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Growth parameters and childhood epilepsy in Hai District, Tanzania: A community-based study

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Summary

Aim—This cross-sectional study examined whether growth parameters were associated with epilepsy in children living in a rural community in sub-Saharan Africa (SSA).

Materials and methods—A cross-sectional study was performed in the Hai District Demographic Surveillance Site (HDSS), Tanzania in which 6–14 year old children with epilepsy (CWE) were identified. Age matched controls were randomly selected from the Hai census database for comparison. Anthropometric measurements were used to assess the nutritional status of the children and body mass index (BMI) calculated. Associations between social, demographic and nutritional factors and epilepsy were assessed using multivariable logistic regression.

Results—112 CWE were identified and were compared with 113 controls. There was no significant difference in the BMI between cases and controls (*T*-test, *p*-value of 0.117). Amongst cases, there were no significant associations between BMI and motor difficulties, antiepileptic drug use, cognitive or behavioural problems, early-onset epilepsy or seizure frequency. In the whole group, BMI was significantly associated with socio-economic status (*p* = 0.037) and age.

Discussion—There was no significant difference found between CWE and matched controls with respect to nutritional status. This suggests that there is no causal association between under

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nutrition and epilepsy in this community. Nutritional assessment is still important as part of the comprehensive care of CWE.

Keywords

Epilepsy; Nutritional status; Africa; Children

Introduction

The World Health Organization (WHO) has identified epilepsy as a health priority given that it is one of the commonest chronic neurological disorders worldwide and that about 85% of affected children live in resource-poor countries (WHO, 2004). It has been postulated that epilepsy in children may be caused in part by malnutrition (Crepin et al., 2007). However the link between nutritional status and epilepsy is likely to be complex as many factors may be involved such as associated motor and feeding difficulties, infectious diseases and the effect of antiepileptic drugs (AED). One early study from sub-Saharan Africa (SSA) found a positive association between malnutrition and epilepsy in a population which included both adults and children although the authors concluded that it was not possible to determine the direction of the association (Crepin et al., 2007). A large survey using questionnaires for people with epilepsy across Africa reported malnutrition in 25% of those less than 15 years old (Quet et al., 2011). Significant risk factors for undernutrition were found to be younger age, poor state of general health, history of adverse perinatal events, cognitive impairment and early age of onset of epilepsy. A recent review of other studies of epilepsy and malnutrition worldwide has highlighted the possibility of a two-way relationship between malnutrition and epilepsy although there is insufficient evidence to characterize this further (Crepin et al., 2009). There has been no previous study from SSA using matched controls to examine the link between malnutrition and epilepsy in childhood, which is when most epilepsy begins.

Materials and methods

Study area and population

We conducted a cross-sectional study of epilepsy in an established demographic surveillance site (DSS) in Hai District, Northern Tanzania. (Burton et al., 2012a) In this study we identified all 6–14 year old children with epilepsy (CWE) living in the district following a household census conducted in early 2009. Age-matched controls were randomly selected from the Hai census database for comparison.

Definitions

Epilepsy was defined according to the epidemiological definition of the International League Against Epilepsy (ILAE), whereby epilepsy is characterized by the onset of at least two unprovoked seizures spaced at least 24 h apart in the last 5 years (ILAE, 1993). Children taking antiepileptic drugs (AEDs) were also considered as having active epilepsy.

Criteria for inclusion and exclusion

During the January 2009 census, a nine-item, previously validated questionnaire to detect possible cases of epilepsy was administered to all households in the Hai DSS (Placencia et al., 1992). Details of children who responded positively to one or more questions in the screening questionnaire, together with those identified by trained enumerators as likely to have epilepsy, were collected (Burton et al., 2012b). Cases of epilepsy were defined as children with active epilepsy aged 6–14 years who were resident in Hai at the time of the census. Those children for whom consent was refused or who were below 6 years of age (to eliminate any children with febrile seizures) were excluded.

Cognitive and behavioural assessment

From February 2010 to June 2010, all children in the epilepsy group and all children in the comparison group were recalled for assessment (Burton et al., 2011). The Rutter questionnaire was used to assess behaviour in cases and controls (Rutter, 1967). Cognitive function was assessed using the Good Enough Harris Drawing Test (Harris and Pinder, 1977); this was chosen because of its good reliability and validity compared with other cognitive tests (Gayton et al., 1974).

Controls

Controls were drawn from a random sample selected from all the children aged 6–14 years who were resident in Hai at the time of the census. Controls were identified through the census and group matched to cases by age (± 1 year), sex and village. From this list of eligible children, with a likely refusal rate of 25%, we estimated we needed 186 to give at least one control for each case.

Assessment

All children had a clinical assessment using a standardized proforma and were examined physically. Their height was measured standing against a wall or lying flat on a bed using a semi-rigid tape measure, their weight was measured using a standard weighing scale and mid upper arm circumference was measured at the mid-point between the shoulder and the elbow using a non-stretchable tape measure. Motor and feeding difficulties were assessed from the history and examination. Children considered to have feeding difficulties were those who took longer than half an hour to take a meal and those with coughing or choking on feeding or drinking.

Ethical approval

Approval for the original study was obtained from the National Institute for Medical Research in Tanzania (NIMR) (application reference NIMR/HQ/R.8c/Vol.II/34). Parents and guardians of cases and controls were given written and verbal information in Kiswahili before signing consent forms agreeing to participation. Approval for this analysis was also obtained from the Clinical Research Committee of the K.C.M. College of Tumaini University. Throughout the analysis patients' anonymity and respect for privacy was observed.

Data analysis

All data were double-entered into a Microsoft Access database (2007 version, USA). The two database copies were compared using Epidata (Version 3.1, Epidata Association, Denmark) and each discrepancy was checked against original data forms. The analysis was performed using STATA v.10 (Statacorp, College Station, TX, USA). There has been no data on under nutrition in children with epilepsy in developing countries to make an accurate power calculation. However, a sample of 190 children (95 in each group) would have 80% power and 95% confidence to detect difference in the proportion of undernourished children with an expected rate of 2.5% in the control group and 15% in the children with epilepsy.

Ethnic groups were classified as Chagga (the predominant tribal group in Hai) against all the others. Education of head of household was used as a surrogate marker for socio-economic status, previous research having shown this to be a key determinant in explaining the between-household variation in expenditure (Adult Morbidity, 2003). Children whose mother or father were single, separated, divorced or widowed were designated as having only one parent resident at home; those who were orphans or had been left with distant relatives were classified as having no parents resident at home. Those scoring less than 70 (>2 standard deviations below the mean) on the drawing test were classed as having cognitive impairment and children with total scores of 13 or more on the Rutter assessment were considered as demonstrating behavioural disorder. Co-morbidities (the greater than coincidental association of two conditions in the same individual) were deemed present if any one or more were present. Early-onset epilepsy was defined as that which started at or before the age of three years. Cases were labelled as having recurrent seizures if they had any ongoing seizures in the three months prior to the assessment. Antiepileptic drug (AED) use was classified as: (i) no AED use, (ii) those receiving sodium valproate or carbamazepine, (iii) those receiving phenobarbitone or (iv) those receiving polytherapy.

Simple descriptive analyses were performed to obtain proportions, chi-square test and Fisher's exact test (when the proportional was less than 5) were used to examine associations between categorical variables. Associations between categorical variables and BMI, the primary outcome of interest, were assessed using linear regression. Variables that were significantly associated with BMI ($p < 0.2$) on univariate analysis were included in the multivariate linear regression models: one for the whole group and one for cases only. Two analyses were undertaken, the first looking at the association between epilepsy and BMI, and the second looking for factors associated with BMI in cases of epilepsy.

Results

Overall, there were 112 children aged 6–14 years with active epilepsy and there were 113 age and sex matched controls (Table 1). The demographic and clinical characteristics of the cases and controls are shown in Table 1 and their BMI in Fig. 1. Out of the cases, 29 (26%) had motor difficulties, of whom 10 (38.5%) also had feeding difficulties. No controls had either motor or feeding difficulties. BMI was not calculated for eight of the cases with feeding difficulties as they had spastic quadriplegia and it was not possible to obtain an accurate height. The BMI in the two children with feeding difficulties with height and weight measurements was 16.4 and 13.4 (7 year old boy and girl, respectively). These were

in the normal range (within 5–95th centile) according to Centers for Disease Control (CDC) 2000 standardized growth charts. Height or weight were not recorded in a further five children (two cases, three controls), and BMI was therefore calculated for 102 cases and 110 controls.

There was no significant difference in the BMI between the cases (mean 15.77, (standard deviation (sd) 2.00; 95% confidence interval (95%CI) 15.38–16.15)) and controls (mean 16.21 (ss 2.01; 95%CI 15.81–16.61); (t -test, $p = 0.117$)). There were also no significant differences between cases and controls in any other anthropometric measures (weight for age z -score, height for age z -score and mid upper arm circumference) (Table 2).

Univariate and multivariable analyses

In the univariate analysis of the data from the controls and children with epilepsy together, BMI was significantly associated with age (increasing with age) and there was a non-significant association with sex (female), case status (having epilepsy) and with educational level of the head of household. On multivariable analysis, BMI was significantly associated with age and with educational level of the head of household (Table 3).

In the children with epilepsy, BMI was significantly associated with age (increased with age) and there was a non-significant association with the presence of motor difficulties, early onset seizures and antiepileptic drug use. On multivariable analysis, BMI was significantly associated with age alone (Table 4).

Discussion

This community-based study of children in the Hai District, Tanzania, found that BMI as a nutritional marker for children aged 6–14 years was not associated with epilepsy. A previous study from Benin, West Africa, found there was a significant association, although it was acknowledged that malnutrition could be a consequence of epilepsy rather than a cause (Crepin et al., 2007). The difference in the findings between these two studies may be due to differences in the environment, study population or study design. The Benin study included mostly adults with a mean age of 25 years, and the contribution of malnutrition to the aetiology of epilepsy with this time lapse is difficult to establish, particularly as most epilepsy in Africa starts in early life (Ngugi et al., 2013). Nutritional status of the general population in Hai may compare favourably with elsewhere in SSA as there is abundant rainfall and a regular food supply throughout the year. HIV prevalence in both populations was not known and could have affected nutritional status.

In this study, BMI was closely associated with age; this relationship is well known and is reflected in all standardized growth charts. In the whole group, BMI was also significantly associated with educational level of the head of household. This was a proxy marker of socioeconomic status which most likely reflects household income, availability of food and the increased prevalence of infectious illness in poorer households. This has been found in other studies of nutrition and epilepsy (Quet et al., 2011).

In CWE we found a non-significant association between BMI and motor difficulties, early onset seizures and current AED use. These most likely reflect the severity of the underlying brain dysfunction with early onset, severe, refractory epilepsy being a marker of this. An evaluation of nutritional status in 17 Italian children aged 3—16 years with refractory epilepsy found that there was more undernutrition in children with refractory epilepsy and neurological impairment (Bertoli et al., 2006). The association with early-onset seizures and motor difficulties was not significantly associated in the multivariable model in this study. This is most likely due to small numbers involved and also to the fact that those with the most severe neurological impairment and associated feeding difficulties could not be included as height could not be reliably measured in them. Other influences on nutrition (Crepin et al., 2009) may be important including cultural attitudes and beliefs about epilepsy which is difficult to assess.

Strengths of the study

This was a community-based study in a prevalent cohort of CWE that also benefited from the inclusion of well-matched controls. Trained enumerators and a validated screening questionnaire were used to identify cases, and case status was confirmed by those with expertise in epilepsy. Both cases and controls were assessed using identical methods and questionnaires. These factors lend strength to the clinical case series and help to minimize bias in the case-control findings.

Limitations

This study examined growth parameters but did not assess nutritional status in terms of other markers such as albumin and prealbumin. Growth parameters may be a reasonable indicator of nutritional status but further work would need to be done to confirm this in the study population. The children with feeding difficulties were all CWE and most of these could not be included in the analysis of BMI as they had motor impairments which made accurate height measurement impossible. The two children with feeding difficulties who had BMI measurements had a BMI that would fit within the normal range on the most recent CDC standardized growth charts. Although this may have reduced the chances of finding an association between poor nutrition and epilepsy, it may be important to exclude children with feeding difficulties altogether as this is likely to be a confounding factor when considering any causal relationship between under-nutrition and epilepsy. There is a time delay between epilepsy onset and this cross-sectional study, and any inferences about causation of epilepsy are difficult to make. The HIV status in this group of children was not assessed, and the contribution of HIV to both epilepsy and nutrition in this population may be important. This study was performed in a distinct population and may not be generalizable to other populations.

Conclusions

This study found that there was no association between growth parameters and epilepsy in this population of Tanzanian children and under nutrition is more likely to be the consequence of other factors. Nutritional assessment is still important in the care of children

with epilepsy, especially in children with associated cerebral palsy who are at higher risk of under-nutrition.

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Figure 1.
Body mass index in controls and children with epilepsy.

Table 1

Descriptive statistics for cases and controls.

Variable	Cases (<i>n</i> = 112); <i>n</i> (%)	Controls (<i>n</i> = 113); <i>n</i> (%)	χ^2	<i>p</i> -Value
<i>Sex</i>	(Missing = 0)	(Missing = 0)		
Male	57 (50.9)	57 (50.4)		
Female	55 (49.1)	56 (49.6)	0.006	0.937
<i>Age</i>	(Missing = 0)	(Missing = 0)		
6 to 10 years	33 (29.5)	41 (36.3)		
11 to 15 years	79 (70.5)	72 (63.7)	1.144	0.285
<i>Tribe</i>	(Missing = 1)	(Missing = 0)		
Chagga	86 (77.5)	101 (89.4)		
Others	25 (22.5)	12 (10.6)	5.758	0.016
<i>Who the child lives with</i>	(Missing = 0)	(Missing = 0)		
Both parents	71 (63.4)	89 (78.8)		
Single parent	7 (6.3)	11 (9.7)		
Relatives	34 (30.4)	13 (11.5)	9.86	0.007
<i>Education of head of household</i>	(Missing = 2)	(Missing = 8)		
None	6 (5.5)	3 (2.9)		
Primary school	93 (84.6)	90 (85.7)		Fisher's
Secondary school	11 (10.0)	12 (11.4)		0.631
<i>Mother's education</i>	(Missing = 4)	(Missing = 10)		
None	8 (8.2)	3 (2.9)		
Primary school	82 (83.7)	95 (92.2)		Fisher's
Secondary school	8 (8.2)	5 (4.9)		0.153
<i>Co-morbidity present</i>	(Missing = 0)	(Missing = 0)		
No	17 (15.2)	82 (72.6)		
Yes	95 (84.8)	31 (27.4)	67.428	0.001
<i>Cognitive impairment</i>	(Missing = 6)	(Missing = 4)		
No	32 (30.2)	93 (93.9)		
Yes	74 (69.8)	6 (6.1)	77.797	0.001
<i>Behavioural disorder</i>	(Missing = 9)	(Missing = 14)		
No	35 (34.1)	80 (80.8)		
Yes	68 (66.0)	19 (19.2)	46.195	0.001

Table 2

Anthropometric measures among cases and controls.

Variables	Cases (<i>n</i> = 112); <i>n</i> (%)	Controls (<i>n</i> = 113); <i>n</i> (%)	<i>p</i> -Value (Fisher's exact)
<i>Weight-for-age z-score</i>	(Missing = 2)	(Missing = 0)	
Normal	50 (45.4)	53 (46.9)	
Underweight	51 (46.4)	56 (49.6)	
Severely underweight	9 (8.2)	4 (3.5)	0.94
<i>Height-for-age z-score</i>	(Missing = 8)	(Missing = 3)	
Normal	62 (59.6)	67 (60.9)	
Stunted	35 (33.7)	41 (37.3)	
Severely stunted	7 (6.7)	2 (1.8)	0.29
<i>Mid-upper-arm circumference</i>	(Missing = 1)	(Missing = 0)	
Normal	110 (99.1)	113 (100.0)	
Acute malnutrition	1 (0.9)	0 (0.0)	0.47

Table 3

Linear regression of BMI to show associations amongst all children (cases and controls).

Variable	Levels	Univariate analysis		Multivariate analysis	
		Coefficient (95% CI)	p-Value	Coefficient (95% CI)	p-Value
Age	Per year of age	0.334 (0.225—0.444)	0.000	0.345 (0.234—0.454)	0.000
Sex	Female	1			
	Male	−0.370 (−0.921 to 0.180)	0.187	−0.398 (−0.907 to 0.112)	0.125
Tribe	Chagga	1			
	Other	−0.470 (−1.199 to 0.257)	0.204		
Religion	Other	1			
	Christian	0.934 (−0.622 to 0.809)	0.797		
Case status	Control	1			
	Case	0.418 (−0.133 to 0.969)	0.136	0.351 (−0.159 to 0.861)	0.177
Education of head of house	None	1			
	Primary/secondary	0.624 (−0.127 to 1.38)	0.103	0.732 (0.046—1.418)	0.037
Education of mother	None	1			
	Primary/secondary	−0.478 (−1.356 to 0.401)	0.285		
Parents resident at home	Both parents	1			
	One or no parents	0.160 (−0.276 to 0.598)	0.469		
Comorbidity present	None	1			
	One or more	0.151 (−0.405 to 0.707)	0.593		
Cognitive impairment	None	1			
	Present	0.102 (−0.485 to 0.690)	0.730		
Behaviour problems	None	1			
	Present	0.259 (−0.308 to 0.826)	0.369		
Motor difficulties	None	1			
	Present	−0.468 (−1.394 to 0.458)	0.320		

Table 4

Linear regression of BMI in children with epilepsy only.

Variable	Levels	Univariate analysis		Multivariate analysis	
		Coefficient (95% CI)	p-Value	Coefficient (95% CI)	p-Value
Age	Per year of age	0.483 (0.330—0.634)	0.000	0.421 (0.239—0.604)	0.000
Sex	Female	1			
	Male	−0.167 (−0.963 to 0.628)	0.676	−0.391 (−0.736 to 0.658)	0.911
Tribe	Chagga	1			
	Other	−0.403 (−1.329 to 0.521)	0.388		
Religion	Other	1			
	Christian	0.276 (−0.771 to 1.32)	0.602		
Education of head of house	None	1			
	Primary/secondary	0.391 (−0.649 to 1.431)	0.458	0.879 (−0.821 to 1.840)	0.073
Education of mother	None	1			
	Primary/secondary	−0.460 (−1.522 to 0.602)	0.392		
Parents resident at home	Both parents	1			
	One or no parents	0.175 (−0.386 to 0.736)	0.538		
Comorbidity present	None	1			
	One or more	−0.193 (−1.291 to 0.905)	0.728		
Cognitive impairment	None	1			
	Present	−0.515 (−1.394 to 0.365)	0.248		
Behaviour problems	None	1			
	Present	−0.161 (−1.031 to 0.710)	0.715		
Motor difficulties	None	1			
	Present	−0.801 (−1.776 to 0.174)	0.106	−0.560 (−1.482 to 0.362)	0.231
Feeding problems	None	1			
	Present	−1.187 (−4.000 to 1.627)	0.405		
Early onset seizures	No	1			
	Present	−1.06 (−1.836 to −0.300)	0.007	0.068 (−0.716 to 0.853)	0.863
Frequent seizures	No	1			
	Present	0.417 (−0.763 to 0.847)	0.918		
Antiepileptic drug use	None	1			
	Single/Multiple	0.323 (−0.978 to 0.743)	0.131	0.320 (−0.048 to 0.689)	0.087