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Prevalence and factors associated with behavioural problems in children with epilepsy attending Mulago hospital, Uganda: A cross-sectional study

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ABSTRACT

Purpose: : To determine the prevalence of behavioural problems and the associated factors in children with epilepsy (CWE).
Methods: : This was a cross-sectional study conducted at Mulago National Referral Hospital, Kampala, Uganda, from December 2019 to May 2020. A total of 300 CWE aged 6 to 17 years were consecutively enrolled and assessed for behavioural problems using the Strengths and Difficulties Questionnaire. We obtained data on the associated factors by using pretested structured questionnaires, the Rosenberg Self-Esteem Scale, the Kilifi Stigma Scale of Epilepsy, the Morisky medication adherence scale and the Tumaini Child Health Screener for childhood disabilities. Simple logistic regression and multivariate analysis was done to determine the associated factors while adjusting for the presence of neurodevelopmental disorders and childhood disabilities.
Results: : Behavioural problems were detected in 108/300 CWE (36%) with more internalizing (28%) than externalizing (21%) behaviour scores noted. The odds of behavioural problems increased with the presence of co-morbid neurodevelopmental disorders or childhood disabilities (cOR: 5.42, p-value < 0.001). Factors associated with occurrence of behavioural problems were high stigma perception (aOR: 4.06, p-value < 0.001) and being seizure-free in the last six months (aOR: 3.43, p-value $=0.031$) while being an adolescent (aOR: 0.33, $p=0.001$) lessened the risk.
Conclusions: : Behavioural problems occur in more than a third of CWE. They are more in the internalizing domain than in the externalizing domain. Their odds increase with high perceived stigma and in the first six months of seizure control.

Introduction

Epilepsy is a worldwide problem that affects approximately 70 million people with the majority (>80%) living in low- and middle-income countries [1]. Worldwide, the age-standardized prevalence is 621•5 per 100 000 population [2]. In Uganda, the estimated overall epilepsy prevalence was 10.3 per 1,000 in 2017 and it was found to decline with age [1]. Children with epilepsy (CWE) have higher rates of behavioural problems than healthy controls, siblings, and other age-matched children with other chronic diseases [3]. In previous studies, behavioural problems were reported in approximately 35-50% of CWE [4]. These problems can impede daily life activities of CWE and affect their families to a major degree [5]. In many cases, these problems create more of a challenge than the epilepsy itself [6].

Behavioural problems may influence the course of treatment of epilepsy by constituting an additional health risk factor, that affects treatment adherence or care-seeking, or they may influence the underlying pathophysiology that triggers symptoms that necessitate further medical attention [7]. Besides, children who display behavioural problems in early childhood are prone to have mental health challenges later

Abbreviations: TUCH, Tumaini Child Health Project; CWE, Children with epilepsy.

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in life [8].

The developing brain may be affected by some epileptic syndromes that are associated with significant cognitive or behavioural declines with a devastating impact [9]. In children with additional impairment, particularly those with intellectual disability, the rates are even higher, over 50% [4]. Among adolescents, a recent study found that schizophrenia, anxiety and mood disorders were most likely associated with behavioural problems [10].

Throughout the world, multiple factors have been associated with increased risk of behavioural problems in CWE which varies with different settings [11–15]. These factors can be broadly divided into seizure-related factors (e.g., type and severity of epilepsy), psychosocial and iatrogenic such as those due to antiepileptic drugs or surgery [4], and the presence of co-morbid neurodevelopmental disabilities [4]. These factors may, independently or in combination, influence the occurrence of behavioural problems.

Although there is relatively adequate information on the prevalence of behavioural problems among CWE in regional studies [16],[17], very little information has been provided regarding their associated factors that might give insights into early diagnosis and prevention [6].

Furthermore, in Uganda, the association between childhood epilepsy and behavioural problems has not been explored ([18]). The aim of this study was to determine the prevalence of behavioural problems and determine the associated factors in CWE compared to children with comorbid Neurodevelopmental disorders or Childhood disability (NDD/CD).

Methods

Study design and study setting

This was a cross-sectional study employing structured pretested questionnaires for data collection. It was carried out over a 6-months period (December 2019 to May 2020) in the Paediatric Neurology Clinic and the Child Psychiatry Clinic at Mulago National Referral Hospital (MNRH), Kampala, Uganda where the majority of CWE with or without behavioural problems are managed.

Study population

Children aged 6 to 17 years with a confirmed diagnosis of epilepsy, attending either clinic during the study period and accompanied by the caregiver. Both idiopathic and syndromic epilepsy were included. However, in further analysis, the factors associated with behavioural problems were identified by controlling for the presence of intellectual disability, other neurodevelopmental disorders, and childhood disability.

Study procedures

CWE whose caregivers provided written informed consent were consecutively enrolled in this study. Where appropriate, assent was sought from children aged 8 years and older. Children not accompanied by their caregiver were excluded.

The child's behaviour was assessed using the Strengths and Difficulties Questionnaire (SDQ) [19]. The original SDQ is a 25 item behaviour screening tool that comprises five subscales (Emotional symptoms, Conduct problems, Hyperactivity, Peer problems, and Pro-social behaviour) each with five items. The SDQ is scored using a three-option Likert response format (not true, somewhat true or certainly true), the score on each subscale ranges from 0 to 10 points so that a higher score indicates a higher risk of behavioural problems. Scores from these items are used to generate the total difficulties score (range 0 to 40), which is the sum of scores from all the subscales except the pro-social scale. The Total difficulties score of $\geq$17 was interpreted as a behavioural problem, while the Total difficulties score of 14-16 was interpreted as borderline [20]. The SDQ has been validated in Uganda and in many countries with excellent reliability for Total Difficulties (alphas $>$ .70); good to excellent for the subscales [21],[22].

A structured pretested questionnaire was the main tool used for obtaining information on sociodemographic data, seizures related factors, pharmacological factors, psychosocial factors, and medical history for each study participant. Additional tools comprised the Rosenberg Self- Esteem Scale [23], the Kilifi Stigma Scale of Epilepsy (SSE) [24], the 8-item Morisky Medication Adherence Scale [25] and the Tumaini Child Health (TUCH) screener for childhood disabilities [26].

The Rosenberg Self-Esteem Scale has been widely used to assess school children's self-image [23]. The current study used the Likert-type scale by Rosenberg (1965), containing 10 items measuring global self-esteem (both positive and negative feelings about the self). The scale ranges from 0-30, with 30 indicating the highest score possible. The higher the score, the higher is the self-esteem [27]. The cutoff used for high self-esteem in this study was $\geq$9 corresponding at 66th percentile. This scale has been widely used in cross-cultural settings and in Uganda with reported good validity and reliability [28].

The Kilifi Stigma Scale of Epilepsy (KSSE) was developed in Kilifi (Kenya) to assess stigma perception among children and adults with epilepsy [24]. It has high internal consistency (Cronbach's a=0.91) and good test-retest reliability (r=0.92) [29]. It is a Likert score scale with 15 items each scored according to the participant's response that is score 0 for "Never", score 1 for "Sometimes" and score 2 for "Always". It has a minimum total score of 0 and maximum of 30 which is calculated by summing up the score of all items. A total score of above the 66th percentile ($\geq$18) of the collected data indicates the presence of high-perceived stigma, whereas that below indicated low-perceived stigma.

The 8-item Morisky Medication Adherence Scale was used to assess the level of adherence to AEDs, which was categorized as low $<$6, moderate: 6-8, or high: $>$8 [25]. The scale has been found reliable and has been used in some non-epilepsy studies in Uganda [30].

The Tumaini Child Health (TUCH) screener is the Ugandan adaptation of the "Ten questions screen'' for childhood disabilities [26],[31]. The "TUCH screener" is a recommended tool for studies of neurodevelopmental disorders in low-resource settings. It screens for autism spectrum disorder; cerebral palsy; epilepsy; cognitive, speech and language, hearing, or vision impairment. The sensitivity of the 23Q ranged from 0.55 to 0.80 [26]. The participants who presented with a positive screen for childhood disability were sent for further assessment in the appropriate clinics, especially the psychiatry clinic; Ear, Nose and Throat; and Ophthalmology within MNRH; or validated with chart review.

Those questionnaires were interviewer-administered to the caregivers of the enrolled children, either in English or in *Luganda* (commonly spoken local language). Two research assistants (a clinical officer and a medical officer) were trained and availed for each clinic day.

The patients were provided with routine care by the clinic staff. Children, who screened positive for behavioural problems, or any childhood disability, were referred for further management in another appropriate clinic. Referral links were established with the Ear, Nose and Throat clinic; Ophthalmology clinic; and social work service within MNRH.

Data analysis

Data were entered into the computer using EPI DATA version 3.1 and exported into STATA version 14 (StataCorpLP, College Station, Texas) for analysis. Descriptive statistics were used to explore baseline characteristics of the study participants. These are presented as frequency, proportions, mean, standard deviation, and interquartile range. A logistic regression model with odds ratios and their 95% confidence intervals was used to measure the strength of association between factors

and behavioural problems. Variables whose p-value of the unadjusted Odds ratio (bivariate level) was less than 0.2 were entered in the multiple logistic regression model using backward elimination with inclusion criteria p=0.2 exclusion p=0.1 and multicollinearity r=0.4. Hosmer-Lemeshow test of goodness of fit was used to test model parsimony. Significance was set at a p-value of < 0.05.

Ethical approval

This study received approval from the School of Medicine Research and Ethics Committee (SOMREC) of Makerere University College of Health Sciences (REC REF 2019-106). Permission to carry out this study was granted by the MNRH Research and Ethics Committee (MHREC 1730).

Results

Baseline characteristics of the study participants

Among the 300 children enrolled, 172 (57.3%) were male, 200 (66.7%) were from an urban residence, 189 (63.0%) were attending school, and 129 (43%) had a comorbid neurodevelopmental disorder or childhood neuro-disability. Their mean age was 11.3 ± 3.8 years, with two thirds (67%) aged between 10-17 years. Other characteristics are presented in Table 1.

Prevalence and impact of behavioural problems

Of the 300 children enrolled, 108 (36%, CI=30.6 to 41.7%) had behavioural problems (See Table 2). These problems were more prevalent in the internalizing domain than in the externalizing domain (28% vs 21%). Of the 300 CWE, 87 CWE (29%) had conduct problems, 61 (20.3%) had peer problems, 72 (24%) presented emotional problems,

Table 1
Baseline characteristics of CWE assessed for behavioural problems (n=300)

Characteristic	Frequency (%)	Characteristic	Frequency (%)
Sociodemographic characteristics		**Baseline seizure characteristics**	
Mean age	11.3±3.8	*Type of seizure*	
Age 10-17 years	201 (67.0)	Generalized onset seizure	186 (62.0)
Male	200 (66.7)	Focal onset seizure	109 (36.3)
Urban	200 (66.7)	Unknown onset	5 (1.7)
School attendance	189 (63.0)	*Frequency of seizure*	
Parent as caregiver	231 (77.0)	≥1 seizure in the last 6 months	226 (75.3)
Baseline co-morbid NDD/CD		Seizure free in the last 6 months	25 (8.3)
Presence of NDD [a]	61 (20.3)	Seizure-free for ≥6 months	49 (16.3)
Childhood disabilities (CD) [b]	68 (22.7)	Seizure-free for ≥6 months	49 (16.3)
No NDD nor CD	171 (57.0)	*Age of seizure onset*	
Baseline psychosocial characteristics		Under-five	155 (51.7)
Low self esteem	145 (48.3)	School age	91 (30.3)
High stigma perception	89 (29.7)	Adolescence	52 (17.3)
Baseline pharmacological characteristics		*Time elapsed since the first seizure*	
Patient on AED	300 (100)	Less than 1 year	24 (8%)
Low to middle adherence to AEDs	108 (36.0)	One to 5 years	112 (37.3)
Ever used traditional medicine	134 (44.8)	More than 5 years	164 (54.7)

[a] **Neurodevelopmental disorder (NDD)** included Autism Spectrum disorder [19], ADHD [9], Intellectual disability [20], communication disorders [4] and learning disabilities [5].

[b] **Childhood disabilities (CD)** included Cerebral palsy (43), Sequelae of stroke, CNS infection or trauma (11), Visual impairment (7), hearing impairment (6) and autonomic syndrome with fecal impaction [1].

Table 2
Prevalence of behavioural problems and distribution of psychosocial characteristics in CWE compared to children with comorbid NDD/CD attending MNRH.

	Overall (n=300)	Presence of NDD/CD* (n=129)	No NDD/CD (n=171)	cOR (95% CI)	P value
SDQ results comparing children with comorbid NDD/CD with those with epilepsy alone					
Total difficulty score (n=300)					
Abnormal	108 (36.0)	74 (57.4)	34 (19.9)	**5.42 (3.25-9.05)**	**<0.001**
Borderline	37 (12.3)	18 (14.0)	19 (11.1)	1.30 (0.65-2.59)	0.459
Normal	155 (51.7)	37 (28.7)	118 (69.0)	0.18 (0.11-0.30)	<0.001
Abnormal scores of the five subsets of behavioural problems (n=300)					
Emotional problem	71 (23.7)	45 (34.9)	26 (15.2)	2.99 (1.71-5.19)	<0.001
Conduct problem	86 (28.7)	56 (43.4)	30 (17.5)	3.61 (2.13-6.10)	<0.001
Hyperactivity	65 (21.7)	50 (38.8)	15 (8.8)	6.58 (3.48-12.45)	<0.001
Peer problem	53 (17.7)	42 (32.6)	11 (6.4)	7.02 (3.44-14.33)	<0.001
Prosocial problem	41 (13.7)	37 (28.7)	4 (2.3)	16.79 (5.80-48.59)	<0.001
Abnormal scores (High and very high score) Broad categories (n=300)					
Internalizing	84 (28.0)	51 (39.5)	33 (19.3)	**2.73 (1.63-4.59)**	**<0.001**
Externalizing	63 (21.0)	49 (38.0)	14 (8.2)	**6.87 (3.58-13.19)**	**<0.001**
Impact score of behavioural problems, Great deal (n=108)					
Difficulties upset or distress the child	43 (39.8)	36 (48.6)	7 (20.6)	9.07 (3.88-21.19)	<0.001
Interfere with home life	40 (37.0)	32 (43.2)	8 (23.5)	6.72 (2.98-15.18)	<0.001
Interfere with friendship	40 (37.0)	26 (35.1)	14 (41.2)	2.83 (1.41-5.68)	0.003
Interfere with classroom learning	41 (37.0)	31 (41.9)	10 (29.4)	5.09 (2.39-10.84)	<0.001
Interfere with leisure activity	41 (37.0)	34 (45.9)	7 (20.6)	8.39 (3.58-19.65)	<0.001
Psychosocial characteristics comparing children with comorbid NDD/CD, and those with epilepsy alone					
Rosenberg Self-esteem scale					
Low (<18)	145 (48.3)	69 (53.5)	76 (44.4)	1.44 (0.91-2.27)	0.121
High (≥18)	121 (40.3)	28 (21.7)	93 (54.4)	**0.23 (0.14-0.39)**	**<0.001**
Not reported	34 (11.3)	30 (23.3)	4 (2.3)	12.65 (4.33-36.98)	<0.001
Kilifi Stigma Scale of Epilepsy					
Low stigma perception (<9)	179 (59.7)	47 (36.4)	132 (77.2)	0.17 (0.10-0.28)	<0.001
High stigma perception (≥9)	89 (29.7)	54 (41.9)	35 (20.5)	**2.80 (1.68-4.66)**	**<0.001**
Not reported	32 (10.7)	28 (21.7)	4 (2.3)		<0.001

(*continued on next page*)

Table 2 (*continued*)

				11.57 (3.94-33.96)	
8-item Moriski Adherence Scale					
Low adherence (<6)	27 (9.1)	16 (12.4)	11 (6.4)	2.06 (0.92-4.60)	0.078
Middle adherence (6-8)	66 (22.0)	29 (22.5)	37 (21.6)	1.05 (0.61-1.82)	0.861
High adherence (>8)	192 (64.0)	77 (59.7)	115 (67.3)	0.72 (0.45-1.16)	0.177
Not reported	15 (5.0)	7 (5.4)	8 (4.7)	1.17 (0.41-3.31)	0.769

* Internalizing SDQ scores: Close to average: 0-5, slightly raised: 6-7, high: 8-9, Very high: 10-20Externalizing SDQ scores: Close to average: 0-8, slightly raised: 9-10, high: 11-12, Very high: 13-20

while 56 (18.7%) had hyperactivity and 41 (13.7%) had abnormal prosocial behavior. The caregivers reported that these behavioural problems impacted negatively on the daily life activities in about 4 out of 10 affected CWE. The presence of NDD/CD is associated with more than five times increased odds of behavioural problems (cOR=5.42, CI=3.25-9.05, p value <0.001), and more likely associated with high stigma perception (cOR=2.80, CI=1.68-4.66, p value <0.001).

Factors associated with behavioural problems in CWE

At bivariate analysis, the factors associated with behavioural problems were high stigma perception, using AED other than Carbamazepine, Valproate or Phenytoin; while age 10-17 years, high self-esteem, high level of adherence and "never used traditional medicine" are protective as shown in Table 3.

Seizure-related factors associated with behavioural problems

Children with "focal onset seizure" were 2 times more likely to present behavioural problems (cOR: 2.31, 95% CI=1.42 to 3.78, p=0.001); while "seizure onset at 6 to 9 years of age", "seizure onset at 10 to 17 years of age", and having an epilepsy syndrome during adolescence presented low odds of behavioural problems, as shown in Table 4.

Comorbidities associated with behavioural problems

The Table 5 below shows that approximately $^{2}/_{3}$ of behavioural problems have either an underlying neurodevelopemental disorder (32.4%) or a childhood disability (33.3%). The major specific underlying disorders are cerebral palsy (33.3%), Autism Spectrum Disorder (13.9%), Intellectual disability (9.3%), and Attention-Deficit-Hyperactivity Disorder (7.4%).

Multivariate analysis of factors associated with behavioural problems while controlling for the presence of NDD/CD

At multivariate analysis, while controlling for the presence of neurodevelopmental disorders and childhood disabilities, the factors associated with behavioural problems were high stigma perception and being seizure-free in the last six months; while CWE with high self-esteem, and older age 10-17 years were less likely to have behavioural problems, see Table 6.

Table 3
Bivariate analysis of socio-demographic, psychosocial and pharmacological factors associated with behavioural problems in CWE attending MNRH

Factor	No (n=192)	Yes (n=108)	cOR (95% CI)	P-value
Sociodemographic characteristics				
Age in years				
6-9 years	46 (24.0)	53 (49.1)	1	
10-17 years	146 (76.0)	55 (50.9)	**0.33 (0.20-0.54**	**<0.001**
Gender				
Male	102 (53.1)	70 (64.8)	1	
Female	90 (46.9)	38 (35.2)	0.62 (0.38-1.00)	0.05
Is the child going to school				
Yes	130 (67.7)	61 (56.5)	1	
No	62 (32.3)	47 (43.5)	1.62 (0.99-2.63)	0.053
Psychosocial factors				
Self-esteem (On Rosenberg self-esteem scale)				
Low (<18)	78 (43.6)	67 (77.0)	1	
High (≥18)	101 (56.4)	20 (23.0	**0.23 (0.13-0.41)**	**<0.001**
Stigma perception (KSSE)				
Low (<9)	139 (77.7)	40 (44.9)	1	
High (≥9)	40 (22.3)	49 (55.1)	**4.26 (2.47-7.35)**	**<0.001**
Pharmacological factors				
Anti-epileptic drugs				
Carbamazepine	125 (65.1)	63 (58.3)	1	
Sodium Valproate	43 (22.4)	28 (25.9)	1.29 (0.73-2.27)	0.373
Phenytoin	12 (6.3)	2 (1.9)	0.33 (0.07-1.52)	0.156
Others*	12 (6.3)	15 (13.9)	**2.48 (1.10-5.62)**	**0.029**
Level of adherence (8-item Moriski adherence scale)				
Low adherence (<6)	12 (6.6)	15 (14.6)	1	
Middle adherence (6-8)	37 (20.3)	29 (28.2)	0.63 (0.25-1.54)	0.31
High adherence (>8)	133 (73.1)	59 (57.3)	**0.35 (0.16-0.80)**	**0.013**
Ever used traditional medicine				
Yes	75 (39.3)	59 (54.6)	1	
No	116 (60.7)	49 (45.4)	**0.54 (0.33-0.87)**	**0.011**

* Others AEDs include lamotrigine, clonazepam, Phenobarbital, Clobazam, Topiramate and Levetiracetam.

Discussion

This study was conducted to determine the prevalence of behavioural problems and the associated factors among children with epilepsy aged 6–17 years, attending two outpatient clinics of the Mulago National Referral Hospital in Uganda. We have illustrated that CWE in Uganda are affected by a huge burden of behavioural problems, which is significantly associated with high perceived stigma and degree of seizure control.

Prevalence of Behavioural problems

To the best of our knowledge this is the first study to document the prevalence of behavioural problems in CWE and identify associated factors in Uganda. Findings of a high prevalence of behavioural problems are suggestive of great distress faced by CWE and their families. These findings are similar to those reported in previous regional studies. A recent study done in Kinshasa/Congo reported a prevalence of 34.6% in CWE aged 6-17 years with externalizing problems (26.9%) higher than internalizing problems (23,1%) [16]. Another study done in Kilifi District, in rural Kenya, showed a significantly greater proportion of

Table 4
Bivariate analysis of seizure-related factors associated with behavioural problems in CWE

Variable	No (n=192)	Yes (n=108)	cOR (95% CI)	P-value
Age at seizure onset				
0 to 5 years	80 (41.7)	77 (71.3)	1	
6 to 9 years	65 (33.9)	26 (24.1)	0.42 (0.24-0.72)	0.002
10 to 17 years	47 (24.5)	5 (4.6)	0.11 (0.04-0.29)	<0.001
Type of seizure				
Generalized onset seizure	132 (68.8)	54 (50.0)	1	
Focal onset	56 (29.2)	53 (49.1)	2.31 (1.42-3.78)	0.001
Unknown onset**	4 (2.1)	1 (0.9)	0.61 (0.07-5.59)	0.663
Time elapsed since the first seizure				
Less than 1 year	16 (8.3)	8 (7.4)	1	
One to 5 years	77 (40.1)	35 (32.4)	0.91 (0.36-2.32)	0.842
More than 5 years	99 (51.6)	65 (60.2)	1.31 (0.53-3.24)	0.555
Frequency of the seizures				
≥1 seizure in the last 6 months	148 (77.1)	78 (72.2)	1	
Seizure free in the last 6 months	13 (6.8)	12 (11.1)	1.75 (0.76-4.02)	0.186
Seizure-free for ≥6 months	31 (16.2)	18 (16.7)	1.10 (0.58-2.09)	0.767
EEG pattern				
Normal	19 (9.9)	13 (12.0)	1	
Generalized	30 (15.6)	14 (13.0)	0.68 (0.26-1.76)	0.429
Focal discharges	39 (20.3)	46 (42.6)	1.72 (0.76-3.93)	0.195
Not done	104 (54.2)	35 (32.4)	0.49 (0.22-1.10)	0.083
Childhood epilepsy syndromes				
Severe ES of childhood[a]	5 (2.6)	6 (5.6)	1	
Benign childhood SSS[b]	8 (4.2)	11 (10.2)	1.15 (0.26-5.11)	0.858
Epilepsy syndromes in adolescence[c]	38 (19.8)	10 (9.3)	0.22 (0.06-0.87)	0.031
Other phenotypes of seizures	141 (73.4)	81 (75.0)	0.48 (0.14-1.62)	0.236
Presence of NDD/CD				
No	137 (71.4)	34 (31.5)	1	
Yes	55 (28.6)	74 (68.5)	5.42 (3.23-9.05)	<0.001

[a] Severe epilepsy syndrome of childhood: Lennox-Gastaut syndrome (5/3), Doose syndrome (0/3).
[b] Benign childhood seizure susceptibility syndrome: Rolandic epilepsy (5/10), Idiopathic childhood occipital of Gastaut (3/1).
[c] Epilepsy syndromes in adolescence: Juvenile myoclonic epilepsy [1], Juvenile absence seizure [14], Epilepsy with generalized tonic-clonic seizure on awakening [24], benign partial seizure in adolescence [5], Epilepsy from cortical brain tumor [1].
** The term "Unknown" is used to denote where it is understood that the patient has Epilepsy but the clinician is unable to determine if the Epilepsy Type is focal or generalized because there is insufficient information available.

CWE aged 6-9 years with behavioural problems (49% vs 26% of controls) [17]. A lower prevalence of behavioural problems (19.1%) was reported in Indonesia by Novriska *et al* in 2014 [15]. In India, Mishra *et al* detected behavioural problems more in externalizing domains (45%) than in internalizing domains (21.2%) in CWE aged 6-14 years [32]. A possible explanation for these differences in frequency of behavioural syndromes may be due to the underlying causes, the context and coping styles of CWE. In view of the growing interest to understand the disadvantaged contexts in which these behavioural problems occur, this study has looked at the associated factors.

Table 5
Neurodevelopmental disorders and childhood disabilities underlying behavioural problems in CWE attenting MNRH

Comorbid neuro-disability	**CWE (n=300)**	**Percentage**	**Behavioural problems (n=108)**	**Percentage**
Neurodevelopmental disorder (NDD)	**61**	**20.3**	**35**	**32.4**
Autism Spectrum disorder	21	7.0	15	13.9
ADHD	9	3.0	8	7.4
Intellectual disability	22	7.3	10	9.3
Communication disorder	4	1.3	1	0.9
Learning disability	5	1.7	1	0.9
Other NDD	0	0.0	0	0.0
Childhood disabilities (CD)	**68**	**22.7**	**36**	**33.3**
Cerebral palsy	43	14.3	25	23.1
Visual impairment	7	2.3	2	1.9
Hearing impairment	6	2.0	3	2.8
Sequalae of CNS infections, stroke, or trauma	11	3.7	5	4.6
Other disability	1	0.3	1	0.9
Total NDD/CD	**129**	**43.0**	**71**	**65.7**
CWE without NDD nor disability	**171**	**57.0**	**37**	**34.3**
Total CWE	**300**	**100**	**108**	**100**

*Children with cerebral palsy complicated with epilepsy and behavioural problems, had cognitive impairment [3], global developmental delay [15], multiple disabilities [4], ASD [1], and ADHD [2].

Table 6
Multivariate analysis of factors associated with behavioural problems in CWE while controlling for the presence of NDD/CD

Variable	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI) While controlling For NDD/CD	P-value
Age in years				
6-9 years	1		1	
10-17 years	**0.23 (0.11-0.49)**	**<0.001**	**0.33 (0.16-0.65)**	**0.001**
NDD/CD				
No	1			
Yes	2.61 (1.30-5.24)	0.07	-	-
Frequency of the seizures in the last six months				
Still has seizures	1		1	
Seizure free in the last 6 months	4.33 (1.31-14.31)	0.016	**3.43 (1.12-10.48)**	**0.031**
Seizure-free for more than 6 months	1.97 (0.79-4.88)	0.143	1.71 (0.71-4.10)	0.229
Stigma				
Low	1		1	
High	4.28 (1.97-9.31)	<0.001	**4.06 (1.94-8.53)**	**<0.001**
Self-esteem				
Low	1		1	
High	0.39 (0.18-0.83)	0.014	**0.36 (0.17-0.75)**	**0.006**

Factors associated with behavioural problems

While controlling for the presence of neurodevelopmental disorders and neuro-disability that limit social communication, this study has demonstrated that high stigma perception and being seizure free in the last six months are the most predominant associated factors. These findings suggest that, although achieving better seizure control has been proven as a key factor in the improvement of psychosocial functioning and behavioural outcome in CWE [33], other factors contribute

significantly to the occurrence of behavioural problems in CWE. Children with epilepsy, who are treated for seizures, should therefore be monitored for other factors that may influence the occurrence of behavioural problems. Besides, a marked improvement in seizure control with treatment can result in behavioural problems, probably as a result of the "release phenomenon". This situation can occur when someone who has been disabled by severe epilepsy for a long period becomes much more able as a result of successful seizure control but has not yet learned how to use their new-found ability in an acceptable way [4].

These findings correlate with studies that looked at both seizure-related factors (duration of illness, seizure frequency, seizure type, and location), and psychosocial factors (parent child relationship, parenting style, underlying family psychopathology, family perception, stigma, self-esteem, coping skills), where psychosocial factors were more important than seizure-related factors [34],[35]. A meta-analysis that looked at the psychopathology in CWE suggested an important role of psychosocial factors besides the epilepsy-related factors [36]. It has been demonstrated that patients with epilepsy who experience high stigma perception are predisposed to suffer from poorer psychological function [37] and subsequently poor quality of life [38]. In Sub-Saharan Africa, the causes of stigma include lack of knowledge about the causes of epilepsy, misconceptions, low socioeconomic status, lack of social support, and poor seizure control [38].

In addition to seizure control, interventions against stigma should include raising awareness and working to change attitudes about epilepsy through education, dispelling myths, and providing more psychosocial support [38].

The presence of co-morbid neurodevelopmental disorders and childhood disabilities presented five times increased odds of behavioural problems. Several studies found that neurodevelopmental disorders are commonly associated with behavioural problems in children with epilepsy. In such co-morbidity, it is difficult to assume that the behavioural problem is caused either by the co-morbid disorders or by epilepsy; as common neurobiological mechanisms may induce the neurologic dysfunction that brings about both seizures and behavioural problems [39]. Ideally, CWE with comorbid NDD or childhood neuro-disabilities should be excluded from this study. However, these study findings highlight the need of addressing the neuro-disabilities as a part of a comprehensive assessment of CWE treated for seizures. The TUCH-screen used in this study was validated in Uganda for community screening of childhood neurodevelopmental disorders [26] for early identification of probable positive cases to be referred for appropriate care. It's validation at the level of primary health centers will require further studies.

Being protected during the adolescent age might result from good seizure control over time and improved adaptation to the illness. The effects of seizures themselves and poor child and family adaptation to the illness have been suggested among the presumed causes of behavioural problems in CWE [39]. In addition, for those who are still having seizures, the relationship between seizures and behavioural problems should be better understood by assessing how frequent are the seizures.

Limitations and directions for further research

We acknowledge that this study was limited in a number of respects by: lack of a specified behavioural syndrome diagnosis. Furthermore, we used the TUCH screening tool which does not provide a definitive diagnosis for neurodevelopmental disabilities which may have been overestimated. Our study being at the main referral hospital of the country in the capital city has a selective bias since other CWE may not have had access to it. Therefore, our findings may not be generalizable to all CWE in Uganda. Hence, there is need for bigger community surveys that may include many more participants from different settings.

We did not measure the maternal mental health; previous studies have reported strong associations between maternal depression and behavioural problems in children [40]. Further studies should employ more robust tools to diagnose more specific behavioural problems and neurodevelopmental disabilities as well as measure maternal mental health. Although this study did not show an association of behavioural problems with pharmacological factors, this could be better understood by a study on AED side effects, which was beyond the scope of our study.

Conclusion and Recommendations

Behavioural problems are common in CWE occurring in more than a third of the children attending MNRH. These problems were more in the internalizing domain (28%) than in the externalizing domain (21%). Underlying neurodevelopmental disorders and neuro-disability are the major contributing factors. The behavioural problems are associated with high stigma perception and being seizure free in the last six months.

In order to reduce the burden of behavioural problems in children with epilepsy, routine care for children with epilepsy should include seizure control, regular behavioural assessment and monitoring, screen for co-morbid neurodevelopmental disorders, and psychosocial support. In addition to that, there should be organized community supportive interventions aimed at stigma reduction, promotion of self-esteem, and psychosocial support to children with epilepsy. Further research studies should be conducted on behavioural side effects of AEDs.

Ethical approval and consent to participate, and for publication

This study was approved by the Makerere University School of Medicine Research and Ethics Committee. Written informed consent was obtained from the child's caregiver in order to participate in the study.

Availability of dataset and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions

JKS contributed to the study design, coordinated the clinical assessment, and patients' enrolment. JKS, JR and AKM did the data analysis and drafted the manuscript. All the authors contributed to the interpretation of data, critical review of the manuscript and approved the final version.

Declaration of competing interest

The authors declare that they have no competing interests.

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