NEUROSCIENCE RESEARCH NOTES

OPEN ACCESS | RESEARCH NOTES ISSN: 2576-828X

Comparative retrospective analysis: exploring the quality of life of people with epilepsy in two cohorts

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Received: 3 November 2023; **Accepted:** 31 January 2024; **Published:** 25 March 2024
Edited by: Battuvshin Lkhagvasuren (Mongolian National University of Medical Sciences, Mongolia)
Reviewed by: Gantsetseg Tumur-Ochir (Mongolian National University of Medical Sciences, Mongolia); Oyuntugs Byambasukh (Mongolian National University of Medical Sciences, Mongolia)
https://doi.org/10.31117/neuroscirn.v7i1.310

Abstract: People with epilepsy (PWE) are reported to have a lower quality of life (QOL). QOL among PWE were primarily observed through cross-sectional studies, and there is little information about the progression of QOL among PWE over the years. This study aimed to investigate the changes in QOL among PWE at a tertiary referral centre. A retrospective observational study was conducted among PWE from the Neurology clinic at the University Malaya Medical Centre. Data were extracted from the Quality of Life in Epilepsy Inventory (QOLIE-31) database for 2016, 2017, and 2020. A total of 88 subjects were included in Cohort 1 (2016 vs. 2017) and Cohort 2 (2017 vs. 2020), respectively. There was a significant improvement in mean scores of QOLIE-31 in Cohort 1 (57.7±12.2 vs. 63.2±14.2; $p<0.001$), in terms of seizure worry, emotional well-being, cognitive functioning, medication effects and social function ($p<0.05$, respectively). However, significant deterioration was observed in Cohort 2 (67.1±15.6 vs. 63.1±14.9; $p=0.008$), in terms of seizure worry and cognitive functioning ($p<0.05$, respectively). Based on the calculated Jacobson Reliable Change Index (RCI) for the QOLIE-31 score, 28.4% from Cohort 2 experienced deterioration of QOL as compared to those from Cohort 1 (8%) ($p<0.001$), which was most likely attributed to the COVID-19 pandemic. This study provides insights into the change of QOL among PWE in Malaysia over time, encompassing the COVID-19 pandemic period.

Keywords: Epilepsy; Quality of life; Patients with epilepsy; QOLIE-31

1.0 INTRODUCTION

Epilepsy is a prevalent neurological disorder, with a global lifetime prevalence of 7.6 per 1000 individuals, making it the fourth most debilitating neurologic illness worldwide in terms of Disability-adjusted Life Years (Fiest et al., 2017; GBD 2017 DALYs and HALE Collaborators, 2018). The prevalence of epilepsy is vastly varied among Asian countries, where it ranges from 1.5 to 14.0 per 1000 individuals (Mac et al., 2007). In Malaysia, the prevalence of lifetime epilepsy is 7.8 in

1000 individuals (Fong et al., 2021). The quality of life (QOL) of people with epilepsy (PWE) is acknowledged as a crucial aspect of clinical management, and more focus has been placed on this over the past few decades. Previous literature reported that PWE experiences a lower QOL when compared to those with other chronic conditions, such as diabetes and heart disease (Hermann et al., 1996; Vickrey et al., 1994). This could be attributed to PWE being susceptible to psychological comorbidities, including depression, anxiety and psychosis (Josephson and Jetté, 2017). These psychological comorbidities are closely associated with poorer treatment outcomes, high discrimination or stigmatisation and poor quality of life (Tsigebrhan et al., 2023; Whatley et al., 2010; van Ool et al., 2016). PWE experience stigmatisation and are plagued by a variety of social and psychological implications, which lower their quality of life (Azuma and Akechi, 2014; Malik et al., 2022; Tombini et al., 2021).

Several cross-sectional studies have been conducted globally to understand the quality of life among PWE and its predictors (Azuma and Akechi, 2014; Chen et al., 2016; Gebre and Haylay, 2018; Honari et al., 2021; Malik et al., 2022; Saadi et al., 2016; Silva et al., 2019; Tombini et al., 2021). Similarly, in Malaysia, QOL among PWE were observed through the cross-sectional studies that are prevailing in a different population at a certain time point, including West and East Malaysia (Lua et al., 2007; Norsa'adah et al., 2013), children with epilepsy (Fong et al., 2018) and during the COVID-19 pandemic (Koh et al., 2021a).

However, there is little information about PWE on the progression of QOL over the years, although a Caucasian study reported that PWE generally experience changes in their QOL over 6 months (Wiebe et al., 2002). Understanding the progression of QOL among PWE is crucial to identifying the impacts of historical medical, socio-cultural or environmental factors and to planning strategies towards achieving better health outcomes for PWE. Therefore, this study aimed to explore the longitudinal changes in QOL among PWE from the University Malaya Medical Centre (UMMC) between 2016 and 2020.

2.0 MATERIALS AND METHODS

2.1 Study design

A retrospective longitudinal observational study was conducted on PWE from the Neurology Clinic of UMMC. Data were extracted from the Quality of Life in Epilepsy Inventory (QOLIE-31) database for the years 2016, 2017 and 2020. The QOLIE-31 database comprises data on the QOL of PWE who visited the Neurology Clinic, UMMC and completed the QOLIE-31 questionnaire in previous studies from 2016 – 2020. Ethical clearance was obtained for each research conducted previously from the Medical Research Ethics Committee, University of Malaya Medical Centre (MREC ID No. 202056-8601).

2.2 Study population

The QOLIE-31 database comprises surveys completed in 2016, 2017, and 2020. Data in 2020 was collected during the beginning of the COVID pandemic and the movement control order (MCO) period. Those subjects who completed at least two QOLIE-31 questionnaires (i.e., Cohort 1: 2016 vs. 2017 and Cohort 2: 2017 vs. 2020) were included. The exclusion criteria were (1) those subjects with duplicate data and (2) those who had partially completed the questionnaire. This study had no dropouts as it involved a sub-analysis that consolidated the repeated data.

2.3 Study instrument

The QOLIE-31 was employed in this study to evaluate the QOL among PWE, using the English or validated Malay or Chinese-translated versions (Liu et al., 2003; Norsa'adah et al., 2013; Vickery et al., 1993). It is a validated questionnaire regarding its reliability and validity in assessing health-related QOL among PWE (Cramer et al., 1998). This self-administered questionnaire consists of 31-item which are categorised into seven subscale domains: seizure worry (5 items); emotional well-being (5 items), energy/fatigue (4 items), medication effects (3 items), cognitive functioning (6 items), social functioning (5 items), and overall QOL (2 items). This questionnaire uses a Likert scale to collect the respondents' responses. The raw scores were converted to scores between 0 and 100 according to the QOLIE-31 scoring manual, where the higher scores indicate a better quality of life (Vickery et al., 1993). The scores from the seven subscales will be then weighted and summated to determine the overall QOL score. On the other hand, a previous study demonstrated that QOLIE-31 can distinguish the changes (from no change to large change) precisely by 95% confidence intervals (Wiebe et al., 2002).

2.4 Data extraction and transformation

Data extraction from the database was done using a designated data collection form. The data was coded using registered identification numbers for each year and were matched. There were 96 subjects included in

Cohort 1 (2016 vs. 2017) and 94 subjects in Cohort 2 (2017 vs. 2020). A total of 8 and 6 subjects were excluded from Cohort 1 and 2, respectively, due to partially completed questionnaires and dataset duplication. With the responses, the raw scores from each item were translated to scores 0 – 100 during the scoring process. Following the inclusion and exclusion criteria, 88 patients from Cohort 1 (2016 vs 2017) and 88 patients from Cohort 2 (2017 vs 2020) were included in this study. The percentage of change in QOLIE-31 score between each year was determined by using the following formula:

$$\text{Percentage of change in score (\%)} = \frac{\text{Score of latest year} - \text{Score of previous year}}{\text{Score of previous year}}$$

The overall QOLIE-31 scores for each subject were further transformed into the Jacobson Reliable Change Index to determine the risk differences compared to the likelihood of participants making a reliable change. An RCI of more than ±1.96 was required for the change to consider statistically reliable at $p < 0.05$ (Noble et al., 2018). A Jacobson Reliable Change Index (RCI) was calculated for overall QOLIE-31 scores (Noble et al., 2018).

$$\text{Reliable Change Index (RCI)} = \frac{X_2 - X_1}{S_{diff}}$$

$$\text{where } S_{diff} = \sqrt{2S_E^2} \text{ and } S_E = S_1\sqrt{1 - r_{xx}}$$

X_1 = first QOLIE score of an individual
X_2 = subsequent QOLIE score of an individual
S_{diff} = SE of differences
S_E = standard error of measurement
S_1 = standard deviation at pre level
r_{xx} = reliability of the scale

2.5 Data analysis

Continuous data were expressed as mean ± standard deviation (SD) or median (interquartile range) if the data were not normally distributed. All data were analysed using the Statistical Package for Social Sciences (SPSS) version 26.0 (IBM Corporation, Armonk, New York, U.S.). The Kolmogorov–Smirnov test determined the normality of data for all the tested variables to select the appropriate tests as the normality of data may affect the validity and reliability of the results obtained from these tests. The Student's T-test or Mann-Whitney U test (if the data were not normally distributed) was used to assess the difference in variables between the two groups. The chi-squared ($\chi 2$) test or Fisher's exact test (when the frequency of respondents was less than 5 for any category) was performed to determine the association between categorical groups, such as gender, ethnicity and seizure control. Paired T-test or related samples Wilcoxon Signed Rank Test (if the data were not normally distributed) was used to assess the significance in differences between two repeated measured variables (i.e., the QOLIE scores) for the same individual. The p-value < 0.05 was considered statistically significant. One-way analysis of variance (ANOVA) or the Kruskal-Wallis test (if the data were not normally distributed) was used to assess the difference in variables between groups (more than two groups). Spearman's correlation (as the data were not normally distributed) was used to measure the strength of linear relationships between two continuous variables (e.g., percentage of changes in QOLIE score and age).

3.0 RESULTS

The demographic and clinical characteristics of included subjects are tabulated in **Table 1**. The median age for Cohort 1 (2016 vs 2017) was 35.5 years [Interquartile range (IQR) = 17.0], with the majority being Chinese (56.8%), employed (70.5%), without a family history of epilepsy (67.0%) and on antiepileptic polytherapy (51.1%). At the same time, Cohort 2 (2017 vs 2020) had a median age of 37.0 years (IQR = 27.0), where the majority were Chinese (47.7%), employed (62.5%), without a family history of epilepsy (60.2%) and on antiepileptic polytherapy (52.3%). No significant demographic and clinical characteristics differences existed between Cohort 1 and 2 ($p>0.05$; **Table 1**).

The changes in the QOLIE-31 score and its subscale scores for both cohorts are summarised in **Table 2**. There was a significant improvement in mean scores of QOLIE-31 in Cohort 1 (57.7±12.2 vs. 63.2±14.2; $p<0.001$), yet a significant deterioration was observed in Cohort 2 (67.1±15.6 vs. 63.1±14.9; $p=0.008$). In Cohort 1, the subscale scores were significantly improved in terms of seizure worry ($p<0.001$), emotional well-being ($p=0.007$), cognitive functioning ($p=0.004$), medication effects ($p=0.001$) and social function ($p<0.001$). On the other hand, the subscales scores significantly deteriorated for seizure worry ($p=0.003$) and cognitive functioning ($p=0.021$) subscales for Cohort 2. In terms of percentage of change, Cohort 1 (median = 10.6; IQR = 25.1) demonstrated a significant positive change in mean

QOLIE-31 score as compared to Cohort 2 (median = -4.3; IQR = 32.9; p<0.001), particularly in seizure worry (p<0.001), emotional well-being (p=0.002), cognitive functioning (p=0.002), medication effects (p=0.033) and social function (p<0.001) subscales. The score changes of each component in the seven subscales of QOLIE-31 are presented in Supplementary File 1.

Table 3 summarises the Jacobson Reliable Change Index (RCI) for the QOLIE-31 scores in Cohort 1 and 2. Based on the calculated RCI, 42.1% from Cohort 1 demonstrated an improvement in QOL compared to those from Cohort 2 (12.5%), whereas 28.4% from Cohort 2 experienced deterioration of QOL as compared to 8% from Cohort 1 (p<0.001). This could be explained by the COVID-19 outbreak that took place in 2020. The QOL of Cohort 2 were measured in 2017 and 2020. Hence, it is highly probable that the decline in QOL experienced by PWE in Cohort 2 can be attributed to the COVID-19 pandemic.

Table 1: Demographic and clinical characteristics of the subjects from Cohort 1 and 2

Characteristic	n (%) Cohort 1* (n = 88)	Cohort 2** (n = 88)	p value[δ]
Gender			
Male	41 (46.6)	42 (47.7)	0.880[a]
Female	47 (53.4)	46 (52.3)	
Age[#], years (median, IQR)	35.5 (17.0)	37.0 (27.0)	0.113[b]
Age of disease onset, years (median, IQR)	18.0 (12.0)	18.0 (18.5)	0.372[b]
Duration of epilepsy[#], years (median, IQR)	13.5 (17.0)	13.0 (17.0)	0.847[b]
Ethnicity			
Malay	20 (22.7)	23 (26.1)	0.522[a,Φ]
Chinese	50 (56.8)	42 (47.7)	
Indian	18 (20.5)	22 (25.0)	
Others	0 (0)	1 (1.1)	
Employment			
Employed	62 (70.5)	55 (62.5)	0.264[a]
Unemployed	26 (29.5)	33 (37.5)	
Type of seizure			
Generalised	22 (25.0)	19 (21.6)	0.534[a,Φ]
Focal	63 (71.6)	68 (77.3)	
Unknown	3 (3.4)	1 (1.1)	
Seizure control			
No seizure for at least 1 year	30 (34.5)	41 (47.1)	0.219[a]
< 1 per month	32 (36.8)	24 (27.6)	
≥ 1 per month	25 (28.7)	22 (25.3)	
Family history of epilepsy			
Yes	29 (33.0)	35 (39.8)	0.347[a]
No	59 (67.0)	53 (60.2)	
Type of AED therapy			
Monotherapy	43 (48.9)	41 (46.6)	0.589[a,Φ]
Polytherapy	45 (51.1)	46 (52.3)	
Unknown	0 (0)	1 (1.1)	

*2016 vs. 2017; **2017 vs. 2020; [#]based on first year of enrolment; [a]Chi-Square test; [b]Mann-Whitney test; [Φ]Statistical analysis was performed by excluding the 'others' or 'unknown' category; [δ]Significant level at p<0.05.
AED: antiepileptic drug; IQR: interquartile range.

Table 2: Changes in QOLIE-31 scores between 2016 – 2020

	Cohort 1, n = 88 [Mean ± SD or Median (IQR)]		p-value*	Cohort 2, n = 88 [Mean ± SD or Median (IQR)]		p-value*	Percentage of Change [Median, (IQR)]		p-value*
	2016	2017		2017	2020		Cohort 1	Cohort 2	
Overall score	57.7 ± 12.2	63.2 ± 14.2	**<0.001[a]**	67.1 ± 15.6	63.1 ± 14.9	**0.008[a]**	10.6 (25.1)	-4.3 (32.9)	**<0.001[c]**
Seizure worry	40.9 ± 23.2	53.0 ± 21.6	**<0.001[a]**	59.0 ± 19.3	50.9 ± 27.1	**0.003[a]**	28.9 (92.4)	-13.5 (67.0)	**<0.001[c]**
Overall quality of life	67.5 (27.5)	72.5 (22.5)	0.175[b]	72.5 (19.4)	72.5 (17.5)	0.253[b]	3.1 (35.3)	0 (21.0)	0.059[c]
Emotional well-being	64.0 (24.0)	68.0 (20.0)	**0.007[b]**	72.0 (20.0)	68.0 (24.0)	0.101[b]	6.7 (31.1)	-4.3 (27.9)	**0.002[c]**
Energy/Fatigue	55.0 (15.0)	57.5 (25.0)	0.800[b]	60.0 (23.8)	60.0 (20.0)	0.461[b]	0 (32.7)	0 (36.4)	0.716[c]
Cognitive functioning	57.7 ± 18.6	63.0 ± 22.3	**0.004[a]**	71.9 (32.2)	62.2 (26.1)	**0.025[b]**	7.6 (40.6)	-7.9 (36.5)	**0.002[c]**
Medication effects	40.1 ± 23.3	51.0 ± 29.7	**0.001[a]**	62.5 (52.8)	61.1 (44.5)	0.389[b]	24.3 (136.1)	0 (109.1)	**0.033[c]**
Social function	58.9 ± 19.9	67.3 ± 19.4	**<0.001[a]**	67.0 (36.8)	65.0 (27.8)	0.097[b]	16.0 (55.6)	-0.5 (34.7)	**<0.001[c]**

SD: Standard deviation; IQR: interquartile range.
*Significance level at p<0.05 (bold text); [a] Paired t-test; [b] Related samples Wilcoxon Signed Rank Test; [c] Mann-Whitney test

Table 3: The reliable change index for QOLIE-31 score in Cohort 1 and 2

Outcome Measures	Group comparison	Number of cases	S_1	r_{xx}	S_E	S_{diff}	RCI (mean ± SD)	n (%)			p value*
								RC-	RC0	RC+	
Quality of Life	Cohort 1 (2016-2017)	88	12.24	0.93	3.24	4.58	1.20 ± 2.46	7 (7.95)	44 (50.00)	37 (42.05)	< 0.001
Quality of Life	Cohort 2 (2017-2020)	88	15.65	0.93	4.14	5.86	-0.68 ± 2.33	25 (28.41)	52 (59.09)	11 (12.50)	

S_1: standard deviation at pre level; r_{xx}: reliability of the scale; S_E: standard error of measurement; S_{diff}: SE of differences; RCI: reliable change index; SD: standard deviation; RC-: deterioration; RC0: unchanged; RC+: improved.
* Chi-Square test; significance level at p<0.05.

In terms of factors affecting the change in QOLIE-31 score, no significant difference was found between gender, age, age of disease onset, ethnicity, employment status, type of seizure, seizure control, family history of epilepsy and type of antiepileptic therapy in Cohort 1 (p>0.05, respectively) (**Table 4**). Interestingly, in Cohort 2, the change in QOLIE-31 score significantly differed between seizure control. Those who were seizure-free had the least deterioration in the median change of QOLIE-31 score (-1.2; IQR = 19.9) as compared to those who had seizure less than once a month (-12.4; IQR = 47.2) and one or more seizure a month (-8.4; IQR = 36.7) (p=0.032). Sub-analysis of the effect of seizure control on change of QOLIE-31 score between two cohorts (**Table 5**). Among those who achieved seizure remission, only the seizure worry subscale significantly deteriorated in Cohort 2 (-3.89; IQR = 48.4) compared to Cohort 1 (32.9; IQR = 35.4; p=0.006). Whereas, among those with infrequent seizures (less than one seizure per month), more subscales were significantly worsened in Cohort 2 compared to Cohort 1.

Table 4: Factors affecting the change in QOLIE-31 score

Factor	Cohort 1			Cohort 2		
	n (%)	Percentage of change in QOLIE-31 score, % (Median, IQR)	p value*	n (%)	Percentage of change in QOLIE-31 score, % (Median, IQR)	p value*
Gender						
Male	41 (46.6)	10.8 (27.5)	0.454[a]	42 (47.7)	-5.0 (30.9)	0.567[a]
Female	47 (53.4)	7.5 (24.8)		46 (52.3)	-2.63 (32.6)	
Age[#], years (median, IQR)	-	ρ = -0.175	0.104[b]	-	ρ = 0.144	0.182[b]
Age of disease onset, years (median, IQR)	-	ρ = -0.032	0.768[b]	-	ρ = 0.028	0.797[b]
Duration of epilepsy[#], years (median, IQR)	-	ρ = -0.138	0.200[b]	-	ρ = 0.129	0.233[b]
Ethnicity						
Malay	20 (22.7)	17.4 (21.3)		23 (26.1)	-6.0 (35.3)	
Chinese	50 (56.8)	9.7 (24.0)	0.596[c]	42 (47.7)	-8.0 (32.4)	0.490[c]
Indian	18 (20.5)	9.1 (33.9)		22 (25.0)	0.7 (24.1)	
Others	0 (0)	-		1 (1.1)	4.8 (-)	
Employment						
Employed	62 (70.5)	10.8 (20.2)	0.217[a]	55 (62.5)	-2.7 (31.9)	0.504[a]
Unemployed	26 (29.5)	0.2 (31.9)		33 (37.5)	-6.0 (31.4)	
Type of seizure						
Generalised	22 (25.0)	8.5 (20.1)	0.638[c]	19 (21.6)	2.9 (22.3)	0.596[c]
Focal	63 (71.6)	10.9 (29.6)		68 (77.3)	-6.2 (32.7)	
Unknown	3 (3.4)	-4.8 (-)		1 (1.1)	-26.7 (-)	
Seizure control						
No seizure for at least 1 year	30 (34.5)	7.8 (25.9)	0.452[c]	41 (47.1)	-1.2 (19.9)	**0.032[c]**
< 1 per month	32 (36.8)	13.3 (23.9)		24 (27.6)	-12.4 (47.2)	
≥ 1 per month	25 (28.7)	5.9 (26.8)		22 (25.3)	-8.4 (36.7)	
Family history of epilepsy						
Yes	29 (33.0)	13.8 (29.4)	0.543[a]	35 (39.8)	-3.8 (16.0)	0.174[a]
No	59 (67.0)	8.9 (24.9)		53 (60.2)	-7.7 (36.8)	
Type of AED therapy						
Monotherapy	43 (48.9)	10.5 (26.3)	0.924[a]	41 (46.6)	-2.1 (27.0)	0.757[c]
Polytherapy	45 (51.1)	10.8 (23.0)		46 (52.3)	-7.8 (37.2)	
Unknown	0 (0)	-		1 (1.1)	3.2 (-)	

IQR: interquartile range; AED: antiepileptic drug.

* Significance level at p<0.05 (bold text); [a] Mann-Whitney U test; [b] Spearman's correlation; [c] Kruskal-Wallis test.

Table 5: The effect of seizure control on the change of QOLIE-31 scores between two cohorts

Seizure Control	Percentage of Change (Median, IQR)		p-value*
	Cohort 1	Cohort 2	
No seizure for at least 1 year, n (%)	30 (34.5)	41 (47.1)	
Overall score	7.8 (25.9)	-1.2 (19.9)	0.083
Seizure worry	32.9 (106.9)	-3.89 (48.4)	**0.006**
Overall quality of life	3.23 (35.4)	0.0 (30.9)	0.907
Emotional well-being	7.9 (52.1)	0.0 (24.7)	0.291
Energy/ Fatigue	0.0 (25.9)	0.0 (36.9)	0.641
Cognitive functioning	5.3 (33.9)	-0.3 (31.0)	0.264
Medication effects	18.5 (95.6)	0.0 (110.2)	0.071
Social function	17.4 (52.9)	0.0 (46.3)	0.173
< 1 per month, n (%)	32 (36.8)	24 (27.6)	
Overall score	13.3 (23.9)	-12.4 (47.2)	**<0.001**
Seizure worry	26.2 (75.5)	-32.4 (73.5)	**<0.001**
Overall quality of life	0.0 (24.7)	-6.5 (20.5)	**0.007**
Emotional well-being	11.8 (22.9)	-7.9 (30.8)	**0.002**
Energy/ Fatigue	0.0 (33.0)	-10.6 (27.2)	0.138
Cognitive functioning	12.5 (44.0)	-9.7 (52.4)	**0.014**
Medication effects	41.5 (142.96)	-6.5 (252.9)	0.211
Social function	14.8 (56.8)	-11.9 (31.7)	**0.003**
≥ 1 per month, n (%)	25 (28.7)	22 (25.3)	
Overall score	5.9 (26.8)	-8.4 (112.2)	**0.013**
Seizure worry	27.6 (103.4)	-25.2 (63.2)	**0.002**
Overall quality of life	6.9 (43.6)	0.0 (26.5)	0.381
Emotional well-being	0.0 (35.8)	-2.0 (38.5)	0.370
Energy/ Fatigue	0.0 (41.6)	7.7 (42.5)	0.609
Cognitive functioning	4.4 (40.3)	-14.0 (154.35)	**0.031**
Medication effects	23.5 (156.9)	1.6 (114.6)	0.924
Social function	16.7 (68.6)	-12.1 (49.8)	**0.013**

IQR: interquartile range. * Mann-Whitney test, significance level at p<0.05 (bold text).

4.0 DISCUSSION

The present study employed QOLIE-31 to assess the longitudinal change in QOL among epilepsy patients. QOLIE-31 is one of the instruments validated by its robustness in precisely distinguishing the different levels of QOL change (Wiebe et al., 2002). The mean QOL overall scores of the second year in both Cohort 1 and 2 were slightly higher than the global mean QOLIE-31 score (59.8 ± 8.0) tested across World Health Organization world regions comprised of low to high-income countries (Saadi et al., 2016). Saadi et al. (2016) reported that the QOLIE-31 scores differed among countries by world region and income category, with Low and Middle-Income Countries (LMIC) associated with worse QOL. They explained that this could be potentially attributed to the economic conditions, resources, healthcare infrastructure, geography and culture in epilepsy care. Nevertheless, there is limited information about the changes in the QOL of PWE over the years. This study highlighted that the QOL of a person with epilepsy fluctuated over time. About 42% of Cohort 1 had improvement in QOL. Our cohort consisted of a mixture of those with newly diagnosed and chronic epilepsy, irrespective of seizure type and psychosocial background. Most cross-sectional studies reported that patients with poor seizure control had poorer QOL (Mohamed et al., 2014). However, our study was the first to show an improvement over the years, and the QOL improvement was likely related to a successful pharmacological or surgical treatment. This was congruent with the findings from a previous study, where treatment response is a critical factor for QOL, and this highlights the importance of an iterative approach in the clinical management of epilepsy (Jacoby et al., 2015). However, those with refractory epilepsy might have a stagnant or worsening QOL.

Future prospective studies may help identify the specific factors causing improvement or worsening QOL.

However, there might be other psychosocial or environmental factors that may affect QOL. For example, one of the major factors that may explain the worsening of the QOL in Cohort 2 is the COVID pandemic that started in 2020 when the second set of the QOLIE data was collected. During the COVID pandemic, there was fear of attending clinic consultations, delay in seeking help during emergencies, and problems collecting their medications (Koh et al., 2021b). In addition, the psychosocial issues related to COVID, such as anxiety and depression, lifestyle restrictions and issues with employment or study, may also affect QOL (Koh et al., 2021b; Xiao et al., 2020). However, those with controlled seizures were shown to be less affected in our study.

Most subscales in QOL improved in cohort 1, including seizure worry, emotional well-being, cognitive functioning, medication effects, and social function. These are common subscales that commonly correlate with improved seizure control (Allain et al., 2007). However, during the COVID pandemic, the seizure worry and cognitive functioning subscales worsened (in Cohort 2). This is likely related to logistic issues such as running out of seizure medications, or psychological problems like anxiety or depression, leading to seizure worsening (Koh et al., 2021b). Similarly, other studies also reported that PWE with mood disorders (such as anxiety and depression) were associated with poorer QOL in addition to epilepsy-related variables, including seizure control, antiepileptic drugs (AEDs) regimen and side effects of AEDs (Chen et al., 2016; Silva et al., 2019).

The impact of various factors associated with patients' demographic characteristics (i.e. age, gender, ethnicity), employment status and epilepsy-related variables (i.e. duration of epilepsy, type of seizure, seizure control and type of AED therapy) were analysed in this study. The result revealed that only seizure control was significantly associated with the negative change in QOLIE score in Cohort 2 during the COVID-19 pandemic. However, this association was not significant in Cohort 1. This further emphasises the potential compounding impact of the COVID pandemic, especially on those with poor seizure control, which is congruent with the findings reported by Koh et al. (2021b). The sub-analysis showed that the COVID-19 pandemic had a negative impact on multiple domains (psychological, social and cognitive) in the quality of life, if the seizures were not in remission. This could be explained by the changes PWE encountered during the pandemic, which affected their physical, social, and emotional functioning (Koh et al., 2021b). Other variables were found to have no association with the change in QOL. There is little literature on these factors affecting longitudinal QOL among PWE. A QOL study conducted in the United States demonstrated that the QOL remained stable over 7 months among newly onset pediatric epilepsy patients. However, seizure activity and side effects of AEDs were negatively associated with QOL domains (Modi et al., 2011). Nonetheless, the impacts of these factors on changes in QOL among adult epilepsy remain unknown. Further investigation is warranted to explore the relationship between these factors and the changes in QOL among PWE over time. In addition, other important predictive factors, including comorbidities and adverse effects of AED, should be considered in the study design.

4.1 Clinical implications

A longitudinal study on QOL in epilepsy is essential to understand comprehensively the long-term medical and psychosocial factors that have a significant impact on people with epilepsy. For example, this study design will be beneficial in understanding the long-term impacts of the COVID-19 pandemic, long-term campaigns such as the Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders (IGAP), medication shortages during political turmoil, or economic recession. Secondly, this study design allows us to understand the changes in QOL in different phases of epilepsy, including newly diagnosed epilepsy and chronic epilepsy.

4.2 Limitations

This study was limited by its small sample size and retrospective design. However, the collection of QOLIE data in various studies on the same cohort allows us to determine the long-term changes in this group of patients. Secondly, most of the studies applied convenient sampling and may not be able to be generalised to the general population.

5.0 CONCLUSIONS

This longitudinal study provides insights into the change of QOL among PWE in Malaysia over time, encompassing the COVID-19 pandemic period. Understanding the progression of QOL among PWE is crucial to identifying strategies to achieve better health outcomes for PWE.

Acknowledgements:
We would like to acknowledge the Impact Oriented Interdisciplinary Research Grant (IIRG) Programme (IIRG003A-2020HWB).

Author Contributions:
Study conceptualisation and methodology: YHY, KSL; Data collection and analysis: MKB, SLF, CA, YHY, KSL; Manuscript drafting, reviewing and editing: YHY, KSL; Funding and resources acquisition: KSL; Supervision: KSL, YHY.

Conflicts of Interest:
The authors declare no conflict of interest.

References

Allain, H., Schück, S., Nachit-Ouinekh, F., Plouin, P., Brunon, A. M., Boulliat, J., Mercier, F., Slama, A., Baulac, M. & El Hasnaoui, A. (2007). Improvement in quality of life after initiation of lamotrigine therapy in patients with epilepsy in a naturalistic treatment setting. *Seizure*, *16*(2), 173–184. https://doi.org/10.1016/j.seizure.2006.11.009

Azuma, H. & Akechi, T. (2014). Effects of psychosocial functioning, depression, seizure frequency, and employment on quality of life in patients with epilepsy. *Epilepsy & Behavior*, *41*, 18–20. https://doi.org/10.1016/j.yebeh.2014.09.025

Chen, H. F., Tsai, Y. F., Hsi, M. S. & Chen, J. C. (2016). Factors affecting quality of life in adults with epilepsy in Taiwan: A cross-sectional, correlational study. *Epilepsy & Behavior*, *58*, 26–32. https://doi.org/10.1016/j.yebeh.2016.02.019

Cramer, J. A., Perrine, K., Devinsky, O., Bryant-Comstock, L., Meador, K. & Hermann, B. (1998). Development and cross-cultural translations of a 31-item quality of life in epilepsy inventory. *Epilepsia*, *39*(1), 81–88. https://doi.org/10.1111/j.1528-1157.1998.tb01278.x

Fiest, K. M., Sauro, K. M., Wiebe, S., Patten, S. B., Kwon, C. S., Dykeman, J., Pringsheim, T., Lorenzetti, D. L. & Jetté, N. (2017). Prevalence and incidence of epilepsy: A systematic review and meta-analysis of international studies. *Neurology*, *88*(3), 296–303. https://doi.org/10.1212/wnl.0000000000003509

Fong, C. Y., Chang, W. M., Kong, A. N., Rithauddin, A. M., Khoo, T. B. & Ong, L. C. (2018). Quality of life in Malaysian children with epilepsy. *Epilepsy & Behavior*, *80*, 15–20. https://doi.org/10.1016/j.yebeh.2017.12.032

Fong, S.-L., Lim, K.-S., Tan, L., Zainuddin, N. H., Ho, J.-H., Chia, Z.-J., Choo, W.-Y., Puvanarajah, S. D., Chinnasami, S., Tee, S.-K., Raymond, A. A., Law, W.-C. & Tan, C.-T. (2021). Prevalence study of epilepsy in Malaysia. *Epilepsy Research*, *170*, 106551. https://doi.org/https://doi.org/10.1016/j.eplepsyres.2021.106551

GBD 2017 DALYs & HALE Collaborators. (2018). Global, regional, and national disability-adjusted life-years (DALYs) for 359 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*, *392*(10159), 1859–1922. https://doi.org/10.1016/s0140-6736(18)32335-3

Gebre, A. K., & Haylay, A. (2018). Sociodemographic, Clinical Variables, and Quality of Life in Patients with Epilepsy in Mekelle City, Northern Ethiopia. *Behavioural Neurology*, *2018*, 7593573. https://doi.org/10.1155/2018/7593573

Hermann, B. P., Vickrey, B., Hays, R. D., Cramer, J., Devinsky, O., Meador, K., Perrine, K., Myers, L. W. & Ellison, G. W. (1996). A comparison of health-related quality of life in patients with epilepsy, diabetes and multiple sclerosis. *Epilepsy Research*, *25*(2), 113–118. https://doi.org/https://doi.org/10.1016/0920-1211(96)00024-1

Honari, B., Homam, S. M., Nabipour, M., Mostafavian, Z., Farajpour, A., & Sahbaie, N. (2021). Epilepsy and quality of life in Iranian epileptic patients. *Journal of Patient-Reported Outcomes*, *5*(1), 16. https://doi.org/10.1186/s41687-021-00292-3

Jacoby, A., Sudell, M., Tudur Smith, C., Crossley, J., Marson, A. G., Baker, G. A. & SANAD Study Group. (2015). Quality-of-life outcomes of initiating treatment with standard and newer antiepileptic drugs in adults with new-onset epilepsy: findings from the SANAD trial. *Epilepsia*, *56*(3), 460–472. https://doi.org/10.1111/epi.12913

Josephson, C. B. & Jetté, N. (2017). Psychiatric comorbidities in epilepsy. *International Review of Psychiatry*, *29*(5), 409–424. https://doi.org/10.1080/09540261.2017.1302412

Koh, M. Y., Lim, K. S., Fong, S. L., Khor, S. B. & Tan, C. T. (2021a). Impact of COVID-19 on quality of life in people with epilepsy, and a multinational comparison of clinical and psychological impacts. *Epilepsy & Behavior*, *117*, 107849. https://doi.org/10.1016/j.yebeh.2021.107849

Koh, M. Y., Lim, K. S., Fong, S. L., Khor, S. B. & Tan, C. T. (2021b). Impact of COVID-19 pandemic on people with epilepsy: An interventional study using early physical consultation. *Epilepsy & Behavior*, *122*, 108215. https://doi.org/10.1016/j.yebeh.2021.108215

Liu, X. Q., Ren, X. N., Zhou, G. L. & Chen, P. Y. (2003). Reliability and validity of quality of life in epilepsy inventory-31 (QOLIE-31). *Chinese Journal of Neuromedicine*, *2*, 106–109.

Lua, P. L., Haron, H., Cosmas, G. & Nawi, N. H. M. (2007). The Impact of Demographic Characteristics on Health-related Quality of Life Profile of Malaysian Epilepsy Population. *Applied Research in Quality of Life*, *2*(4), 247–271. https://doi.org/10.1007/s11482-008-9041-y

Mac, T. L., Tran, D.-S., Quet, F., Odermatt, P., Preux, P.-M. & Tan, C. T. (2007). Epidemiology, aetiology, and clinical management of epilepsy in Asia: a systematic review. *The Lancet Neurology*, *6*(6), 533–543. https://doi.org/https://doi.org/10.1016/S1474-4422(07)70127-8

Malik, N. I., Fatima, R., Ullah, I., Atta, M., Awan, A., Nashwan, A. J. & Ahmed, S. (2022). Perceived stigma, discrimination and psychological problems among patients with epilepsy. *Frontiers in Psychiatry*, *13*, 1000870. https://doi.org/10.3389/fpsyt.2022.1000870

Modi, A. C., Ingerski, L. M., Rausch, J. R. & Glauser, T. A. (2011). Treatment factors affecting longitudinal quality of life in new onset pediatric epilepsy. *Journal of Pediatric Psychology, 36*(4), 466–475. https://doi.org/10.1093%2Fjpepsy%2Fjsq114

Mohamed, S., Gill, J. S. & Tan, C. T. (2014). Quality of life of patients with epilepsy in Malaysia. *Asia-Pacific Psychiatry*, *6*(1), 105–109. https://doi.org/10.1111/j.1758-5872.2012.00192.x

Noble, A. J., Reilly, J., Temple, J. & Fisher, P. L. (2018). Cognitive-behavioural therapy does not meaningfully reduce depression in most people with epilepsy: a systematic review of clinically reliable improvement. *Journal of Neurology, Neurosurgery & Psychiatry*, *89*(11), 1129–1137. https://doi.org/10.1136/jnnp-2018-317997

Norsa'adah, B., Zainab, J. & Knight, A. (2013). The quality of life of people with epilepsy at a tertiary referral centre in Malaysia. *Health and Quality Life Outcomes*, *11*, 143. https://doi.org/10.1186/1477-7525-11-143

Saadi, A., Patenaude, B. & Mateen, F. J. (2016). Quality of life in epilepsy-31 inventory (QOLIE-31) scores: A global comparison. *Epilepsy & Behavior*, *65*, 13–17. https://doi.org/10.1016/j.yebeh.2016.09.032

Silva, B., Canas-Simião, H., Cordeiro, S., Velosa, A., Oliveira-Maia, A. J. & Barahona-Corrêa, J. B. (2019). Determinants of quality of life in patients with drug-resistant focal epilepsy. *Epilepsy & Behavior*, *100*(Pt A), 106525. https://doi.org/10.1016/j.yebeh.2019.106525

Tombini, M., Assenza, G., Quintiliani, L., Ricci, L., Lanzone, J. & Di Lazzaro, V. (2021). Epilepsy and quality of life: what does really matter? *Neurological Sciences*, *42*(9), 3757–3765. https://doi.org/10.1007/s10072-020-04990-6

Tsigebrhan, R., Derese, A., Kariuki, S. M., Fekadu, A., Medhin, G., Newton, C. R., Prince, M. J. & Hanlon, C. (2023). Co-morbid mental health conditions in people with epilepsy and association with quality of life in low- and middle-income countries: a systematic review and meta-analysis. *Health and Quality Life Outcomes*, *21*(1), 5. https://doi.org/10.1186/s12955-022-02086-7

van Ool, J. S., Snoeijen-Schouwenaars, F. M., Schelhaas, H. J., Tan, I. Y., Aldenkamp, A. P. & Hendriksen, J. G. M. (2016). A systematic review of neuropsychiatric comorbidities in patients with both epilepsy and intellectual disability. *Epilepsy & Behavior*, *60*, 130–137. https://doi.org/https://doi.org/10.1016/j.yebeh.2016.04.018

Vickrey, B. G., Hays, R. D., Rausch, R., Sutherling, W. W., Engel Jr, J. & Brook, R. H. (1994). Quality of Life of Epilepsy Surgery Patients as Compared with Outpatients with Hypertension, Diabetes, Heart Disease, and/or Depressive Symptoms. *Epilepsia*, *35*(3), 597–607. https://doi.org/https://doi.org/10.1111/j.1528-1157.1994.tb02480.x

Vickrey, B. G., Perrine, K. R., Hays, R. D., Hermann, B. P., Cramer, J. A., Meador, K. J. & Devinsky, O. (1993). *Quality of Life in Epilepsy (QOLIE)-31 scoring manual (version 1.0)*. RAND.

Whatley, A. D., DiIorio, C. K. & Yeager, K. (2010). Examining the relationships of depressive symptoms, stigma, social support and regimen-specific support on quality of life in adult patients with epilepsy. *Health Education Research*, *25*(4), 575–584. https://doi.org/10.1093/her/cyq001

Wiebe, S., Matijevic, S., Eliasziw, M. & Derry, P. A. (2002). Clinically important change in quality of life in epilepsy. *Journal of Neurology, Neurosurgery & Psychiatry*, *73*(2), 116–120. https://doi.org/10.1136/jnnp.73.2.116

Xiao, Z., Ding, D., Li, S. & Hong, Z. (2020). Management of people with epilepsy during the COVID-19 pandemic: a national survey among epileptologists in China. *Acta Epileptologica*, *2*(1), 19. https://doi.org/10.1186/s42494-020-00030-0