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Hospital-based epilepsy care in Uganda: A prospective study of three major public referral hospitals

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ABSTRACT

Objective: This study sets out to describe the current demographics of people with epilepsy (PWE) attending hospital-based care in Uganda and the epilepsy treatment practices within three of the largest Ugandan public referral hospitals.

Methods: In a six-month prospective cohort study, 626 children and adults attending epilepsy clinics at Mulago National Referral Hospital, Butabika National Referral Mental Hospital and Mbarara Regional Referral Hospital were enrolled. Using a study questionnaire, data were collected at baseline and at 3 weeks, 3 months, and 6 months following enrollment. Specific data surrounding individual patient demographics, clinical characteristics and severity of epilepsy, and treatment of epilepsy with antiepileptic drugs (AEDs) were collected.

Results: Female patients totaled to 50.8%, with a nearly equal gender distribution at each hospital. There was no statistical difference in gender or age between sites. The majority of PWE had completed primary school, with less than 15% of patients completing more than a secondary education. Seizure severity was high, with most patients having multiple seizures per week at the initial onset of epilepsy, and greater than 90% of patients reporting a loss of consciousness with seizures. The majority of patients (54.95%) also reported a developmental or learning delay. Most patients were on 1 AED (46.01%) or 2 AEDs (36.90%), with carbamazepine being the most frequently prescribed AED. There was a trend towards improved seizure severity over the follow-up period, as assessed by the corresponding Personal Impact of Epilepsy Scale (PIES) subscale.

Conclusions: People with epilepsy attending hospital-based care in Uganda tend to have severe forms of epilepsy requiring management with AEDs. Current hospital-based practices show a positive trend for seizure burden and quality of life of PWE in Uganda. Further interventions to improve overall access to biomedical care are required to continue to advance the management of PWE across all communities.

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1. Introduction

Epilepsy is a common neurological disease worldwide that affects people of all ages, and the highest burden can be found in low- and middle-income countries (LMICs), particularly in rural areas [1,2]. In Uganda, the prevalence of epilepsy in children under 15 years of age was reported to be about 2%, while in eastern Uganda, an epilepsy prevalence of 10.3 per 1000 was noted; the highest prevalence was among the youngest children aged 0–5 years [3,4]. Throughout Sub-Saharan Africa, higher rates of birth-related injuries, adverse neurological sequelae of infectious exposures (including malaria, neurocysticercosis, and human immunodeficiency virus (HIV)), and road traffic injuries are thought to contribute to the significantly higher incidence and prevalence of epilepsy [2–12]. Although medical treatment in the form of antiepileptic drugs (AEDs) provides adequate seizure control in approximately 70% of people with epilepsy (PWE), the treatment gap in developing countries is high, but the exact figure has been elusive to conclude. The reasons underlying this are complex and multifactorial [13].

Seizure control remains a challenge as multiple barriers impede timely and appropriate treatment. Some of these barriers include the lack of specialized healthcare staff, limited investigative facilities, poor access to medication, and prohibitive costs associated with chronic treatment [6,10,11,14–16]. Many health centres also find difficulty in recognizing seizure events beyond generalized tonic–clonic seizures due to restricted access to diagnostic tools such as electroencephalogram (EEG) and magnetic resonance imaging (MRI), and tools that are available may function poorly, making the interpretation of results difficult [17]. These barriers subsequently lead to high seizure frequencies, worsen epilepsy stigma, and widen the treatment gap further.

Furthermore, many of the most common first-tier AEDs are unavailable consistently within Uganda, causing healthcare providers to prescribe inadequate regimens or expensive alternate medications. In turn, this may lead patients and their families to turn to familiar and more readily accessible traditional medicines [10,18,19]. This requires out of pocket purchases, further straining the finances of PWE and their families [16]. In addition, patients may be vulnerable to counterfeit medicines with subtherapeutic activity, as even with appropriate adherence, subtherapeutic blood–drug levels are regularly reported, indicating insufficient quality of AEDs [18]. A lack of understanding around the need for strict adherence to treatment regimens, including misconceptions regarding the need to continue treatment even when seizure frequency has reduced, may also negatively impact seizure control [2,18]. Ultimately, poorly controlled seizures negatively impact the lives of PWE. Understanding the impact of seizures on the life of PWE would enable us to develop targeted strategies to control seizures and improve quality of life.

In the face of these multiple challenges, closing the treatment gap for epilepsy will evidently require a multifaceted strategy targeting both social and health system issues. In order to act responsibly, the current landscape of hospital-based care in these regions must be thoroughly understood, prior to taking steps towards change on either an individual or community level. In this context, this study sets out to describe the patient demographic and clinical characteristics of PWE, and the impact of epilepsy on the lives of PWE attending hospital-based care in Uganda, in three major public referral hospitals.

2. Methods

2.1. Study design

In 2017 through 2018, we conducted a six-month prospective cohort study at three public hospitals in Uganda, and enrolled 626 PWE who met the study inclusion criteria. The inclusion criteria consisted of provision of written informed consent, children and adults seeking care for epilepsy in the hospital clinics, and the respondent (patient or caregiver) had to speak at least one of the study languages (English, Luganda, or Runyankole). All PWE who meet the inclusion criteria were included regardless if they were new or existing patients at the clinic sites. Using a study questionnaire, we collected data on demographic and clinical characteristics at our baseline, three weeks, three months, and six months. During follow-up, we monitored changes in self-reported metrics of seizure severity and quality of life from baseline. These three time points were based upon expert feedback, likelihood of follow-up, and meaningful time for seizures to respond to medication regimens. All follow-up data were captured over the phone using scripts and trained research assistants fluent in the respondents preferred language.

2.2. Setting

Study participants were recruited through convenience sampling at the available clinics from three sites: Mulago National Referral and Teaching Hospital (MNRH), Butabika National Referral Mental Hospital (BNRMH), and Mbarara Regional Referral Hospital (MRRH). The MNRH is located in Kampala, the capital city of Uganda. It is the main national referral hospital for the entire country and functions as a teaching hospital for Makerere University College of Health Sciences. It has an official bed capacity of 1790 and offers a range of services in most medical and surgical subspecialties along with emergency care, intensive care, dentistry, and pediatrics. The MNRH provides specialist inpatient and outpatient epilepsy care for pediatrics and adults in Neurology and Psychiatry clinics.

The BNRMH is also located in Kampala and serves as the only national referral mental hospital in Uganda. It is a public hospital and serves as a psychiatric teaching hospital for Makerere University College of Health Sciences. It has an official bed capacity of 900 and sees a higher total volume of patients with epilepsy relative to the other hospitals in the study.

The MRRH is a public regional referral hospital for the districts of Mbarara, Bushenyi, Ntungamo, Kiruhura, Ibanda, and Isingiro, with an official bed capacity of 600. It is located in Mbarara and is a teaching hospital for Mbarara University of Science and Technology. It has a neurology clinic and a psychiatry clinic staffed by physicians and nurses that care for PWE.

2.3. Data collection and study questionnaires

We collected demographic and clinical factors that included age, gender, socioeconomic status (SES), district of residence, urban or rural residence, primary caretaker, education level, and patient employment status or guardian employment status. Socioeconomic status was captured as the possession of five proxy items (radio, TV, phone, access to electricity, and running water), with respondents able to respond yes or no to each item.

Clinical characteristics included age at onset, duration of epilepsy, seizure pattern (generalized or focal), seizure frequency, neurological deficits (vision, developmental delay, motor impairment), symptomatic epilepsy, prior history of epilepsy, and seizure control. Furthermore, indicators for treatment history were assessed, such as current medications used, and initial number of medications prescribed. In addition, we recorded the current treatment plan (i.e., AEDs or surgery) as well as information on dosage and frequency of AEDs prescribed if relevant.

The Personal Impact of Epilepsy Scale (PIES) is a 25-question tool that can be administered to patients of all ages to measure the influence that epilepsy has on their life [20]. We administered this tool in the language preferred by the study respondent. For all PIES analyses, we restricted our sample to those who reported a seizure within the past three months ($n = 430$). This decision was made given that PIES has only been tested on PWE who are currently experiencing seizures [21,22]. The PIES is evaluated using the overall total score, along with the four subscales: 1) Impact of seizures; 2) Medication side effects; 3) Impact of comorbidities; and 4) Overall quality of life. Each question

Table 1
Demographic characteristics.

		Hospital study sites			p-Value
	Full sample (n = 626)	Butabika (n = 346)	Mulago (n = 210)	Mbarara (n = 70)	
	n (%)	n (%)	n (%)	n (%)	
Gender					
Female	318 (50.80)	180 (52.02)	105 (50.00)	33 (47.14)	0.721
Male	306 (48.88)	165 (47.69)	104 (49.52)	37 (52.86)	
Age					
Mean (sd)	23.00 (13.22)	22.59 (13.56)	24.09 (12.99)	21.84 (12.15)	0.319
0–5	47 (7.51)	28 (8.09)	14 (6.67)	5 (7.14)	
6–10	70 (11.18)	42 (12.14)	21 (10.00)	7 (10.00)	
11–18	136 (21.73)	77 (22.25)	39 (18.57)	20 (28.57)	
19–30	226 (36.10)	125 (36.13)	77 (36.67)	24 (34.29)	
31–40	84 (13.42)	46 (13.29)	28 (13.33)	10 (14.29)	
41–50	29 (4.63)	8 (2.31)	18 (8.57)	3 (4.29)	
51–60	23 (3.67)	16 (4.62)	7 (3.33)	0 (0.00)	
>60	6 (0.96)	4 (1.16)	1 (0.48)	1 (1.43)	
Education					
No education	110 (17.57)	71 (20.52)	24 (11.43)	15 (21.43)	0.250
Primary	271 (43.29)	150 (43.35)	92 (43.81)	29 (41.43)	
Secondary - O level	155 (24.76)	81 (23.41)	58 (27.62)	16 (22.86)	
Secondary - A level	20 (3.19)	10 (2.89)	9 (4.29)	1 (1.43)	
Vocational training	28 (4.47)	15 (4.34)	9 (4.29)	4 (5.71)	
Higher education	40 (6.39)	17 (4.91)	18 (8.57)	5 (2.38)	
SES indicator					
0	4 (0.64)	3 (0.87)	0 (0.00)	1 (1.43)	<**0.001**
1	18 (2.88)	5 (1.45)	3 (1.43)	10 (14.29)	
2	68 (10.86)	28 (8.09)	24 (11.43)	16 (22.86)	
3	103 (16.45)	63 (18.21)	31 (14.76)	9 (12.86)	
4	162 (25.88)	102 (29.48)	45 (21.43)	15 (21.43)	
5	271 (43.29)	145 (41.91)	107 (50.95)	19 (27.14)	

The text in bold represents statistical significance.

is scored from 0 to 100, and a higher score indicates greater well-being for the overall score and all subsections. The PIES has good internal consistency and test–retest reliability, although to date, this is the first time it has been used in East Africa [20].

2.4. Data analysis

All analyses were performed using STATA version 16 along with Excel 2016. Continuous data are summarized with means and standard deviations (sd), and categorical data are summarized with counts and percentages.

The PIES was scored according to the recommended scoring framework and summarized using means and sd for the total score and all subsections. The PIES total score and subsection scores were used as the primary outcome at the follow-up time periods. We analyzed the total and subsections of PIES to fully understand the differences between outcomes at each hospital. To evaluate changes to the PIES scores over the follow-up period, we used a repeated measures mixed model because of disadvantages inherent to using a repeated measures analysis of variance (ANOVA) approach with our data.

2.5. Ethical approval

Ethical approval was provided by local Ugandan institutional review boards where the studies were conducted and at the partner institutions in the United States. All study participants provided written consent before they were enrolled into the study, and participants between 12 and 18 years additionally provided assent.

3. Results

3.1. Sample

Initial recruitment resulted in 650 PWE interested in participating in the study, with 642 meeting all study criteria and providing written consent. Of the 642 that participated in the study, 16 respondents were excluded from the final analysis because of incomplete baseline demographic and survey data. Our sample for analysis was 626 PWE with 346 from BNRMH, 210 from MNRH, and 70 from MRRH.

3.2. Demographics

Of the 626 PWE in our sample, 318 (50.80%) were female with a nearly equal gender distribution at each hospital site (Table 1). The average age was 23.00 years old ranging from 21.84 years old at MRRH to 24.09 years old at MNRH with 253 (40.41%) of all PWE in our study under 18 years old. The MRRH saw the largest percentage (45.71%) of PWE under 18 compared with BNRMH (42.48%) and MNRH (35.24%). There was no statistically significant difference in either gender or age between sites (p-value = 0.721 and 0.319, respectively).

A majority of our sample, 381 (60.86%), either had no formal education (110, 17.57%) or only completed primary school (271, 43.29%) at the time of the baseline survey (Table 1). In the overall sample, 68 (10.86%) completed some form of vocational training or higher education with the greatest percentage, 12.86%, at MNRH and the lowest percentage, 8.09%, at MRRH. Despite these differences, there was no statistically significant difference in education level between sites (p-value = 0.250).

Socioeconomic status was captured as the number of total SES proxy items (i.e., electricity, running water), out of five, that a PWE possessed in their household. A majority of our sample, 433 (69.17%), possessed either 4 or 5 of the items with BNRMH and MNRH having around 70% of their PWE who possessed 4 or 5 items (Table 1). The MRRH had the greatest percentage of PWE possessing 2 or less items (38.58%). There was a statistically significant difference in SES between sites (p-value <0.001).

3.3. Seizure characteristics

At our baseline visit, we asked respondents to report how many seizures they had per week when their seizures first started and how

Table 2
Seizure characteristics.

		Hospital study sites			p-Value
	Full sample (n = 626)	Butabika (n = 346)	Mulago (n = 210)	Mbarara (n = 70)	
	Mean (sd)	Mean (sd)	Mean (sd)	Mean (sd)	
Number of seizures per week					
Initial	11.17 (21.70)	15.54 (25.71)	5.10 (13.41)	7.29 (13.24)	<**0.001**
At baseline visit	2.33 (9.05)	2.65 (9.93)	2.10 (8.68)	1.31 (3.95)	0.494
Loss of consciousness	n (%)	n (%)	n (%)	n (%)	
Yes	578 (92.33)	332 (95.95)	180 (85.71)	66 (94.29)	<**0.001**
No	44 (7.03)	11 (3.18)	29 (13.81)	4 (5.71)	
Developmental or learning delay					
Yes	344 (54.95)	165 (47.69)	153 (72.86)	26 (37.14)	<**0.001**
No	277 (44.25)	181 (52.31)	52 (24.76)	44 (62.86)	
Number of AEDs					
1	288 (46.01)	145 (41.91)	93 (44.29)	50 (71.43)	<**0.001**
2	231 (36.90)	134 (38.73)	80 (38.10)	17 (24.29)	
3	72 (11.50)	54 (15.61)	18 (8.57)	0 (0.00)	
4	9 (1.44)	6 (1.73)	3 (1.43)	0 (0.00)	

The bold text in this table represents statistically significant results.

many seizures per week they were currently having. The initial seizure frequency ranged from 5.10 (sd = 13.41) seizures per week at MNRH to 15.54 (sd = 25.71) seizures per week at BNRMH with a full sample average of 11.17 (sd = 21.70) seizures per week (Table 2). Given that everyone in our sample had reached biomedical care, and almost none of our respondents were new to treatment, the overall current seizure frequency at the baseline visit was lower than the reported initial seizure frequency. Current seizure frequency at the baseline visit ranged from 1.31 (sd = 3.95) seizures per week at MRRH to 2.65 (sd = 9.93) seizure per week at BNRMH with a full sample average of 2.33 (sd = 9.05) seizures per week.

Nearly our entire sample, 578 (92.33%), self-reported that they experienced loss of consciousness during their seizures (Table 2). The lowest percentage experiencing loss of consciousness with their seizures was reported at MNRH, 85.71%. There was a statistically significant difference in loss of consciousness experienced by PWE across study sites (p-value <0.001).

There was a statistically significant difference between sites (p-value <0.001) for those self-reporting a significant developmental or learning delay (Table 2). There were 344 (54.95%) of the overall sample that reported a delay with MNRH having the highest percentage (72.86%).

3.4. AED prescription

As noted above, PWE in our sample had already reached biomedical care; therefore, >95% of our sample was already receiving medication for their seizures. In our full sample, 288 (46.01%) and 231 (36.90%) were on AED monotherapy or a two-AED regimen, respectively. This same percentage was seen at both BNRMH and MNRH, but at MRRH, 71.43% were on AED monotherapy. It was observed that at BNRMH and MNRH, some PWE were on 3 or 4 AEDs, while this pattern was not seen in any PWE at MRRH. This difference in the prescription of AEDs was statistically significant between study sites.

When examining AED prescription practices, carbamazepine was the most frequently prescribed AED, making up more than half of all prescribed AEDs across all sites and age groups (Fig. 1). Other commonly prescribed AEDs included phenytoin (23%), sodium valproate (19%), lamotrigine (3%), and phenobarbitone (3%). Almost one-fifth of

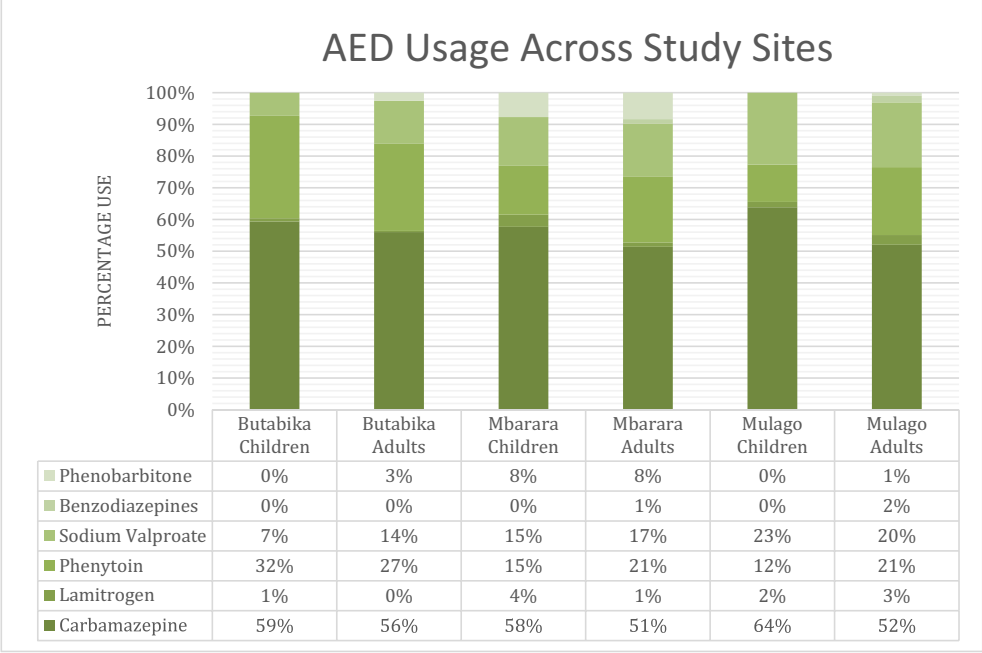

Fig. 1. Antiepileptic drug (AED) use across study sites by age.

patients also received folic acid. Some differences were observed in prescribing practices between the three different study sites. The MRRH and MNRH reported a significantly larger amount of phenytoin being prescribed: 38% and 40%, respectively, compared with only 11% at BNRMH. In contrast, BNRMH showed more frequent use of sodium valproate and lamotrigine. Phenobarbitone was more frequently reported in MNRH than it was in the other two health care centres. In analyzing the differences in prescription practices between adults and children, it was found that carbamazepine was more frequently prescribed in the pediatric group (62% compared with 50% of AED prescriptions in the adult group), and sodium valproate was more frequently prescribed in the adult group.

3.5. PIES baseline scoring

There were 430 PWE included in our PIES analyses following restriction of our sample to those who reported a seizure within the past three months. For the baseline PIES scoring, we had 245 PWE from BNRMH, 136 from MNRH, and 49 from MRRH (Table 3). The average Total PIES score at baseline for the full sample was 175.80 (sd = 41.40). The BNRMH had the highest Total PIES score average (180.86, sd = 39.41), while MRRH had the lowest (146.03, sd = 44.47), and this difference was statistically significant (p-value <0.001). For the Seizure Severity subscale, the average score was 43.77 (sd = 16.73); MNRH had the highest Seizure Severity subscale score average (45.55, sd = 16.32), while MRRH had the lowest (35.09, sd = 17.52); this difference was statistically significant (p-value <0.001). For the Adverse Events subscale, the average score was 70.78 (sd = 18.07); MNRH had the highest Adverse Events subscale score average (72.66, sd = 17.98), and MRRH had the lowest (60.37, sd = 19.50); this difference was statistically significant (p-value <0.001). For the Comorbidities subscale, the average score was 61.24 (sd = 19.17); BNRMH had the highest Comorbidities subscale score average (64.52, sd = 18.45), and MRRH had the lowest (50.57, sd = 20.76); this difference was statistically significant (p-value <0.001). For the Quality of Life subscale, the average score was 38.02 (sd = 19.29); MRRH had the highest Quality of Life subscale score average (43.37, sd = 25.91), and MNRH had the lowest (36.95, sd = 18.99); this difference was not statistically significant (p-value: 0.115).

3.6. PIES changes at follow-up

During our three follow-up time points, we were able to retain >90% of PWE at each time point, with the largest number of people (n = 40) missing the 3-month follow-up. Statistically significant differences at the 3-week follow-up between sites were seen within the Seizure Severity subscale (p-value = 0.005) and the Adverse Events subscale (p-value = 0.038) (Table 3). There were no significant differences noted within the PIES Total score, Comorbidities subscale, or Quality of Life subscale among sites at the 3-week follow-up. Statistically significant differences at the 3-month follow-up between sites were seen within the Comorbidities (p-value <0.001) and the Quality of Life subscales (p-value <0.001). There were no significant differences noted within the PIES Total score, Seizure Severity subscale, or Adverse Events subscale between sites at the 3-month follow-up. Statistically significant differences at the 6-month follow-up between sites were seen within the Comorbidities (p-value = 0.046) and the Quality of Life subscales (p-value <0.001). There were no significant differences noted within the PIES Total score, Seizure Severity subscale, or Adverse Events subscale between sites at the 6-month follow-up.

In examining the change in scores over each of our follow-up time points, there was an upward trend in the Total PIES score, but this trend was not statistically significant (Fig. 2). Within the Seizure Severity subscale, there was a greater upward trend in the subscale score, especially for MRRH, but this trend was also not statistically significant (Fig. 3). Both the Adverse Events and the Comorbidities subscale scores remained fairly stagnant over time without any statistical significance (Figs. 4 and 5). The Quality of Life subscale showed an upward trend for both BNRMH and MNRH and a downward trend for MRRH; despite these trends, there was no statistical significance (Fig. 6).

4. Discussion

Addressing the epilepsy treatment gap is paramount in LMICs where the disease burden is high and stigma reinforces the underlying contributing factors. In our study, we examined the current treatment that Ugandans receive at three of the largest public hospitals that care for PWE. Understanding the current demographics, treatment practices, and the impact these practices have on PWE is a first step in addressing the overall treatment gap. People with epilepsy will not remain in biomedical care if they do not see an improvement in their symptoms given the multitude of challenges they already face. Our study illustrated that there is a difference in the type of patients that are seen at the various hospitals; on the whole, the patients seeking care have severe forms of epilepsy, medication usage varies between sites, and overall treatment has a positive impact on seizure severity, but full, sustained seizure control is an elusive target.

4.1. Hospital differences

Uganda's public healthcare infrastructure is set up in a tiered, decentralized, referral model. This set up allows for care to be provided closer to patients and theoretically reduces their need to travel long distances. While PWE can benefit from this structure, many PWE in Uganda must seek care at regional and national referral hospitals because of the lack of healthcare providers trained to care for epilepsy in the lower level health facilities. This fact is what led us to focus on the three hospitals we used in this study, as each of them has multiple providers that care for PWE. We included two national referral hospitals and a regional referral facility, which provided us with a representative idea of the type of PWE that seek care at these facilities. Expectedly, we were able to recruit more PWE from the two national hospitals as they see a greater number of PWE.

Important to note in the Ugandan context is that epilepsy is perceived and even categorized within the Ministry of Health as a mental health condition, leading many PWE to be managed primarily by psychiatrists and psychiatric nurses. This is reflected in the fact that BNRMH sees a higher number of PWE compared with the other two hospitals. While this arrangement is beneficial in the management of the psychiatric comorbidities that often accompany epilepsy, and positioning epilepsy care within mental health takes advantage of the larger number of psychiatrists in Uganda compared with neurologists and pediatricians, it also helps to propagate the social stigma around epilepsy [17]. At this time, entirely removing the care of PWE from psychiatrists may not be feasible given the current number of epilepsy specialists, though promoting and integrating epilepsy training in a wider range of health professions may be a realistic goal [17].

4.2. Population differences

Within our sample, we saw almost an even gender distribution across all sites, which is a key finding given that for many conditions in Uganda, gender influences care-seeking [6,11]. This suggests that care-seeking behaviors for PWE are unlikely to be influenced by gender within Uganda.

The burden of epilepsy impacts the attainment of formal education for PWE throughout most of the world, and even more so in LMICs [10]. In our sample, a majority of the patients across all hospital sites only completed primary school, with less than 15% receiving more than a secondary education, which is less than would be expected in the general Ugandan population [23]. The stigma associated with epilepsy heavily influences PWE's ability to attend school, as often children

Table 3
Personal Impact of Epilepsy Scale scoring.

	Baseline	3-Week follow-up	3-Month follow-up	6-Month follow-up
	n; mean (sd)	n; mean (sd)	n; mean (sd)	n; mean (sd)
Total				
Full sample	430; 175.80 (41.40)	412; 179.38 (44.26)	390; 181.99 (43.22)	398; 183.46 (51.77)
BNRMH	245; 180.86 (39.41)	237; 176.68 (44.00)	228; 180.53 (45.55)	229; 183.02 (49.73)
MNRH	136; 177.42 (39.56)	134; 183.43 (40.61)	121; 186.07 (33.47)	132; 185.86 (50.75)
MRRH	49; 146.03 (44.47)	41; 181.70 (55.89)	41; 178.10 (54.37)	37; 177.65 (66.88)
p-Value	<**0.001**	0.348	0.434	0.684
Seizure severity				
Full sample	430; 43.77 (16.73)	412; 50.90 (19.05)	390; 54.29 (18.86)	398; 58.07 (20.34)
BNRMH	245; 44.53 (16.33)	237; 49.70 (18.14)	228; 54.15 (18.59)	229; 57.98 (18.84)
MNRH	136; 45.55 (16.32)	134; 50.23 (17.45)	121; 53.03 (17.16)	132; 58.01 (20.51)
MRRH	49; 35.09 (17.52)	41; 60.09 (26.01)	41; 58.78 (24.26)	37; 58.81 (27.99)
p-Value	<**0.001**	**0.005**	0.238	0.973
Adverse events				
Full sample	430; 70.78 (18.07)	412; 65.93 (18.83)	390; 64.32 (15.97)	398; 63.17 (18.27)
BNRMH	245; 71.82 (17.19)	237; 64.10 (18.28)	228; 63.55 (15.89)	229; 62.63 (17.72)
MNRH	136; 72.66 (17.98)	134; 69.30 (19.16)	121; 65.77 (14.23)	132; 63.83 (17.59)
MRRH	49; 60.37 (19.50)	41; 65.51 (19.83)	41; 64.27 (20.70)	37; 64.19 (23.69)
p-Value	<**0.001**	**0.038**	0.468	0.784
Comorbidities				
Full sample	430; 61.24 (19.17)	412; 62.54 (19.35)	390; 63.35 (18.67)	398; 62.22 (20.40)
BNRMH	245; 64.52 (18.45)	237; 62.88 (19.44)	228; 62.80 (19.66)	229; 62.41 (19.80)
MNRH	136; 59.20 (18.30)	134; 63.91 (17.31)	121; 67.23 (13.51)	132; 64.02 (18.99)
MRRH	49; 50.57 (20.76)	41; 56.10 (23.88)	41; 54.95 (23.02)	37; 54.65 (26.88)
p-Value	<**0.001**	0.071	<**0.001**	**0.046**
Quality of Life				
Full sample	430; 38.02 (19.29)	412; 43.75 (21.90)	390; 43.59 (18.73)	398; 45.04 (19.33)
BNRMH	245; 37.55 (17.77)	237; 43.46 (22.30)	228; 43.20 (18.26)	229; 46.07 (17.86)
MNRH	136; 36.95 (18.99)	134; 45.52 (21.65)	121; 47.73 (17.68)	132; 46.40 (18.82)
MRRH	49; 43.37 (25.91)	41; 39.63 (20.14)	41; 33.54 (20.62)	37; 33.78 (25.83)
p-Value	0.115	0.307	<**0.001**	<**0.001**

The bold text in this table represents statistical significance.

with epilepsy are not allowed to remain in mainstream education and are not accepted in their local community [17], limiting future job and financial prospects. Keeping young PWE out of school also reduces a community's general knowledge of epilepsy, as students are not exposed to or taught about epilepsy early in life. In one survey of central Uganda, while many people could recognize a seizure, a third of people would not know what to do, and only 5.6% of people would take the seizing person to a hospital [24]. As such, developing strategies to ensure that PWE are able to attend school will not only benefit PWE directly but also help in addressing the stigma present in the general population by promoting insight into the condition and its medical management.

4.3. Seizure characteristics

We evaluated seizure severity by examining both the total number of current seizures at baseline and utilizing the PIES seizure subscale. Our sample's seizure severity was high with most PWE experiencing multiple

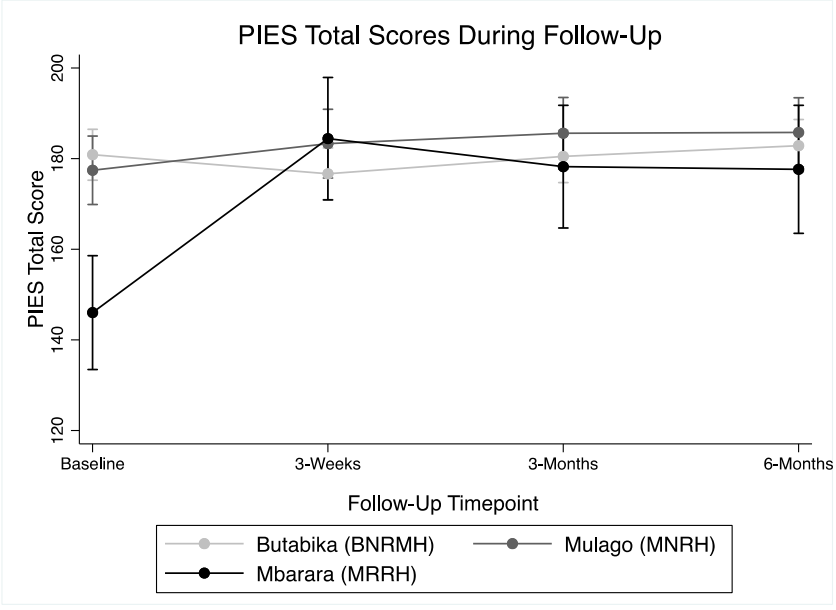

Fig. 2. PIES Total scores during follow-up.

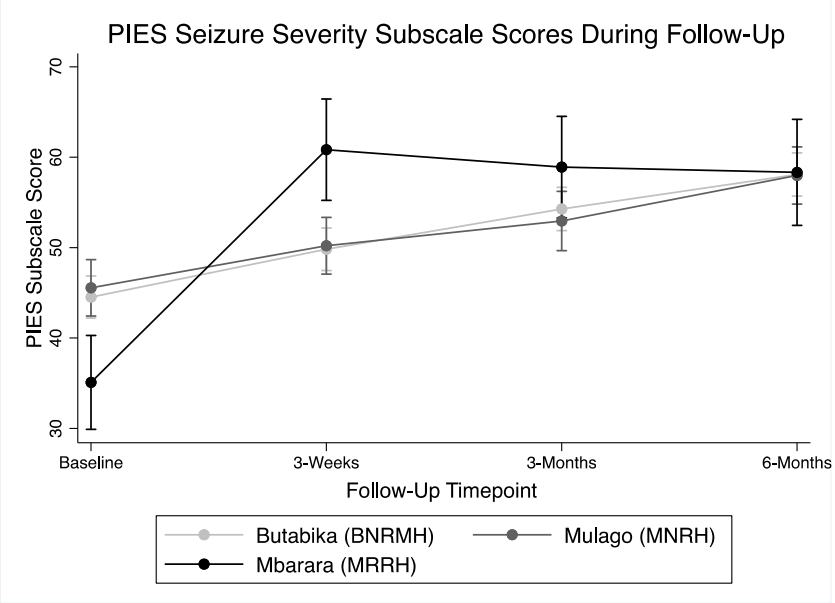

Fig. 3. PIES Seizure Severity subscale scores during follow-up.

seizures per week upon hospital presentation, and a 43.77 (sd = 16.73) score on the PIES severity scale. The median initial seizure frequency at BNRMH was twice as high as the observed median initial frequency at the other two sites. However, the median current seizure frequency was noted to be the same across the three study sites. Additionally, most PWE experienced loss of consciousness as part of their seizure semiology suggesting that most people experience generalized seizures, although we did not fully categorize the type of epilepsy. It might be expected that severe epilepsy is present in our cohort due to the recruitment of patients from tertiary facilities, where healthcare providers should be seeing more severe cases due to a higher number of referrals from peripheral centres. However, an alternative or contributory explanation is that PWE do not seek care until their condition is quite severe. Prior literature in LMICs and Uganda specifically points to the latter [4,24,25]. If this is the case, it follows that there are many PWE living with less severe forms of epilepsy, and likely many with primarily only focal seizure episodes that are not receiving care and not being captured by this study. If this is in fact true, then we are likely underestimating the current epilepsy treatment gap.

Another key finding in our study was the delay in skill and learning ability associated with epilepsy. Our findings reveal that a delay in skill or learning ability can be found in the majority of people living with epilepsy. This was especially apparent at MNRH where over 70% of patients reported a skill or learning delay. This association underscores the importance that PWE receive appropriate multidisciplinary care to better control their seizures, reduce side effects, preserve and develop neurocognitive function and use of compensatory strategies, and avoid neuronal damage caused by repeated insults to the brain.

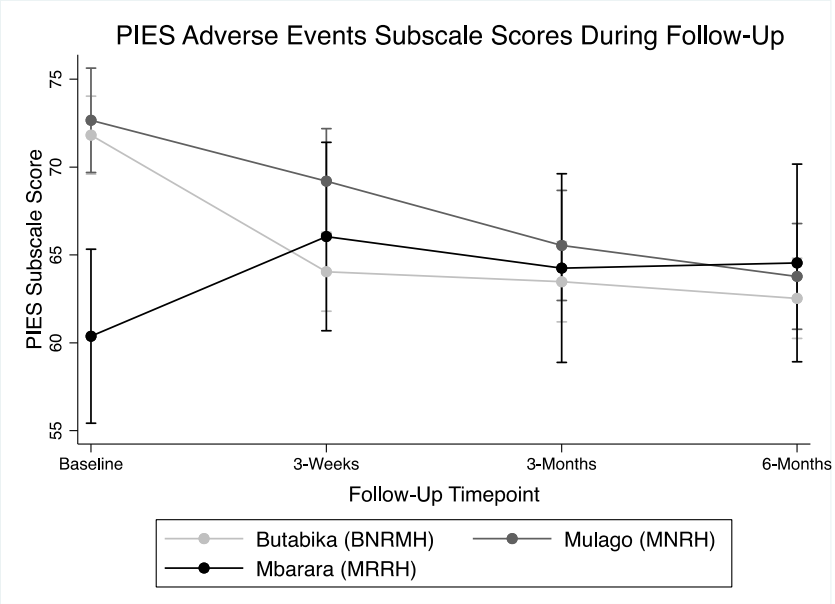

Fig. 4. PIES Adverse Events subscale scores during follow-up.

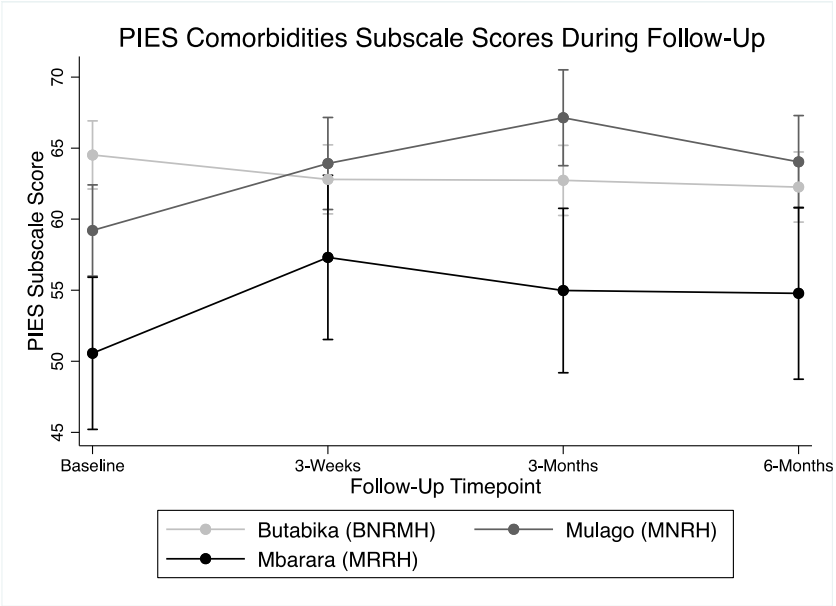

Fig. 5. PIES Comorbidities subscale scores during follow-up.

4.4. AED prescription

All of the most frequently prescribed AEDs at the three hospital sites are on the World Health Organization (WHO) Model list of essential medicines. Carbamazepine was clearly shown to be the most frequently prescribed AED, with other commonly used AEDs, including phenytoin and sodium valproate. In our study, there was an obvious difference in the use of phenytoin across the different hospitals: In BNRMH, phenytoin was used considerably less and only accounted for 11% of the total amount of prescribed AEDs. This number was considerably higher in the two other centres: 40% and 38%, respectively. Despite its antiepileptic effects, phenytoin is noted to have considerable side effects and for this reason is generally not prescribed as the first or second AED of choice in higher-income countries; however, because of its relatively lower cost, it is often prescribed in LMICs.

The relative availability of AEDs has a profound impact on prescription patterns and treatment of epilepsy. In one study on children with epilepsy in Central Uganda, 66.9% of caregivers reported that at some point during their care, there was a lack of their child's AEDs at their clinic or hospital pharmacy, where AEDs are normally provided free of cost, thus requiring out-of-pocket purchase of the required AEDs at private shops instead [18]. In a wider survey of hospitals, the 2014 Hospital and Health Centre IV Census Survey [26] aimed to assess the healthcare service capacity of 147 hospitals and 188 level IV primary care facilities in Uganda. Of 13 medicines considered to be important in the treatment of mental and neurological illness, including diazepam, carbamazepine, phenytoin, phenobarbital, and valproate, a startling 1% of the 335 facilities surveyed had all medicines available. National referral hospitals had the highest mean availability of medicines, with 81% of medicines being available, versus only 47% of medicines available in level IV

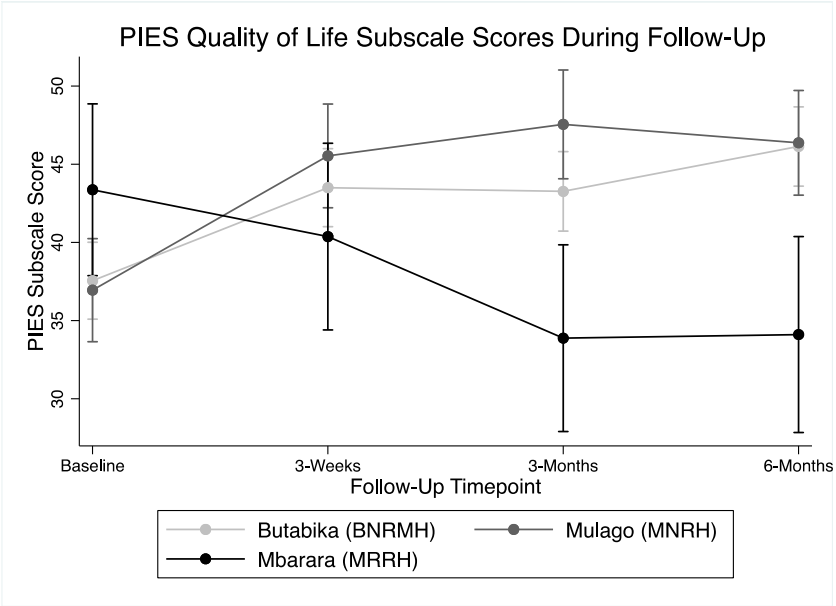

Fig. 6. PIES Quality of Life subscale scores during follow-up.

primary care facilities. When further examining availability by medication, 80% of facilities had phenytoin available, whereas only 15% had valproate available. In being a national psychiatric referral hospital, it is likely that BNRMH has considerably improved access to a wider variety of AEDs such as sodium valproate and carbamazepine when compared with MRRH, a regional hospital, and MNRH, a national though multidisciplinary referral hospital. Ultimately, this difference is likely a downstream effect of a complex interplay between variations in local policy, administrative control, and supplier options among hospitals and regions. Such differences in AED utilization and availability should be investigated further so that the most cost-effective treatment can be established.

4.5. Impact of treatment

Antiepileptic drugs and other treatments are provided to PWE in the hope that treatment will reduce seizures, have minimal side effects, and improve quality of life. We selected the PIES tool as our key outcome indicator because it possesses questions that elucidate the primary goals of treatment, and the total score can be used as a proxy for overall impact [20]. Our overall PIES Total score average was 175.80 (sd = 41.40), which illustrated that the PWE in our study were impacted significantly by their seizures. Within the subscales of PIES at baseline, Quality of Life had the lowest average (38.02, sd = 19.29) followed by Seizure Severity (43.77, sd = 16.73), Comorbidities (61.24, sd = 19.17), and Adverse Events (70.78, sd = 18.07) with the highest average (Table 3). This illustrates that for PWE in our sample, quality of life had the greatest impact. Notably given limited AED choices, minimal impact was attributed to side effects from medications and other treatments used to manage their seizures. Aside from seizures, for PWE, health-related quality of life is largely dependent on social and psychological factors. Another study in Uganda has also shown that these areas become increasingly more important than seizure control for patients who are already on medication, as even with appropriate seizure control, other limitations arising from stigma and social isolation exist [25]. Ultimately, management plans that address overall quality of life, and not just seizure frequency and medication side effects, are necessary.

Generally, treatment provided at the three sites improved the overall PIES scores and the Seizure Severity subscale scores, although this was not statistically significant given that our sample was a mix of PWE with variable baseline levels of seizure control. Importantly, the types of AEDs prescribed were similar across sites, and BNRMH and MNRH being located within Kampala, the capital city, likely provided those PWE with greater access to ancillary services. These facts would lead one to conclude that PWE would be worse off at MRRH. We found this to be true at baseline for the PIES Total score and all subscales except for Quality of Life. Despite the initial poor PIES scores at MRRH at baseline, PWE at MRRH had the greatest improvements in nearly all PIES subscales. An inability to divide our sample by age at onset of seizures, length of time on AEDs, and type of epilepsy is likely masking the true impact of treatment in this population and preventing us from uncovering the underlying differences influencing treatment outcomes at each site. Further examination of the current available treatments in Uganda and their impact on PWE is warranted to help develop strategies for reducing the epilepsy treatment gap.

4.6. Limitations

While our study has many strengths, there are a few key limitations that require discussion. Most importantly, we focused our efforts on developing our cohort through convenience sampling at three key public hospitals, where a proportion of PWE may be unable to seek care because of distance and inaccessibility. Despite obtaining full follow-up data on more than 90% of the original cohort, there are likely more PWE being treated at lower level health facilities not being captured. It is possible that these people have less severe forms of epilepsy as they are not being subsequently referred to the major hospitals included here; this may be reflected in the fact that there are few seizures with preserved awareness captured in the current cohort.

Another key limitation is that we relied on self-reporting for our data collection. Additionally, patients were not subcategorized by epilepsy type, limiting our ability to examine differences in outcomes based on specific subtypes. We also were not able to adequately collect the length of seizures episodes and the amount of time that patients were in treatment, which limited our ability to evaluate the differential impact of AED prescriptions on new versus existing cases. Lastly, the variety in training and background of healthcare providers at each hospital was not examined, which may impact overall management of patients with epilepsy including AED choice and level of seizure control achieved.

Overall, we believe that this study helps to elucidate treatment practices in the most resourced hospitals in Uganda, and how it may impact outcomes for PWE. The demographics and current seizure outcomes of PWE attending hospital-based care in Uganda are well described in our sample.

5. Conclusion

Epilepsy can be managed cost-effectively with appropriate treatment and consistent follow-up care. Despite this, the epilepsy treatment gap is substantial in many LMICs where a multifactorial network of challenges widens the gap. We were able to show how epilepsy is currently managed in public referral hospitals in Uganda and the impact of current treatment practices. Specifically, we found that, while not statistically significant, current treatment practices have a positive impact on PWE. This finding suggests that for the population of patients that make it to biomedical care, if improvements in AED availability and basic resources are made, then PWE will show greater improvements that are significant statistically and pragmatically. Additionally, our findings suggest that more work needs to be done to improve educational attainment, reduce stigma, expand the availability of medications, and develop strategies to better track the impact of treatment for PWE. These changes would allow for a better understanding of and how to effectively address the treatment gap in Uganda.

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Declaration of competing interest

None.

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