Quality of life of persons with epilepsy in Mahenge, an onchocerciasis-endemic area in Tanzania : a cross-sectional study

Quality of life of persons with epilepsy in Mahenge, an onchocerciasis-endemic area in Tanzania: a cross-sectional study

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Abstract

Objective: This study investigated the quality of life (QoL) of adults with epilepsy living in Mahenge, an onchocerciasis-endemic area in Tanzania with a high prevalence of onchocerciasis-associated epilepsy (OAE).

Methods: Between February and December 2020, persons with epilepsy (PWE) were recruited from four rural villages in Mahenge: Mdindo, Msogezi, Mzelezi and Sali. For PWE who could not answer the questionnaire due to their mental or physical disability, a family member was asked to answer the questions instead. The Quality of Life in Epilepsy Inventory-31 (QOLIE-31) questionnaire used contained seven domains. The raw domain scores were transformed to 0–100% subscales, with higher scores indicating better QoL. The global QoL was calculated from the subscales using the overall QOLIE-31 score formula.

Results: In total, 96 PWE were enrolled in the study with a median age of 28 (range: 18–60) years, of whom 45 (47%) were male. The questionnaires were answered by PWE (54.8%) or one of their family members (45.2%). Most PWE were single (81%), and half never attended school. About two-thirds (65%) of PWE were suspected of having OAE, and a third (31%) had a history of head nodding seizures. Most PWE were treated with phenobarbital (85.4%) and had high treatment adherence (96.9%). Still, the number of seizures per week ranged from 0 to 7, with a median of one. The mean global QOLIE-31 score was 66.9 (range: 38.3–92.1) out of 100.0. Predictors of lower QoL were living in Sali Village and experiencing seizures the week before the interview. In contrast, completing primary school and switching to second-line anti-seizure medication were predictors of higher QoL.

Conclusion: In order to improve the QoL of PWE in Mahenge, it is vital to optimise anti-seizure medication regimens to decrease the frequency of seizures and to increase the schooling of PWE.

Keywords: Epilepsy, onchocerciasis-associated epilepsy; nodding syndrome; quality of life; education; Africa

1. Introduction

Epilepsy is one of the most common neurological conditions worldwide [1] and an important public health problem in sub-Saharan Africa [2]. It is characterised by abnormal and brief brain electrical activity that can lead to recurrent seizures with cognitive, neurological and psychological

repercussions [3]. Epilepsy prevalence is higher in low- and middle-income countries and rural settings [4], such as sub-Saharan Africa. The reported prevalence of epilepsy in Africa varies widely due to variations in methodologies and definitions used in studies, the presence of epilepsy stigma and misconceptions and the epidemiology of its risk factors, such as heredity, head injuries and parasitic infections [4-6].

Besides increasing the risk of premature death, epilepsy is a source of stigma and social discrimination [7], impacting the quality of life (QoL) of PWE and their families. In turn, QoL is a broad, subjective concept defined as the "individual's perceptions of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, and concerns" [8]. With the turn of the millennium, greater attention has been given to the QoL of PWE. The latter has been related to demographic variables, the presence of stigma, poor knowledge of the condition, type and frequency of seizures, age of onset and treatment status [9]. Studying the QoL of PWE can contribute to a greater understanding of this public health problem and improve the quality of medical care, treatment and resource allocation. To date, no assessment of the QoL of persons with OAE in sub-Saharan Africa has been done.

Epilepsy is unique among major brain disorders. Although there is no cure, several effective and inexpensive anti-seizure medications are available [10]. These treatments could make 70% of persons with epilepsy (PWE) seizure-free [11]. Unfortunately, many PWE in low-income countries cannot access them and consequently suffer substantial personal, social and economic burdens [7]. In addition to the treatment gap, one in every four epilepsy cases can be prevented [7], such as onchocerciasis-associated epilepsy (OAE) [12].

Onchocerciasis is a neglected tropical disease caused by the nematode *Onchocerca volvulus* and spread by blackflies (*Simulium* spp.). The disease burdens millions in sub-Saharan Africa, where over 99% of the infections are found [13]. Also known as river blindness, onchocerciasis causes skin and eye disease and has been recently associated with epilepsy (OAE) [14]. Onchocerciasis-associated epilepsy is characterised by seizures, cognitive impairment and neurological symptoms, including nodding and Nakalanga syndromes [15]. It was estimated that 381,000 (95% CI: 159,000–1636,000) persons were affected by OAE in 2015 [16].

Onchocerciasis can be controlled and eventually eliminated through the implementation of community-directed treatment with ivermectin (CDTi). Ivermectin kills *O. volvulus* offspring (microfilariae) and prevents adult worms from producing microfilariae for several months. In the Mahenge mountains of Tanzania, an onchocerciasis-endemic area, the prevalence of epilepsy is several times higher than in the rest of the country [17, 18]. In 2017, a house-to-house survey in the rural villages of Mdindo and Msogezi found an epilepsy prevalence of 35 per 1,000 people [18]. A similar survey in 2018 documented an epilepsy prevalence of 28.8 per 1,000 people in Mzelezi Village and 36.6 per 1,000 people in Sali Village [19]. Furthermore, most (77.9%) PWE in these four rural villages met the criteria for OAE [19]. A community-based epilepsy treatment programme was established in these villages in 2019 to address the high prevalence of epilepsy and the challenges faced by PWE in accessing anti-seizure medication [20]. Under this programme, community healthcare workers were trained to identify epilepsy cases and provide appropriate treatment with anti-seizure medication.

The implementation of the above-mentioned community-based programme aimed to improve the accessibility and availability of anti-seizure medication for PWE in these villages to improve their QoL. Nevertheless, in Tanzania, including the Mahenge Area, a high level of epilepsy-related stigma, epilepsy misconceptions and a large anti-seizure treatment gap has been reported [7, 17, 20, 21],

which likely undermines the QoL of PWE in the area. In this study, we focused on investigating the QoL of PWE in the onchocerciasis-endemic area of Mahenge. We hypothesised that OAE and active epilepsy might have a negative impact on the QoL of PWE in Tanzania, while the availability of anti-seizure medication may improve it. We also aimed to explore the education gap among PWE in Mahenge and its impact on the QoL.

2. Material and methods

2.1 Study settings, sampling and data collection

The Mahenge mountains in the Morogoro region, Tanzania, are home to one of the country's most historically and currently onchocerciasis-endemic populations [22]. Study participants were recruited from four rural villages in Mahenge: Mdindo, Msogezi, Mzelezi and Sali (Figure 1). Targeted sampling was used to identify adult PWE and invite them to participate in the study. Participants were interviewed between February and December 2020. Each interview started by asking the PWE for their sociodemographic (Supplementary Material 1) and clinical (Supplementary Material 2) characteristics, followed by the QoL questionnaire (Supplementary Material 3). A few questions regarding the care for PWE were also asked to the caregivers of the PWE interviewed (Supplementary Material 4). When the PWE could not answer the questionnaire because of their mental or physical disability, one of their family members was asked to complete it instead. Before answering the questionnaires, the study details were explained to the participants, and written informed consent was obtained.

Figure 1 – Location of the four villages included in the study in Mahenge: Mdindo, Msogezi, Mzelezi and Sali [23].

Since February 2019, anti-seizure medication has been freely available in Mahenge. Phenobarbital was given as the first-line medication for all types of seizures. If the latter drug did not prevent seizures or produce side effects, the PWE would be advised to the second-line treatment with carbamazepine, sodium valproate or phenytoin.

2.2 Operational definitions

Persons with epilepsy were suspected of having OAE if they developed their first seizure at the age of 3–18 years [24]. The duration of epilepsy was calculated by subtracting the age of onset of the first seizures from the current PWE age. The types of seizures were classified according to the latest International League Against Epilepsy classification [3]. The date of interview was grouped in quadrimesters (four months periods): 1) January to April 2020; 2) May to August 2020 and; 3) September to December 2020.

2.3 Instrument of measure of the quality of life

In order to evaluate the QoL of PWE, the Quality of Life in Epilepsy Inventory-31 version 1.0 (QOLIE-31, US English QoLie-31 copyright 1993, RAND) questionnaire was used. This measure of QoL has been extensively applied worldwide [25] and validated in multinational settings [26]. The questionnaire contains 31 items divided into one item of subjective overall health and seven subscales: 1) seizure worry; 2) emotional wellbeing; 3) energy/fatigue; 4) cognitive functioning; 5) medication side effects; 6) social functioning and; 7) overall quality of life. Raw domain scores were calculated and transformed to 0–100 linear subscales, with higher scores indicating better QoL [27]. The global QoL was then

calculated as 0–100 scales by adding the seven subscale scores using the overall QOLIE-31 formula (Supplementary Material 5). Higher QOLIE-31 scores indicated a better QoL.

The questionnaire was translated from English into Swahili and later back-translated into English (Supplementary Material 3). The local team, fluent in Swahili, pre-tested the questionnaire to ensure the interpretability and understanding of its items.

2.4 Statistical analysis

The sociodemographic and clinical features of the participants were described. Categorical variables were expressed as absolute and relative (%) frequencies and continuous variables as mean and standard deviation (SD) if normally distributed or median and interquartile range (IQR) otherwise. The normality of the distribution of continuous data was visually checked with a histogram and formally tested with the Shapiro-Wilk test and the moments formula for skewness. The associations between baseline variables and the global QOLIE-31 score were tested in bivariate linear regression. Similarly, the associations among baseline variables were explored to avoid collinearity later in the regression analysis. Finally, a correlation matrix of the QOLIE-31 global and seven subscales scores was done using Pearson's correlation coefficients to verify that all subscales measured different domains of PWE life and contributed to the global QOLIE-31 score.

A backward-selection multivariable linear regression model adjusted for sex and age was used to investigate the relationship between the global QoLIE-31 scores and the sociodemographic and clinical features of the participants. The models were compared by: 1) their adjusted R-squared to ascertain the proportion of variance explained and prevent overfitting; 2) their Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC), which provided a comparison of the fit of different regression models (lower values likely to be better models for the current dataset), and; 3) their F-statistics, which p-value indicated whether the regression model provided a better fit than a model without independent variables. All the variables with significant regression coefficients (p-value <0.05) and the ones confounding those associations were maintained in the final multivariable model. Sparse values of categorical variables were aggregated with other values, when possible, to improve the performance and stability of the model. The final multivariable model was used to explore the sex variable as an effect modifier. Significant and almost significant (0.05–0.15) variables were described for males and females. The same backward-selection regression approach was used to determine the positive and negative predictors of each of the seven subscales of QOLIE-31 (Supplementary Material 6).

The regression assumptions were verified after regression by visually inspecting the diagnostic plots, and no collinearity among predictors was confirmed by calculating the generalised variance-inflation factors. All statistical analyses were performed in R and RStudio (versions 4.0.5 and 2022.02.3, respectively).

3. Results

3.1 Description of the study population

The study included 96 PWE with a mean age of 31 (range: 18–60) years, of whom 45 (47%) were male (Table 1). The questionnaires were answered by PWE (56.3%) or one of their family members (parents, siblings, grandparents or children) (43.7%). Each of the four study villages had more than ten participants, with Sali recording the least and Mzelezi the most. An even number of persons were interviewed over the three quadrimesters of 2020. Most PWE were single (81%), and half never attended school.

Table 1 — Sociodemographic characteristics of the PWE.

Characteristics of the PWE		**Participants (n=96)**
Age (per year) Mean (SD)		31 (10)
Sex (Male) N (%)		45 (46.9%)
Village N (%)	Mdindo	27 (28.1%)
	Msogezi	24 (25.0%)
	Mzelezi	32 (33.3%)
	Sali	13 (13.6%)
Quadrimester interviewed in 2020 N (%)	January to April	28 (29.2%)
	May to August	31 (32.3%)
	September do December	37 (38.5%)
Education N (%)	Never went to school	48 (50.0%)
	Primary/standard education	48 (50.0%)
Marital status N (%)	Single	78 (81.3%)
	Married	18 (18.8%)
Who responded to the questionnaire N (%)	PWE	54 (56.3%)
	Caregiver or parent of PWE	36 (37.5%)
	Sibling or partner of PWE	6 (6.2%)

Abbreviations: IQR – interquartile range; N – number; PWE – persons with epilepsy; SD – standard deviation.

The care for PWE was given mainly by their parents (65.9%), often spending three to ten hours daily with the PWE (Table 2). The median family size was six (range: 1–12) elements, with most households subsisting on farming.

Table 2 — Characteristics provided by the PWE caregivers.

Characteristics of the caregivers	**Participants (n=96)**

Caregiver of PWE N (%) 5 missing values	Father	22 (24.2%)
	Mother	38 (41.7%)
	Brother	3 (3.3%)
	Sister	5 (5.5%)
	Other (PWE, partner, grandparent or children)	23 (25.3%)
Caregiver occupation N (%) 11 missing values	Farmer	77 (90.6%)
	Petty trader	7 (8.2%)
	Other	1 (1.2%)
Caregiver time caring for PWE N (%) 12 missing values	Less than 3 hours	3 (3.6%)
	3 to 10 hours	80 (95.2%)
	More than 10 hours	1 (1.2%)
PWE family size Median (IQR) members		6 (4–7)

Abbreviations: IQR – interquartile range; N – number; PWE – persons with epilepsy.

3.2 Clinical characteristics of the PWE

The median duration of epilepsy was 15 (IQR: 7–20) years, with most participants (64.6%) having epilepsy for at least a decade (Table 3). The most common main type of seizure was generalised tonic-clonic seizures (72.9%). About two-thirds (64.6%) of PWE were suspected of having OAE, and almost a third (30.2%) had a history of head nodding seizures. The median age at epilepsy diagnosis was 15 (IQR: 10–22) years.

Most PWE were treated with phenobarbital (85.4%) and followed the anti-seizure medication daily dosage (96.9%). Persons with epilepsy had a median of one seizure (range: 0–7) the week prior to the interview.

Table 3 — Clinical characteristics of the PWE.

Characteristics of the PWE		**Participants (n=96)**
Age at epilepsy diagnosis (years) Median (IQR)		15 (10–22)
Duration of epilepsy N (%)	0–5 years	18 (18.8%)

	6–10 years		18 (18.8%)
	11–20 years		34 (35.4%)
	>20 years		26 (27.0%)
History of head nodding seizures N (%)			29 (30.2%)
Main type of seizures N (%)	Generalised onset (motor)	Tonic-clonic seizures	70 (72.9%)
		Myoclonic seizures	9 (9.4%)
	Generalised onset (non-motor)	Absence	10 (10.4%)
	Focal onset (aware)		7 (7.3%)
Weekly number of seizures before the interview Median (IQR) seizures			1 (0–2)
Anti-seizure medication N (%)	First-line	Phenobarbital	82 (85.4%)
	Second-line	Carbamazepine	9 (9.4%)
		Sodium valproate	4 (4.2%)
		Phenytoin	1 (1.0%)
Takes therapy daily N (%)			93 (96.9%)
Suspected OAE N (%)			62 (64.6%)

Abbreviations: IQR – interquartile range; N – number; PWE – persons with epilepsy; OAE – onchocerciasis-associated epilepsy.

3.3 Mean Global Quality of Life scores of PWE

The mean global QOLIE-31 score was 66.9 (range: 38.3–92.1) out of a maximum possible of 100.0 points (Table 4). All subscales contributed to the global QoL score (Table S6.1), as seen by the significant Pearson's correlation coefficients between the Global QoL and its seven subscales. Still, some subscales seem to have contributed more (Cognitive; Energy/Fatigue, Emotional Wellbeing; and Social Functioning), in line with the weights given to each subscale in the global QoL formula. The correlations between QOLIE-31 subscales were weaker, suggesting they assessed separate domains of PWE life in Mahenge. The highest QOLIE-31 subscale was for medication effects, followed by social functioning. The lowest subscales were seizure worry, energy/fatigue and cognitive functioning. Lastly, the global QoL score was not significantly correlated with the Subjective Overall Health item,

the only item in the questionnaire not used to calculate the former. Nevertheless, the Subjective Overall Health item was moderately correlated with the Overall QoL subscale, as both are measuring the perceived QoL.

Table 4 — Quality of life QOLIE-31 scores of PWE per subscale and global.

QOLIE-31	Mean (SD)	Skewness†	Median (IQR)	Pearson's correlation coefficients						
				Global QoL	Overall QoL subscale	Seizure worry subscale	Emotional Wellbeing subscale	Energy/Fatigue subscale	Cognitive subscale	Medication effects subscale
Global QoL	66.9 (13.0)	-0.05	67.0 (56.8–77.0)							
Overall QoL subscale	66.6 (17.0)	-0.44	70.0 (55.0–80.0)	0.35*						
Seizure worry subscale	57.1 (25.3)	-0.19	60.7 (40.3–76.0)	0.46*	-0.01					
Emotional Wellbeing subscale	70.0 (19.1)	-0.15	68.0 (56.0–84.0)	0.69*	0.26*	0.19				
Energy/Fatigue subscale	63.4 (18.4)	0.33	60.0 (50.0–75.0)	0.73*	0.25*	0.19	0.63*			
Cognitive subscale	60.8 (22.4)	-0.33	63.3 (44.5–80.0)	0.84*	0.16	0.28*	0.42*	0.51*		
Medication effects subscale	87.8 (17.1)	-1.35	100.0 (77.8–100.0)	0.31*	-0.01	0.02	0.16	0.19	0.28*	
Social functioning subscale	75.7 (17.6)	-0.85	80.0 (67.0–85.0)	0.67*	0.00	0.35*	0.31*	0.36*	0.41*	0.27*
Subjective overall health	68.2 (21.3)	-0.95	70.0 (50.0–80.0)	0.18	0.54*	0.15	0.13	0.14	0.08	-0.05

Abbreviations: IQR – interquartile range; QOLIE-31 – 31-item quality of life in epilepsy inventory; QoL – Quality of life; SD – standard deviation.
† Skewness calculated with the moment formula. *Significant Pearson's correlation coefficients (p-value < 0.05).

3.4 Association between sociodemographic and clinical variables of PWE and their QOLIE-31 global scores

Predictors of lower QoL among PWE were living in Sali and experiencing seizures the week before the interview (Table 5). In contrast, completing primary school and switching anti-seizure medication to the second-line treatment were predictors of higher QoL.

Table 5 – Bivariate and multivariable linear regression of the sociodemographic and clinical variables associated with quality of life QOLIE-31 global scores among PWE in Mahenge, Tanzania.

Sociodemographic and clinical variables	Beta (95% CI)	
	Univariable	Multivariable
Intercept		65.54 (53.95–77.13)***
Age (years)	0.17 (-0.10–0.43)	0.04 (-0.22–0.29)
Male (sex)	-0.59 (-5.91–4.73)	-0.04 (-4.66–4.59)
Village		
Mdindo	Reference	Reference
Msogezi	-8.10 (-15.20– -1.01)*	-2.88 (-9.46–3.70)
Mzelezi	-3.64 (-10.25–2.97)	0.26 (6.21–6.72)
Sali	-9.62 (-18.16– -1.08)*	-10.84 (-19.02– -2.66)*
Primary education	9.81 (4.90–14.73)***	7.41 (2.61–12.22)**
Who responded to the questionnaire		
PWE	Reference	Reference
Parent/caregiver	-6.90 (-12.44– -1.36)*	-2.56 (-7.99–2.88)
Sibling/partner	-0.31 (-9.91–9.28)	9.27 (-0.05–18.60)
Weekly number of seizures before the interview	-2.53 (-4.23– -0.83)**	-2.33 (-4.06– -0.60)**
Anti-seizure medication		
First-line therapy (Phenobarbital)	Reference	Reference
Second-line therapy (Carbamazepine, Sodium Valproate or Phenytoin)	9.48 (1.96–17.00)*	10.26 (2.91–17.60)**
Quadrimester interviewed in 2020‡		
January to April	Reference	

May to August	-4.28 (-10.98–2.42)
September to December	-5.94 (-12.37–0.50)
Main type of seizures	
Generalised onset (motor)	Reference
Generalised onset (non-motor)	-1.18 (-7.90–5.54)
Focal onset (aware)	5.44 (-4.86–15.74)
History of head nodding	-2.16 (-7.92– -3.61)
Number of family members in the household	-0.93 (-2.05–0.19)
Has a partner	3.61 (-3.16–10.37)
Daily time spent by the caregiver with the PWE	
<3 hour	Reference
3–10 hours†	3.37 (-11.34–18.08)
Caregiver	
Father	Reference
Mother	-2.61 (-9.42–4.21)
Siblings	-0.22 (-10.72–10.29)
Other (self/grandparent/partner/child)	0.66 (-6.27–8.25)
Caregiver occupation	
Farmer	Reference
Petty trader¥	-1.52 (-10.98–7.94)
Duration of epilepsy	
0–5 years	Reference
5–10 years	-3.40 (-12.24–5.44)
11–20 years	-0.81 (-8.82–7.20)
>20 years	-2.57 (-10.70–5.56)
Suspected OAE	-4.49 (-0.99–9.96)

Abbreviations: Beta – regression coefficients; PWE – persons with epilepsy; 95% CI – 95% confidence interval; OAE – onchocerciasis-associated epilepsy.
† The participant who reported >10 hours a day spent carrying for the PWE was included in the 3-10 hours group.
¥ The caregiver with "other" profession was included in the petty trader group.
* Significant p-value <0.05; ** Significant p-value <0.01; *** Significant p-value <0.001.

The inclusion of sex (male/female) in the regression analysis did not yield statistically significant p-values, nor did it show any interaction with the other coefficients in the model. Many of the statistically significant coefficients observed in the main regression model, which included both male and female participants, remained significant in the female-specific model (Table 6). Particularly, female PWE living in Sali Village and experiencing seizures the week before the interview had lower QoL. On the other hand, the use of second-line anti-seizure medication was associated with a positive impact on QoL. Additionally, completing primary school education and having the questionnaire answered by a sibling or partner showed a nearly significant association with higher QoL among female PWE. Conversely, the male-specific model only found a significant positive association between completing primary school education and QoL.

Table 6 – Sex as an effect modifier of quality of life using the multivariable linear regression for QOLIE-31 global scores.

Sociodemographic and clinical variables	**Beta (95% CI)**	
	Female	**Male**
Intercept	66.10 (50.48–81.71)*	64.50 (42.09–86.91)*
Age (years)	0.10 (-0.27–0.46)	-0.05 (-0.50–0.41)
Village		
Mdindo	Reference	Reference
Msogezi	-4.16 (-12.66– 4.34)	-0.71 (-13.72– 12.30)
Mzelezi	-1.19 (-10.06–7.68)	-2.48 (-9.72–14.68)
Sali	-12.67 (-23.34– -1.99)*	-7.54 (-25.40–10.31)
Primary education	5.06 (-1.90–12.01)†	10.07 (1.66–18.48)*
Who responded to the questionnaire		
PWE	Reference	Reference
Parent/caregiver	-4.22 (-12.11–3.67)	-2.76 (-11.66–6.15)
Sibling/partner	12.15 (-1.06–25.35)†	3.29 (-13.85–20.42)
Weekly number of seizures before the interview	-2.58 (-5.13– -0.34)*	-0.97 (-4.04–2.10)
Anti-seizure medication		

First-line therapy (Phenobarbital)	Reference	Reference
Second-line therapy (Carbamazepine, Sodium Valproate or Phenytoin)	13.15 (3.23–23.08)*	6.31 (-7.15–19.76)

* Significant p-value <0.05; † Almost significant p-value of 0.05–0.15.

3.5 Predictors of the QOLIE-31 seven subscales

Consistent with the main analysis, living in Sali and experiencing seizures the week before completing the QoL questionnaire were associated with lower scores in various subscales of the QOLIE-31 (Table 7). Although larger family sizes were associated with lower scores in two subscales, the variable was also linked with higher scores in the overall QoL subscale. Furthermore, completing primary school education, having lived longer with epilepsy and taking second-line anti-seizure medication were positive predictors for several QOLIE-31 subscales. For detailed information on regression coefficients and their corresponding 95% confidence intervals for each subscale model, please refer to Supplementary Material 6.

Table 7 – Significant predictors of higher and lower scores on QOLIE-31 subscales among PWE in Mahenge, Tanzania, using bivariate linear regression.

QOLIE-31 subscales	Predictors of a higher score	Predictors of a lower score
Overall QoL	• Duration of epilepsy of >20 years • Larger family size	• Age • Questionnaire filled by parent/caregiver
Seizure worry	• Age • Focal onset (aware) seizures	• Larger family size • Questionnaire filled by parent/caregiver
Emotional Wellbeing	• Attended primary education • Duration of epilepsy of 10–20 years	• Generalised onset (nonmotor) seizures • Living in Sali Village • Weekly seizures before the interview
Energy/Fatigue	• Attended primary education • Second-line anti-seizure medication	
Cognitive	• Attended primary education • Second-line anti-seizure medication	• Living in Sali Village
Medication effects	• Questionnaire filled by parent/caregiver	• Living in Sali Village • Weekly seizures before the interview
Social functioning	• Attended primary education	• Larger family size

Abbreviations: QoL – quality of life. OAE – onchocerciasis-associated epilepsy.

4. Discussion

We explored the QoL of PWE in the onchocerciasis-endemic area of Mahenge. The mean global QoL score was 66.9 (SD: 13.0) out of 100, with higher subscale scores in medication effects and social functioning. The high social functioning subscale score may be due to interventions to reduce epilepsy stigma and promote PWE integration into society carried out in the area [20]. The exceptionally high QoL for medication effects suggests that PWE are satisfied with the anti-seizure medication provided

in Mahenge since 2019, which is also reflected by the high treatment compliance rate (97%) observed in our study and previously reported in 2020 (94%) [20].

Caregivers of PWE assigned significantly lower scores on the seizure worry and overall QoL subscales while giving higher scores on the anti-seizure medication effects subscale. The lower scores on the overall QoL and seizure worry subscales could be attributed to the concerns of the caregivers about the occurrence of seizures. It is possible that caregivers, being closely involved in the care of PWE, have heightened worries about seizure events, which might reflect in their assessments of the QoL. On the other hand, caregivers rated higher on the medication effects subscale, indicating a greater awareness of the potential side effects of anti-seizure medications. The involvement of family members in providing sustainable and effective epilepsy care is crucial, as evidenced by the significant amount of time reported in caregiving activities for PWE. The observed differences in subscale scores between caregivers and PWE may also be influenced by the cognitive capacities of PWE. Research suggests that individuals with reduced cognitive capacities tend to overestimate their well-being, which could contribute to variations in the perceived QoL scores [28, 29].

Ultimately, the introduction of anti-seizure medication in Mahenge since 2019 has the potential to not only reduce seizure frequency and improve the QoL of PWE but also positively impact the QoL of caregivers. As PWE experience fewer seizures and potentially gain more independence, caregivers may experience a decrease in their worries, concerns and time taken caring for PWE. The impact of these changes on the QoL of caregivers should be investigated in a follow-up study that specifically explores their QoL. Lastly, PWE on second-line anti-seizure medication (carbamazepine, sodium valproate or phenytoin) exhibited higher levels of QoL than those on phenobarbital. This shift to second-line treatment may have been due to phenobarbital-related side effects or insufficient seizure control [30]. Further research is necessary to determine the most suitable anti-seizure medication for PWE residing in onchocerciasis-endemic areas.

The observed lower QoL scores among PWE from Sali Village compared to those from the villages of Mdindo and Mzelezi could be related to the availability and accessibility of healthcare services in these villages. Sali Village has a clinic staffed by a nurse who provides anti-seizure medication to PWE. On the other hand, in Mdindo and Mzelezi villages, the distribution of anti-seizure medication is conducted by trained community workers. This disparity in healthcare provision suggests that PWE in Sali Village may have easier access to medical resources or better monitoring of their condition due to the presence of a dedicated healthcare professional. It is, therefore, plausible that PWE with more severe disease or higher healthcare needs may be more inclined to seek care at the Sali Clinic, where they can receive direct support and supervision from a nurse. This preference for the Sali Clinic among individuals with greater disease severity could contribute to the lower QoL scores observed in this village. However, further investigation is required to confirm this hypothesis and explore other factors that may be influencing the QoL of PWE in Sali Village, such as epilepsy-related stigma.

It is important to address the factors preventing PWE from attending school. Persons with epilepsy with primary school education had higher QoL. Moreover, attending primary school was positively associated with four of the seven QOLIE-31 subscales. This association aligns with the results of other African studies [31, 32]. Still, half of PWE in Mahenge never attended school, coincident with the findings of a survey conducted in the area in 2020 [20]. This educational gap is likely due to the persistent high epilepsy stigma in the area [20, 33]. Although the sample size was small, Mmbando *et al.* described in 2018 that children with epilepsy aged 7–10 years were more likely not to enrol for primary education (83%) than children of the same age without epilepsy (16%) [18]. Providing optimal anti-seizure treatment and interventions to decrease epilepsy stigma and misconceptions may

increase schooling rates and prevent children with epilepsy from dropping out of school. These measures could improve the QoL of PWE.

Longer duration of epilepsy was associated with higher emotional wellbeing and overall QoL subscale scores, as previously reported [34]. It may be that PWE learn to live with epilepsy by developing coping mechanisms over time and finding the optimal treatment for their seizures. On the other hand, experiencing seizures in the week before completing the QoL questionnaire was associated with lower QoL, especially among women. The frequency of seizures has been shown before to have a detrimental impact on QoL [32, 35, 36]. Thus, providing anti-seizure medication to PWE is vital to reduce seizure episodes and improve QoL. It is estimated that the proportion of persons with active epilepsy who are not appropriately treated, the treatment gap [37], is over 75% in low-income countries [38]. Increasing treatment coverage would reduce epilepsy-related premature death and promote individual wellbeing and independence, consequently benefiting the QoL of PWE. This would also meet the third Sustainable Development Goal of "ensuring a healthy life and promoting wellbeing for all at all ages" [39].

Eliminating onchocerciasis would ultimately improve the QoL of the at-risk populations by possibly preventing OAE and onchocerciasis skin and eye clinical manifestations. Although the underlying mechanism of OAE is yet to be described [12], evidence in Uganda and South Sudan suggests that its incidence can be decreased by implementing onchocerciasis elimination measures such as CDTi and vector control [40, 41]. A CDTi coverage of at least 80% for several years is required to eliminate *O. volvulus* transmission [42] and meet the WHO target for onchocerciasis elimination [43]. In Mahenge, the incidence of epilepsy significantly decreased after increasing the frequency of CDTi to biannual in 2017 [44]. Hence, onchocerciasis elimination programs should prioritise strengthening their programme in onchocerciasis-endemic areas in Africa with a high prevalence of epilepsy and ongoing *O. volvulus* transmission.

Our study had some limitations. First, the number of study participants was small. Therefore, the relationship between QoL and the type of seizures could not be assessed. Second, we lacked sufficient information about the potential causes of epilepsy to determine if the participants had OAE. Hence, participants could only be suspected of having or not having OAE. Still, participants suspected of having OAE are very likely to have OAE based on previous studies in the area, where most epilepsy cases were OAE [19]. The gold standard for confirming the diagnosis of OAE includes conducting additional laboratory tests, such as electroencephalography (EEG) or imaging studies, to exclude other potential causes of epilepsy. This is particularly important for ruling out epileptic syndromes, which typically manifest before the age of three [45, 46], and neurocysticercosis, which commonly occurs during adulthood [47, 48]. Consequently, the OAE case definition only considers PWE who experienced their first seizure between the ages of three and 18 years. Third, due to the high adherence to anti-seizure medication among participants, we were unable to explore the association between drug adherence and QoL. However, this association has been established in several settings in developed and developing countries [31].

Fourth, seizure frequency was self-reported, introducing the possibility of recall bias. To minimize this bias, participants were asked to report the number of seizures experienced in the week preceding the completion of the QoL questionnaire. Fifth, a substantial proportion (45.2%) of the questionnaires were completed by the caregivers of PWE, who may not fully capture the QoL experienced by their family member with epilepsy themselves. We accounted for this in our multivariable analysis. Sixth, the use of backward regression in our analysis may be susceptible to overfitting and assumes independence among predictor variables. To address this, we limited the number of variables in the model, adjusted for age, sex and village, and assessed collinearity between variables before

conducting the regression analysis. Lastly, the predictors identified in the main regression model appeared to be more representative of the female population, possibly due to the smaller sample size of males and the influence of variables not assessed in this study in the QoL of males with epilepsy in Mahenge.

5. Conclusion

The QoL of PWE was inversely related to their frequency of seizures. To prevent seizures, anti-seizure medication should be optimised. Phenobarbital may not be the ideal anti-seizure medication in the Mahenge area for all PWE. Thus, more research is needed to identify the optimal anti-seizure treatment for the different types of seizures observed in onchocerciasis-endemic areas. Improved control of seizures may also lead to increased schooling of PWE, a strong predictor of better QoL. Ultimately, eliminating onchocerciasis transmission will prevent the epilepsy disease burden and improve the QoL of the affected communities.

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Ethical Approval Statement

Ethical approval was obtained from the Ethics Committee of the National Institute for Medical Research, Tanzania (NIMR/HQ/R.8a/Vol.IX/3341) and the Ethics Committee of the Antwerp University Hospital, Belgium B300201942516.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Availability of data

After de-identification, all individual participant data underlying the results reported in this article will be made available immediately and indefinitely via the Zenodo repository following publication for anyone who wishes to access the data for any purpose.

Author contributions

The study was conceptualized by Dan Bhwana (DB), Bruno P Mmbando (BM) and Robert Colebunders (RC). The data collection was coordinated and implemented by DB, Carmen-Nabintu Chigoho (CC) and Bruno Mmbando (BM) and analysis and interpretation of data were completed by Luís-Jorge Amaral (LA), Messaline F. Fomo (MF). The original draft was written by: LA and MF. Reviewing and editing was done by LA, DB, MF, BM, and RC. All authors read and approved the final version of this paper.

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Supplementary Material

Supplementary Material 1 — Questionnaire given to the PWE regarding their sociodemographic characteristics.

Supplementary Material 2 – Questionnaire given to the PWE regarding the clinic characteristics of epilepsy.

Supplementary Material 3 — QOLIE-31 translated version.

Supplementary Material 4 — Questionnaire given to the caregivers of the participating PWE.

Supplementary Material 5 — Calculation of QOLIE-31 global score.

Supplementary Material 6 – Multivariable analysis of the QOLIE-31 subscales.