disability. The scholastic performance was graded as good;, average;, below average, and poor/fail as per the marks percentage in the final exams of the previous academic year. At school level, marks percentage in the range 55–75% was taken as average as there is a lot of heterogeneity in the system of evaluation in various schools in India. Marks percentage in the range of 35–55% was graded as below average, while above 75% was graded as good and below 35% was considered poor/fail. The study was conducted after the approval of the institutional review board and ethics committee clearance.

### 2.2. Data collection

Sociodemographic data, such as age, gender, socioeconomic status, urban/rural, paternal and maternal education, occupation, family income, and type of family – nuclear or joint – were recorded. Clinical data pertaining to epilepsy – seizure types, semiology, onset, frequency, duration, course, AEDs taken, compliance/adherence and their adverse effects; past history of febrile seizures, head trauma, or meningitis; family history of seizures; development; scholastic performance; and existing comorbidities were collected. Seizure severity was assessed with the Hague seizure severity scale developed by Carpay et al. [29]. It is a 13-item scale and is a parent-completed questionnaire based on parental perception of severity of seizures in the last 3 months. High scores indicate more severe seizures. This scale is reliable and valid and has been widely used in epilepsy-related research. It has been employed in a previous study in India although it has not been validated in the Indian population [30]. The presence and severity of adverse events of the AEDs was assessed by the Adverse Event Profile (AEP) scale [31]. The AEP is a 19-item instrument that assesses the presence and severity of the adverse effects during the previous 4 weeks. Higher scores indicate increased AED-related adverse effects. Adherence to AEDs was assessed by a modification of the Brief Adherence Rating scale [32]. The number of days AED was missed/skipped or the doses reduced in the past 1 month were documented. Good adherence was considered if AED was skipped less than 7 days, occasional lapses if skipped 7–13 days, frequent lapses if skipped 14–20 days, and very poor adherence if AED was skipped >20 days. Poor adherence was considered if AED was skipped for >7 days in the past month. A complete clinical examination and investigations including electroencephalogram (EEG) and imaging (computerized tomography [CT]/magnetic resonance imaging [MRI] of the brain in relevant cases) were conducted.

### 2.3. QOL assessment

Assessment of QOL was done with Quality of Life in Children with Epilepsy (QOLCE) questionnaire. This epilepsy-specific questionnaire for measuring QOL was developed by Sabaz et al. in 2000 [33]. It is a parent-reported instrument to measure HRQOL of children 4–18 years of age. It covers 5 domains ;: physical function, emotional wellbeing, cognitive function, social function, and behavior. There are also 2 generic subscales for general overall QOL and general health. It was initially validated in an Australian sample and then subsequently adapted and validated in an American sample. The QOLCE US has 16 subscales (13 multi-item scales and 3 single-item scales) and 79 items. Questions are answered by the parents about the previous 4-week time period. Scoring is from 0 to 100 points with higher scores indicating better QOL. An overall QOL score was computed by adding each subscale score for each individual and then dividing by respective number of items. This scale is a reliable and valid measure and is sensitive to differences in epilepsy. The QOLCE questionnaire is considered to demonstrate high psychometric values with reliability index for a complete questionnaire (Cronbach $\alpha$ coefficient) amounting to 0.93 [34–36]. The National Institute of Neurological Disorders and Stroke Common Data Elements have recommended using the QOLCE for the assessment of QOL in pediatric epilepsy. This scale has been used in various studies in India and has been validated [27]. The questionnaire was completed by the parent in the presence of the primary investigator, and overall and individual subscale scores were determined.

### 2.4. Statistical analysis

Descriptive statistical analysis was carried out in the present study using IBM SPSS Version 22 and R software Version 3.4.2. Results were considered statistically significant with a two-sided *P*-value of less than 0.05. Independent sample *t*-test was employed for comparison of variables between 2 categories, and one way analysis of variance (ANOVA) was used for comparison of variables with more than 2 categories. Spearman correlation analysis was performed for assessing associations between QOLCE score and other variables. Linear regression with backward elimination was used to predict QOLCE score from other variables.

## 3. Results

### 3.1. Demographic data

A total of 110 eligible CWE participated in the study. The youngest participant was 4 years, and the oldest was 18 years of age. The mean age was 12.1 ± 4.14 years. Demographic data of the participants are shown in Table 1.

Of the study participants, 35.5% were from upper middle socioeconomic status followed by lower middle (33.6%), lower (26.4%), and upper (4.5%) as per the revised Kuppuswamy's scale [37]. Educational status of the participants' parents was noted. Majority of the fathers (52.7%) had completed high school, and 23.6% were illiterate. Among the mothers, 65.5% had completed high school, and 18.2% were illiterate. Of the participants, 75.5% were from a nuclear family type, and 24.5% were from a joint family type.

### 3.2. Epilepsy and AED-related results

The mean age of onset of epilepsy was 8.05 ± 4.74 years. Epilepsy-related variables are elaborated in Table 1. Majority (64.6%) of the children had onset of epilepsy within 10 years of age. The mean duration of epilepsy was found to be 4.1 ± 3.5 years; 73.6% of the participants had a duration of 1–10 years followed by <1 year (20%) and >10 years (6.4%). Presence of a single seizure type was noted in 93.6% of the participants, and 6.4% had multiple seizure types. Of the study population, 63.6% had focal onset seizure; 30.9% had a generalized onset, and 5.5% had an unknown onset. Prodromal symptoms were noted in 13.6% of the children with headache being the most common. Aura was noted in 25.5% of the children and dizziness was the most common type of aura. Focal onset of seizures with impaired awareness was the most common (31.8%) followed by focal onset nonmotor seizures with impaired awareness (19.1%) and generalized onset motor tonic–clonic seizures (15.5%). The severity of seizures was assessed by the Hague seizure severity score with the mean score of 34.6 ± 6.3 in the study population; 21.8% of the children had been seizure-free for 1 year; 49.1% had less frequent seizures of 1–5 per year, and 29.1% had frequent seizures of >5 per year. Of the patients, 80.9% did not have any hospitalizations for seizures, whereas 19.1% of the patients were hospitalized once or more; 22.7% of the study population had history of status epilepticus in the past.

**Table 1**
Demographic and clinical data of the study participants.

| Variables | | N = 110 |
|---|---|---|
| Mean age ± SD (years) | | 12.1 ± 4.14 |
| Gender – male | | 68 (61.8%) |
| Age distribution | 4–9 years | 29 (26.4%) |
| | 10–12 years | 28 (25.5%) |
| | 13–18 years | 53(48.2%) |
| Residence | Urban | 67 (60.9%) |
| | Rural | 43 (39.1%) |
| Family type | Nuclear | 83 (75.5%) |
| | Joint | 27 (24.5%) |
| Socioeconomic status | Upper | 5 (4.5%) |
| | Upper middle | 39 (35.5%) |
| | Lower middle | 37 (33.6%) |
| Mean duration of epilepsy ± SD (years) | | 4.1 ± 3.5 |
| Mean age of onset of epilepsy ± SD (years) | | 8.05 ± 4.74 |
| Type of seizure | Single | 103 (93.6%) |
| | Multiple | 7 (6.4%) |
| Type of seizure onset | Focal | 70 (63.6%) |
| | Generalized | 34 (30.9%) |
| | Unknown | 6 (5.5%) |
| Seizure frequency in the last year | Nil | 24 (21.8%) |
| | 1–5 | 54 (49.1%) |
| | 6–12 | 10 (9.1%) |
| | ≥12 | 22 (20%) |
| Last observed seizure | < 1 week | 34 (30.9%) |
| | 1 week – 1 month | 12 (10.9%) |
| | 1–6 months | 30 (27.3%) |
| | 6–12 months | 9 (8.2%) |
| | >1 year | 25 (22.7%) |
| Mean Hague seizure severity score ± SD | | 34.6 ± 6.3 |
| AED | Monotherapy | 71 (63.6%) |
| | Polytherapy | 39 (36.4%) |
| Duration of AED use | <5 years | 88 (80%) |
| | 5–10 years | 19 (17.3%) |
| | >10 years | 3 (2.7%) |
| Mean Adverse event profile score | | 29.7 |
| Adherence to AED | Good | 68 (61.8%) |
| | Occasional lapses | 38 (31.5%) |
| | Frequent lapses | 2 (1.8%) |
| | Very poor | 2 (1.8%) |

Of the participants, 64.5% were on single AED, whereas 35.5% were on multiple AEDs. The most common AEDs were valproate (16.4%), phenytoin (16.4%), carbamazepine (14.5%), levetiracetam (11.8%), phenobarbitone (3.6%), and oxcarbazepine (1.8%). Common combinations were carbamazepine with clobazam, phenytoin with clobazam, and levetiracetam with clobazam. Eighty percent of the children were on AEDs for <5 years, 17.3% from 5 to 10 years, and 2.7% of the children had been on AEDs for more than 10 years. Adverse effects of the AEDs were assessed in the study population using the AEP score. The mean AEP score was found to be 29.7 ± 7.8 (mean ± standard deviation). Of the children, 56.4% had an AEP score in the interval of 26–35. Of the participants, 61.8% had good drug compliance; 36.4% had AED changes in the past, and 28.2% had discontinued AEDs in the past.

Past history of febrile seizures was present in 17.3% of the patients, meningitis in 7.3%, and head injury in 0.9% of the patients. Family history of febrile seizures or epilepsy was present in 30% of the population. Past history of developmental delay was present in 20.9% of the patients. Significant birth history in the form of adverse events, like hypoxic ischemic encephalopathy, preterm delivery, low birth weight, small for gestational age, sepsis, meningitis, hypoglycemia, etc., in the neonatal period were present in 15.5% of the patients.

### 3.3. Comorbidities

Comorbidities, either psychiatric or neurological, were present in 10% of the participants with ADHD being the most common (5.4%). One child had psychosis with suicidal ideation. Among the neurological comorbidities, hemiparesis was observed in two, ataxia in one, and aphasia in one of the participants. With respect to scholastic performance, 71.8% of the study participants were studying in age appropriate class; 16.4% of the children had good scholastic performance; 30% had average scholastic performance; 27.3% had below average performance, and academic failure noted in 20.9% of the participants; 5.5% of the children had dropped out from school because of various reasons.

### 3.4. Etiology

Abnormal EEG findings were noted in 37.3% of the study participants. Abnormal imaging findings (CT/MRI brain) were noted in 32.3% of the patients. Etiology of epilepsy was unidentified in 55.4% of the patients. Perinatal insult was identified as the probable etiology in 13.5% of the study population. Childhood absence epilepsy was noted in six of the patients, benign partial epilepsy of childhood with centrotemporal spikes in two, juvenile myoclonic epilepsy in two, juvenile absence epilepsy in one, and idiopathic generalized epilepsy with generalized tonic–clonic seizures only in one. Hot water epilepsy was present in two children. Among the structural causes, neurocysticercosis was noted in five, postencephalitic sequelae in five, mesial temporal sclerosis in four, cerebral tuberculoma in two, hippocampal atrophy in one, posttraumatic remote symptomatic seizures in one, neuronal heterotopia in one, and focal cortical dysplasia in one of the children.

**Table 2**
QOLCE subscale scores in the study population.

| QOLCE Sub scale score | Mean | Standard Deviation | Minimum | Maximum |
|---|---|---|---|---|
| Physical restriction | 65.19 | 16.06 | 13.80 | 97.20 |
| Energy/fatigue | 71.59 | 22.48 | 12.5 | 100 |
| Attention/concentration | 73.03 | 23.29 | 10 | 100 |
| Memory | 86.49 | 18.50 | 20.80 | 100 |
| Language | 83.05 | 22.06 | 21.80 | 100 |
| Other cognitive | 77.10 | 25.27 | 16.6 | 100 |
| Depression | 77.97 | 15.28 | 18.70 | 100 |
| Anxiety | 79.81 | 17.34 | 29.10 | 100 |
| Control/helplessness | 81.08 | 16.83 | 31.20 | 100 |
| Esteem | 77.84 | 11.64 | 40.0 | 100 |
| Social interactions | 79.59 | 24.38 | 0.0 | 100 |
| Social activity | 66.21 | 25.75 | 0.0 | 100 |
| Stigma | 85.45 | 27.76 | 0.0 | 100 |
| Behavior | 74.88 | 14.32 | 36.60 | 100 |
| General health | 41.36 | 30.93 | 0 | 100 |
| Quality of life | 40.45 | 29.32 | 0 | 100 |
| Total QOLCE score | 72.57 | 13.65 | 24.90 | 93.72 |

### 3.5. Quality of life

The mean total QOLCE score was 72.6 ± 13.6 (mean ± standard deviation). The minimum total QOLCE score was 24.9, and the maximum was 93.7 (Table 2). Among the subscale scores, memory had the highest mean of 86.5, and the lowest mean was observed for QOL item (40.4).

Older children reported significantly lower energy levels ($P < 0.001$) and greater depression ($P = 0.007$), anxiety ($P < 0.001$), and helplessness ($P = 0.008$). Early age of onset of epilepsy was associated with higher scores among the anxiety ($P = 0.023$), behavior ($P = 0.008$), language ($P = 0.047$), and social activities ($P = 0.015$) subscales. Duration of epilepsy had a negative correlation with the energy subscale scores with Pearson's coefficient of −0.23 and $P$ of 0.015. Children with severe seizures (as assessed by the Hague seizure severity score in this study) had lower energy ($P = 0.05$), depression ($P = 0.021$), anxiety ($P = 0.036$), and QOL ($P = 0.024$) subscale scores. Duration of AED use was observed to have a negative correlation with energy ($P = 0.008$), anxiety ($P = 0.003$), control/helplessness ($P = 0.049$), esteem ($P = 0.026$), social activities ($P = 0.031$), and general health ($P = 0.035$) subscale scores. The AEP score was higher in children with greater adverse effects of AEDs and vice versa; AEP score had a significant negative correlation with the all the QOLCE subscale variables ($P \leq 0.001$).

The total QOLCE score was compared with the various clinical variables to study if there was any significant association. It was found that there was a significant association between duration of epilepsy, seizure frequency, presence of recent seizures, history of developmental delay, duration of AED intake, adherence to AEDs, the number of AEDs, AEP score, and hospitalization for seizures with total QOLCE score (Tables 3 and 4).

**Table 3**
Total QOLCE score correlated with the following variables.

| Variable | | Total QOLCE score (Mean ± SD) | *P*-value |
|---|---|---|---|
| Number of AEDs taken | Single | 75.7 ± 12.59 | 0.001 |
| | Multiple | 66.9 ± 13.75 | |
| Seizure frequency in the last year | Nil | 79.33 ± 12.58 | 0.008 |
| | 1–12 per year | 71.98 ± 11.42 | |
| | ≥ 12 per year | 66.99 ± 17.8 | |
| Last seizure | <1 week | 67.6 ± 14.08 | 0.014 |
| | 1 week to 1 month | 76.5 ± 7.96 | |
| | 1–6 month | 73.0 ± 13.13 | |
| | 6–12 months | 67.2 ± 16.42 | |
| | >1 year | 78.8 ± 12.3 | |
| History of developmental delay | No | 74.2 ± 12.61 | 0.014 |
| | Yes | 66.38 ± 15.79 | |
| Adherence to AEDs | Good | 76.02 ± 12.45 | 0.001 |
| | Poor | 66.97 ± 13.77 | |
| Hospitalization | Nil | 74.09 ± 12.70 | 0.015 |
| | Present | 66.12 ± 15.87 | |

**Table 4**
Total QOLCE score correlated with the following variables.

| Variable | | Total QOLCE score |
|---|---|---|
| Epilepsy duration | Pearson correlation(r) | −0.19 |
| | *P* | 0.045 |
| Duration of AED intake | r | −0.25 |
| | *P* | 0.009 |
| AEP Score | r | −0.69 |
| | *P* | <0.001 |

From the univariate analysis, the variables found to be significant at 20% level of significance were included for the construction of the final model. Ordinary least square regression with backward elimination was performed. The predictors of QOL that emerged from the regression analysis were AEP score, presence of hospitalization, developmental delay, and adherence to AEDs (Table 5). This model explained 59% of the variance in the total QOLCE score.

## 4. Discussion

Epilepsy affects the physical, cognitive, psychological, emotional, and social spheres of the growing child. These effects can best be assessed by determining the QOL as reported by the patient. The mean total QOLCE score was 72.6 ± 13.6. The mean total QOLCE score in the present study is higher than the scores noted in other studies from Indian subcontinent, which have employed the QOLCE scale for assessment of QOL [27,38,39]. The difference may be due to the variation in the age groups sampled in the various studies, the overall sample sizes, and inherently different cultural milieus. Among the subscale scores, memory had the highest mean of 86.5 followed by stigma (85.4), language (83.05), and control/helplessness (81.07), and the lowest mean was observed for QOL item (40.4), general health (41.36), and physical restriction (65.19). Similar low score in general health and physical restriction has been noted in studies conducted in India [27,38]. This is in contrast to the study by Sabaz et al. where lower mean subscale scores were observed in memory, language, attention/concentration, and other cognitive functions [33]. This may be explained by the relatively weaker social/infrastructure support system available for children with epilepsy in India.

There was no significant association of the total QOLCE score with gender, or any of the demographic variables such as residence, socioeconomic status, paternal/maternal education, or family type. Similar results were noted in other studies [27,38–40]. However, there have been studies that have noted a significant association between maternal education, rural residence, and marital status of parents with overall QOL [27,38,39]. The findings in various studies may differ due to use of different scales for QOL assessment, variation in sample size, and probably regional differences.

The mean total QOLCE score was lower in the age group of 13–18 years (70.83 ± 15.78), followed by 10–12 years (73.51 ± 11.50), and the highest in the younger age group of 4–9 years (74.82 ± 11.08). However, the correlation of the total QOLCE score with age

**Table 5**
Regression analysis of the variables affecting the total QOLCE score.

| Variable | Estimate | Standard error | t value | *P*-value |
|---|---|---|---|---|
| Adherence to AEDs | −6.56 | 1.77 | −3.68 | <0.001 |
| AEP score | −1.07 | 0.11 | −9.65 | <0.001 |
| Developmental delay | −6.09 | 2.10 | −2.90 | <0.01 |
| Hospitalization | −6.65 | 2.19 | −3.03 | <0.01 |

Multiple $R^2$: 0.59, Adjusted $R^2$: 0.57.
Residual standard error: 8.88 on 105 degrees of freedom.
F-statistic: 38.04.

was not significant. Lower mean total QOLCE score has been noted among older children in another study [38]. Older children had lower energy, greater depression, anxiety, and helplessness with the respective scores being significantly correlated with age in our study. Similar results have been observed in other studies [27,38]. Older children are more knowledgeable about the disease and also are sensitive to stigma and negative societal attitude toward the disease. Children are likely to meet with increasing scholastic responsibilities with age, which may result in a sense of pressure to meet expectations. These factors may contribute to higher anxiety, depression, and feeling of helplessness.

It was observed that children who had early age of onset of epilepsy had less anxiety and better language, social activity, and behavior scores than children with later age of onset of epilepsy. This may be due to better adaptation to the illness in children who have an earlier onset. The duration of epilepsy had a significant negative correlation with the mean total QOLCE score ($P = 0.045$). Duration of epilepsy has been demonstrated to affect the QOL of CWE in study by Cianchetti et al. [41]. In the present study, it was found that children with long duration of epilepsy had lower energy subscale scores ($P = 0.015$).

The severity of seizures did not have a significant correlation with mean total QOLCE score. However, children with more severe seizures had significantly lower energy and QOL subscale scores and greater depression and anxiety. Similar findings have been noted in other studies [22,33]. There was no significant association between the type of seizure (focal/generalized) and the total QOLCE score. Children with frequent seizures, as expected, had significantly lower total QOLCE score ($P = 0.008$). Short duration of the interval since last seizure was also associated with lower total QOLCE score ($P = 0.014$) also noted by Aggarwal et al. [27]. Children who have had a recent seizure are more likely to be affected by it and perceive greater inconvenience than children who had a seizure in the distant past.

Children who were on single AED had a higher mean total QOLCE score of 75.7 ± 12.59 compared with those who were on multiple AED who had a mean total QOLCE score of 66.9 ± 13.75. The difference was significant with $P$ of 0.001. Similar association was noted in various studies conducted across the world [9,25,26,40]. Sabaz et al. also noted a negative correlation of number of medications taken with the memory and language subscale scores. The duration of AED intake had a significant negative association with the mean total QOLCE score ($P = 0.009$). Children who have been on AEDs for prolonged duration are more likely to experience adverse effects of the AEDs, which can hamper their physical, cognitive, behavioral, and even emotional functions. In the present study, the subscale scores sharing a negative correlation with duration of AED intake were energy, anxiety, control, esteem, social activity, and general health. Those who had change of AEDs prescribed or discontinuation of AEDs did not have any significant difference in total QOLCE score. The children who had good compliance/adherence to AEDs had significantly better total QOLCE score ($P = 0.001$). The QOL of CWE is found to be associated with the number of failed AEDs in the study conducted by Sherman et al. [40]. Good compliance with medications will lead to better control of the seizures and hence improve the QOL. The AEP score had a significant negative correlation with the total QOLCE score ($P < 0.001$). This is consistent with earlier studies [22,24]. The AEP score had a significant negative correlation with all the subscale scores.

Children with history of developmental delay had significant negative association with the total QOLCE score ($P = 0.014$). Similar finding of lower developmental level associated with poor QOL in CWE has been observed by Sherman et al. [40]. Children who were hospitalized for seizures had lower mean total QOLCE score (66.12 ± 15.87) compared with children who were never hospitalized (mean total QOLCE score of 74.09 ± 12.70). The association was significant with $P = 0.015$. Among all the predictors of QOL, AEP score and adherence to AEDs had the most significant association with the total QOLCE score ($P < 0.001$) making them the most significant predictors of the QOL in CWE.

In the present study, QOLCE scale was used for the assessment of QOL in CWE, which is an epilepsy-specific scale, unlike other studies, which have used generic scales for assessment of QOL. An epilepsy-specific scale is more sensitive and better suited for assessment of the various predictors of QOL in epilepsy. Our study objective was to comprehensively assess the QOL in CWE and determine the predictors of QOL. The predictors identified were related to the epilepsy severity, duration, and AED intake, which are modifiable to a certain extent. Identifying the predictors can help in implementing appropriate management of the condition. Measures to improve the QOL of CWE should be a part of the treatment protocol of epilepsy in children. It also would be useful to develop specific interventions for reducing the burden of AEDs and their adverse events. Screening for comorbid conditions and routine cognitive and psychological assessment during follow-up will help in earlier recognition of factors, which can impair QOL.

A limitation of the study was the population sampling, which was predominantly from an urban population, and the limited sample size. Another observation is that psychiatric and behavioral problems may also develop secondary to epilepsy disease per se and hence may be confounding factors in assessment of the adverse effects of AEDs. The QOLCE scale is a parent-reported scale, which may be associated with parental bias. Assessment of QOL with child-reported scales may lead to different conclusions.

## 5. Conclusion

Epilepsy and use of multiple AEDs in the course of treatment have a detrimental impact on the health, scholastic performance, and the QOL of a growing child. The QOL is most compromised by polytherapy, poor compliance to medication, adverse effects of AEDs, hospitalization, and presence of developmental delay.

## Acknowledgment

The authors would like to thank all the children and their parents for their contribution.

## Conflict of interest

The authors declare no conflict of interest. Further, the authors received no financial support for the research, authorship, and/or publication of this article.

## References

[1] Aaberg KM, Gunnes N, Bakken IJ, Lund Søraas C, Berntsen A, Magnus P, et al. Incidence and prevalence of childhood epilepsy: a nationwide cohort study. Pediatrics 2017;139(5) [pii: e20163908].

[2] Russ SA, Larson K, Halfon N. A national profile of childhood epilepsy and seizure disorder. Pediatrics 2012;129(2):256–64.

[3] Gadgil P, Udani V. Pediatric epilepsy: the Indian experience. J Pediatr Neurosci 2011; 6(Suppl. 1):S126–9.

[4] Camfield C, Breau L, Camfield P. Impact of pediatric epilepsy on the family: a new scale for clinical and research use. Epilepsia 2001;42(1):104–12.

[5] Austin JK, Dunn DW, Caffrey HM, Perkins SM, Harezlak J, Rose DF. Recurrent seizures and behavior problems in children with first recognized seizures: a prospective study. Epilepsia 2002;43:1564–73.

[6] Bautista RE, Shapovalov D, Shoraka AR. Factors associated with increased felt stigma among individuals with epilepsy. Seizure 2015;30:106–12.

[7] Fernandes PT, Salgado PC, Noronha AL, Sander JW, Li LM. Stigma scale of epilepsy: validation process. Arq Neuropsiquiatr 2007;65(Suppl. 1):35–42.

[8] Wu KN, Lieber E, Siddarth P, Smith K, Sankar R, Caplan R. Dealing with epilepsy: parents speak up. Epilepsy Behav 2008;13(1):131–8.

[9] Speechley KN, Ferro MA, Camfield CS, Huang W, Levin SD, Smith ML, et al. Quality of life in children with new-onset epilepsy: a 2-year prospective cohort study. Neurology 2012;79(15):1548–55.

[10] Kaufmann R, Goldberg-Stern H, Shuper A. Attention-deficit disorders and epilepsy in childhood: incidence, causative relations and treatment possibilities. J Child Neurol 2009;24(6):727–33.

[11] Beghi M, Cornaggia CM, Frigeni B, Beghi E. Learning disorders in epilepsy. Epilepsia 2006;47(Suppl. 2):14–8.

[12] Caplan R, Siddarth P, Gurbani S, Hanson R, Sankar R, Shields WD. Depression and anxiety disorders in pediatric epilepsy. Epilepsia 2005;46(5):720–30.

[13] Pellock JM. Defining the problem: psychiatric and behavioral comorbidity in children and adolescents with epilepsy. Epilepsy Behav 2004;5(Suppl. 3):S3–9.

[14] Dunn DW, Austin JK, Harezlak J, Ambrosius WT. ADHD and epilepsy in childhood. Dev Med Child Neurol 2003;45(1):50–4.

[15] Ettinger AB, Weisbrot DM, Nolan EE, Gadow KD, Vitale SA, Andriola MR, et al. Symptoms of depression and anxiety in paediatric epilepsy patients. Epilepsia 1998;39(6):595–9.

[16] Fastenau PS, Shen Jianzhao, Dunn DW, Austin JK. Academic underachievement among children with epilepsy: proportion exceeding psychometric criteria for learning disability and associated risk factors. J Learn Disabil 2008;41(3):195–207.

[17] Bailet LL, Turk WR. The impact of childhood epilepsy on neurocognitive and behavioral performance: a prospective longitudinal study. Epilepsia 2000;41(4):426–31.

[18] Fastenau PS, Johnson CS, Perkins SM, Byars AW, deGrauw TJ, Austin JK, et al. Neuropsychological status at seizure onset in children: risk factors for early cognitive deficits. Neurology 2009;73(7):526–34.

[19] Schouten A, Oostrom KJ, Pestman WR, Peters AC, Jennekens-Schinkel A, Dutch Study Group of Epilepsy in Childhood. Learning and memory of school children with epilepsy: a prospective controlled longitudinal study. Dev Med Child Neurol 2002;44(12):803–11.

[20] Love CE, Webbe F, Kim G, Lee KH, Westerveld M, Salinas CM. The role of executive functioning in quality of life in pediatric intractable epilepsy. Epilepsy Behav 2016;64(Pt A):37–43.

[21] Ravens-Sieberer U, Erhart M, Wille N, Wetzel R, Nickel J, Bullinger M. Generic health-related quality-of-life assessment in children and adolescents: methodological considerations. PharmacoEconomics 2006;24(12):1199–220.

[22] Jovanovic M, Jocic-Jakubi B, Stevanovic D. Adverse effects of antiepileptic drugs and quality of life in pediatric epilepsy. Neurol India 2015;63(3):353–9.

[23] Ferro MA. Risk factors for health-related quality of life in children with epilepsy: a meta-analysis. Epilepsia 2014;55(11):1722–31.

[24] Modi AC, Ingerski LM, Rausch JR, Glauser TA. Treatment factors affecting longitudinal quality of life in new onset pediatric epilepsy. J Pediatr Psychol 2011;36(4):466–75.

[25] Miller V, Palermo TM, Grewe SD. Quality of life in pediatric epilepsy: demographic and disease-related predictors and comparison with healthy controls. Epilepsy Behav 2003;4(1):36–42.

[26] Reilly C, Atkinson P, Das KB, Chin RF, Aylett SE, Burch V, et al. Factors associated with quality of life in active childhood epilepsy: a population-based study. Eur J Paediatr Neurol 2015;19(3):308–13.

[27] Aggarwal A, Datta V, Thakur LC. Quality of life in children with epilepsy. Indian Pediatr 2011;48:893–6.

[28] Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, et al. Operational classification of seizure types by the international league against epilepsy: position paper of the ILAE Commission for Classification and Terminology. Epilepsia 2017;58(4):522–30.

[29] Carpay HA, Arts WF, Vermeulen J, Stroink H, Brouwer OF, Peters AC, et al. Parent-completed scales for measuring seizure severity and severity of side-effects of antiepileptic drugs in childhood epilepsy: development and psychometric analysis. Epilepsy Res 1996;24(3):173–81.

[30] Dwivedi R, Ramanujam B, Chandra PS, Sapra S, Gulati S, Kalaivani M, et al. Surgery for drug-resistant epilepsy in children. N Engl J Med 2017;377(17):1639–47.

[31] Baker GA, Middleton A, Jacoby A. Initial development, reliability, and validity of a patient based adverse event scale. Epilepsia 1994;35:80.

[32] Byerly MJ, Nakonezny PA, Rush AJ. The brief adherence rating scale (BARS) validated against electronic monitoring in assessing the antipsychotic medication adherence of outpatients with schizophrenia and schizoaffective disorder. Schizophr Res 2008;100:60–9.

[33] Sabaz M, Cairns DR, Lawson JA, Nheu N, Bleasel AF, Bye AM. Validation of a new quality of life measure for children with epilepsy. Epilepsia 2000;41(6):765–74.

[34] Cramer JA, Camfield C, Carpay H, Helmstaedter C, Langfitt J, Malmgren K, et al. Principles of health-related quality of life: assessment in clinical trials. Epilepsia 2002;43:1084–95.

[35] Cowan J, Baker GA. A review of subjective impact measures for use with children and adolescents with epilepsy. Qual Life Res 2004;13:1435–43.

[36] Talarska D. The usefulness of quality of life childhood epilepsy (QOLCE) questionnaire in evaluating the quality of life of children with epilepsy. Adv Med Sci 2007;52(Suppl. 1):191–3.

[37] Oberoi SS. Updating income ranges for Kuppuswamy's socio-economic status scale for the year 2014. Indian J Public Health 2015;59(2):156–7.

[38] Nadkarni J, Jain A, Dwivedi R. Quality of life in children with epilepsy. Ann Indian Acad Neurol 2011;14(4):279–82.

[39] Arya V, Gehlawat VK, Kaushik JS, Gathwala G. Assessment of parent reported quality of life in children with epilepsy from Northern India: a cross-sectional study. J Pediatr Neurosci 2014;9:17–20.

[40] Sherman EM, Griffiths SY, Akdag S, Connolly MB, Slick DJ, Wiebe S. Sociodemographic correlates of health-related quality of life in pediatric epilepsy. Epilepsy Behav 2008;12(1):96–101.

[41] Cianchetti C, Messina P, Pupillo E, Crichiutti G, Baglietto MG, Veggiotti P, et al. The perceived burden of epilepsy: impact on the quality of life of children and adolescents and their families. Seizure 2015;24:93–101.