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Link between Epilepsy and Malnutrition in a Rural Area of Benin

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Summary: *Purpose:* Epilepsy and malnutrition are both important public health problems in sub-Saharan Africa. A relationship between epilepsy and malnutrition has been suspected for many years. Our objective was to investigate the association between epilepsy and malnutrition in Djidja, Benin.

Methods: A matched population-based cross-sectional case–control survey was performed: cases (patients with epilepsy) were matched to controls according to sex, age ± 5 years, and village of residence. The World Health Organization's criteria for malnutrition was used. Anthropometric measurements (weight, height, mid arm upper circumference, triceps skinfold thickness) were taken. Bioelectrical impedance analysis, a standardized food and social questionnaire and a clinical examination were done. Statistical analysis (conditional logistic regression) was performed using SAS 8.0.

Results: A total of 131 cases and 262 controls were included. The prevalence of malnutrition was higher in cases than in controls (22.1% vs. 9.2%, p = 0.0006). Social factors were significantly different between cases and controls. Feeding difficulties were more frequent and health status was worse in cases. Seven variables were associated with epilepsy: (i) nutritional factors: mid arm upper circumference (prevalence odds ratio (pOR) = 0.7, CI: 0.6–0.9), cereal consumption <3 times during the 3 days before the study (pOR = 4.2, CI: 1.8–10.0), <3 meals/day (pOR = 4.2, CI: 1.6–10.9), tooth decay (pOR = 2.9, CI: 1.1–7.4), food taboos (pOR = 25.0, CI: 8.3–100.0), (ii) social factors: surrogate respondent (pOR = 16.8, CI: 3.1–90.3) and no second job (pOR = 7.1, CI: 2.3–22.3).

Conclusion: Epilepsy and nutritional status are linked in sub-Saharan Africa. Programs to improve the nutritional status of people with epilepsy are needed. **Key Words:** Epilepsy—Malnutrition—Sub-Saharan Africa—Benin—Developing countries.

Both epilepsy and malnutrition are important public health problems in sub-Saharan Africa with major medical, sociocultural, and economic implications (Meinardi et al., 2001; Preux and Druet-Cabanac, 2005; FAO, 2006). The prevalence of epilepsy is high in sub-Saharan Africa where it varies between 10 and 55 per 1,000 (Preux and Druet-Cabanac, 2005), whereas in industrialized countries, it is about 5–10 per 1,000 (Sander, 2003). In developed countries, about 5% of the population is underweight (Stratton et al., 2003). According to the Food and Agriculture Organization, one-third of the African population is underfed (FAO, 2006). A relationship between epilepsy and malnutrition in developing countries has been suspected for many years (Hackett et al., 1997; Pal et al, 1998; Hackett and Iype, 2001; Birbeck and Kalichi, 2003; Nkwetngam Ndam, 2004; Preux and Druet-Cabanac, 2005). Malnutrition may contribute to the high prevalence of epilepsy in such countries via several mechanisms (Hackett and Iype, 2001). However, because of attitudes toward epilepsy and food taboos in sub-Saharan Africa, epilepsy may also contribute to malnutrition (Dike, 1999). Nevertheless, the few attempts to find a link between epilepsy and malnutrition in developing countries have resulted in inconsistent data (Hackett et al., 1997; Pal et al, 1998; Hackett and Iype, 2001; Nkwetngam Ndam, 2004). The objective of the present study is to establish whether such a link exists in a rural area of Benin.

SUBJECTS AND METHODS

Study design

The study took place in Benin, in West Africa, during February and March 2005 and was conducted in the rural city of Djidja Centre (composed of 11 villages within an area of 160 km^2) about 150 km from Cotonou (capital of the country).

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Before beginning the study, approval of the Ministry of Health of Benin, the body responsible for ethical advice in the absence of an official ethics committee, was obtained. Firstly, a door-to-door survey, using the validated Questionnaire of Investigation of Epilepsy in Tropical Countries (Preux, 2000; Diagana et al., 2006), was carried out in all 11 villages of Djidja Centre to find subjects with epilepsy. Figures from the last census performed in 2002, were used to estimate the proportion of people screened in the study area. This phase was performed by local physicians. All of them received basic training in the detection of epilepsy. This training was provided over 2 days by a neurologist from the Department of Neurology of the University Hospital of Cotonou (Benin). Patients who had at least one positive response to the questionnaire were then interviewed by a neurologist who either confirmed or rejected the diagnosis of epilepsy. Final diagnosis was based on the history and a witness's account of the suspected seizures.

Secondly, a matched cross-sectional case–control study was performed using both the cases confirmed during the door-to-door survey and the controls.

Cases and controls

Cases were people with epilepsy and controls were people without epilepsy. The definition of epilepsy was based on the occurrence of at least two seizures in more than 24 h, as recommended by the International League Against Epilepsy (ILAE) (Commission on Epidemiology and Prognosis of the ILAE, 1993). All types of seizures were included. The exposure factor studied was malnutrition. It was defined as recommended by the World Health Organization (WHO, 1995): body mass index (BMI) $<$ 18.5 kg/m^2 for adults ($>$19 years old), BMI for age *z*-score $<$–2 *z*-score for adolescent (10–19 years old) and weight for height *z*-score or height for age *z*-score $<$–2 *z*-score for children ($<$10 years old). For both children and adolescents, we used the National Centre for Health Stat/WHO reference (Hamill et al., 1979), which is still recommended by WHO for developing countries. *z*-scores were calculated using Epi-info 2000 (Centre for Diseases Control and Prevention, Atlanta, CA). BMI, body mass index for age, weight for height *z*-score, and height for age *z*-score were then used to define the binary variable "malnutrition" that was used in the analysis. Clinical investigations and a food and social questionnaire were performed for both cases and controls.

People with epilepsy were immediately included in this study once epilepsy had been confirmed. No potential cases refused to participate in the investigation. Controls were matched with cases based on sex, age ($\pm$ 5 years) and village of residence. The chiefs of the 11 villages were involved in this process. They suggested possible controls according to the matching criteria (at least four eligible controls for each case). Then, after allocating a number to each eligible control, one investigator (SC) randomly selected the controls for each case among them. Inclusion criteria for both cases and controls, specified they were to live in Djidja Centre, to have participated in the door-to-door survey, and not being pregnant. After being thoroughly informed of its purposes, requirements, and procedures, all subjects gave their consent to participate in the study.

Measurements

In order to avoid interoperator variability, only one trained operator (SC) using standard procedures (Lohman et al., 1996) performed anthropometric measurements, bioelectrical impedance analysis, clinical examination, and the food and social questionnaire for both cases and controls.

Anthropometric measurements

Wearing minimal clothing, the subjects were weighed to the nearest 0.1 kg with a mechanical scale (Seca 220, Seca, Hamburg, Germany), which was set at zero before each measurement. Height was measured to the nearest millimeter (Seca). Arm circumference (right arm at mid distance between acromion and olecranon with the arm bent) was measured with a tape that recorded millimeters. Additionally, we used a Lange caliper to measure triceps skinfold thickness on the right side of the body according to standard methods (Zillikens and Conway, 1991). Triceps skinfold thickness was measured three times in succession, and the retained value represented an average of the three measurements (WHO). Mid arm upper circumference was calculated from triceps skinfold thickness and arm circumference (Gurney and Jelliffe, 1973).

Bioelectrical impedance analysis

Bioelectrical impedance analysis (BIA) was performed on the two sides of the body using a body composition analyzer (50 kHz, BIA 101 RJL System, Eugédia, Chambly, France) with a four-electrode arrangement in a supine position. The stuck electrodes were paired, one pair acting as current electrodes and the other pair acting as detector electrodes. The electrodes were placed on the hand, wrist, foot, and ankle of each subject according to the standard placement for adults stated in the manufacturer's guidelines. At each site, the skin was cleaned with alcohol before the electrodes were placed. Only resistance (Rx) and reactance (Xc) data at 50 kHz was used in the calculation of the present study. The retained values represented an average measurement of both sides. Total body water was calculated using the Zillinkens and Conway equation (Zillikens and Conway, 1991)

$$\text{Total body water} = -9.212 + 0.576 \times (\text{height}^2/\text{Rx}) + 0.128\text{Xc} + 0.017 \times \text{weight}$$

Height was measured in centimeters and weight in kilograms. This equation allows the estimation of total body water. Assuming a constant hydration of the fat-free mass (FFM) at 74% (Clasey et al., 1999), we estimated it using the formula FFM = TBW/0.74. Because of a lack of validated equations for African children and adolescents, we performed BIA in adults only (Zillikens and Conway, 1991; Dioum et al., 2005). The results of the BIA were only used as descriptive data.

Social and food questionnaire

Cases and their matched controls were interviewed using a standardized questionnaire. The questionnaire assessed social data such as occupation (the existence of a second job, very frequent in Benin, was recorded), marital status, education, and included a food questionnaire (a 3-day dietary recall). This questionnaire also explored the different food items in Benin, alimentary difficulties and food taboos, which are important in sub-Saharan Africa. It was also noted if a surrogate respondent answered, which sometimes occurs in an African context when studying epilepsy (Ndour et al, 2004; Nkwetngam Ndam, 2004).

Clinical examination

A physician did a clinical examination in order to look for clinical signs that are frequently associated with malnutrition such as oedema, hair depigmentation, dry skin, and to estimate the dental state (Melchior, 2001).

Statistical analysis

Statistical analysis was performed using SAS System for Windows (release 8.0; SAS Institute, Inc., Cary, NC). Results for quantitative variables were expressed as means ± standard deviation (SD), and results for qualitative variables, as percentages. Univariate conditional logistic regression was applied. Variables that had a $p \leq 0.10$ in the univariate analysis were included in a multivariate regression model. Multivariate conditional logistic regression was fitted using status (case or control) as the dependent variable and malnutrition, anthropometric, nutritional, clinical, and social data as independent variables (Hosmer and Lemeshow, 1989). We then used a step-by-step descending procedure. At each step a nonsignificant variable was removed. The choice was based on the higher p-value in the model. Before continuing the procedure, we examined the modification of the coefficients of the other variables to rule out possible confusion. The level of significance was fixed at 0.05 for all the statistical analysis and the final multivariate model.

RESULTS

Sociodemographic data

A total of 11,668 individuals (94% of the population in the area) were screened for epilepsy. The neurological evaluation confirmed 148 people with epilepsy (prevalence of epilepsy: 12.7%; 95% CI: 10.8 – 14.8). This study included 131 people with epilepsy and 262 controls. The other 17 people with epilepsy were excluded because of pregnancy (an exclusion criteria). The male/female ratio was 1.05. The mean age of subjects with epilepsy was 25.4 ± 16.2 years (range: minimum 1 year; maximum 75 years). The mean age of controls was 25.5 ± 16.6 years (1–80 years). For cases, 17% were children (22), 18% adolescents (24), and 65% adults (85). For controls, there were 15% children (39), 24% adolescents (64), and 61% adults (159). Social characteristics are shown in Table 1.

Neurological data

Most subjects with epilepsy had generalized tonic–clonic epilepsy. All, but one, had had at least one seizure during the last 5 years (active epilepsy). A certain degree of neurological impairment (abnormal mild neurological signs, cognitive impairment) was found in 26% of the subjects. Almost 82% had had their first seizure before the age of 20. Only 42% took antiepileptic treatment at the time of the study (54% of cases were on phenobarbitone, 39% on traditional treatment, and 7% on both traditional and modern treatment). The median number of seizures per year was 12 (Table 2).

Nutritional data

Baseline characteristics are shown in Table 3. Malnutrition was more prevalent in cases than in controls: 22.1% of the cases were malnourished versus 9.2% of the controls ($p = 0.0006$). The crude pOR for malnutrition was 2.9 (95% CI: 1.6–7.4). In adults, 23.5% of cases (20) and 6.9% of controls (11) had BMI < 18.5 kg/m^2 ($p = 0.0012$). In adolescents, only six (6/24) had BMI for age <–2Z and all were cases ($p = 0.01$). In children, 13.6% of the cases (n = 3) versus 30.8% (n = 12) of the controls were

TABLE 1. *Sociodemographic data of the subjects, Benin, 2005*

	Cases (%)	Controls (%)	p
Ethnic group: Fon[a]	90.1	94.7	0.13
Religion: Christian	48.5	52.5	0.55
Married	36.9	54.0	<0.0001
Illiteracy	74.0	58.0	0.0020
Surrogate respondent	28.2	14.5	0.0003
Occupation: none	37.4	22.6	0.0050
Second job	8.4	25.6	<0.0001
Alcohol consumption	9.9	21.4	0.0015
Tobacco consumption	8.4	6.1	0.38

[a]Fon is the major ethnic group in Benin.

TABLE 2. *Type of seizures of the cases, Benin, 2005*

Type of seizure	People with epilepsy n	%
Tonic–clonic seizure	92	70.2
Myoclonic seizure	3	2.3
Atonic seizure	2	1.5
Absence seizure	7	5.3
Other type of generalized seizures	2	1.5
Focal seizure	6	4.6
Focal seizure with secondary generalization	9	6.9
Unclassified seizure	2	1.5
Status epilepticus	4	3.1
Multiple seizures	4	3.1

malnourished (nonsignificant). Height for age *z*-score and weight for height *z*-score were not statistically different between cases and controls in children. In adults, significant differences were found between cases and controls in total body water, FFM, and fat mass (Table 3).

Results from statistical comparisons between cases and controls for the different factors studied are summarized in Table 5. In the 3 days before the survey, cases ate significantly less: tubers (61.8% [81] vs. 74.4% [195]), leguminous plants (55.7% [73] vs. 67.6% [177]), meat/fish (80.9% [106] vs. 89.3% [234]), and sweets (34.4% [45] vs. 47.0% [123]). Cases also ate less often than controls (<3 meals/day: pOR = 2.5, 95%CI: 1.5–4.3). Alimentary difficulties (difficulties to eat enough) were more frequent in cases than in controls (p = 0.02). In addition, cases had more food taboos than controls (55.8% [n = 73] vs. 13.8% [n = 36], p = 0.0001). Consumption of boiled meat and/or "gummy sauces" was forbidden for 85% of the cases who had food taboos. The people with epilepsy believed that disobedience to their food taboos could lead to the occurrence of seizures. In controls, food taboos varied and were usually linked to religion. There were no significant differences between malnourished people with epilepsy and nonmalnourished people with epilepsy with regard to neurological data (Table 4).

Among the cases, those who had tonic–clonic seizures had more food taboos (80.3% vs. 53.9%, p = 0.009). No significant difference in the prevalence of food taboos was found between malnourished people with epilepsy and nonmalnourished people with epilepsy (56.4% vs. 53.6%). People with epilepsy and on treatment were found to have more food taboos (52.1% vs. 29.1%, p = 0.0094). People with epilepsy who had their first seizure before the age of 20 also had more food taboos (60.3% vs. 26.1%, p = 0.0015).

Clinical examination

Four clinical signs, frequently associated with malnutrition, were statistically more frequently observed in cases than in controls: hair depigmentation (19.2% for cases vs. 10.0% for controls; p = 0.01), curly hair (25.2% vs. 11.5%; p = 0.0007), dry skin (25.9% vs. 11.9%; p = 0.0004), and tooth decay (62.3% vs. 48.8%; p = 0.003).

Multivariate statistical analysis

Seven factors were linked to epilepsy: mid arm upper circumference, cereal consumption <3 times during the 3 days before the study, <3 meals/day, tooth decay, food taboos, surrogate respondent and not having a second job. The adjusted pOR are shown in Table 5.

DISCUSSION

Epilepsy and malnutrition represent two major health problems in Benin because of their serious medical, social, cultural, and economic implications (Meinardi et al., 2001; Preux and Druet-Cabanac, 2005; FAO, 2006). This study underlines a relationship between epilepsy and nutritional status.

The minimum estimated number of subjects was 155 cases and 465 controls. This number of cases was not achieved because of a lower prevalence of epilepsy than expected. The number of controls was not achieved because of logistical problems during the study, in particular lack of time and lack of staff. It was then decided to reduce the number of controls to two for each case. However in the end, the study achieved sufficient power due to a

TABLE 3. *Anthropometric and bioelectrical impedance analysis measurements of the subjects, Benin, 2005*

	Cases (m ± SD)	Controls (m ± SD)	p
Adults: BMI[a] (kg/m^2)	20.4 ± 2.8	21.8 ± 2.7	0.0020
Adolescents: BMIFA[b] (Z-score)	–1.3 ± 1.2	–0.5 ± 0.8	0.0100
Tricipital skinfold (mm)	8.9 ± 4.6	9.7 ± 5.4	0.0390
Mid arm upper circumference (cm)	20.4 ± 4.9	21.9 ± 4.6	<0.0001
Total body water[c]	30.6 ± 6.3	33.1 ± 6.0	0.0001
Fat-free mass[c]	41.4 ± 8.6	44.7 ± 8.1	0.0001
Fat mass[c]	10.9 ± 5.7	12.4 ± 5.3	0.0220
Children (*z*-score): HAZ[d]	–0.68[e] (q1 = –1.45; q3 = –0.17)	–1.03[e] (q1 = –1.56; q3 = –0.41)	0.81
WHZ[f]	–1.06[e] (q1 = –1.6; q3 = –0.15)	–0.81[e] (q1 = –2.1; q3 = 0.60	0.47

[a]Body-mass index; [b]body-mass index for age; [c]only in adults; [d]height-for-age *z*-score; [e]median: first and third quartile; [f]weight-for-age *z*-score.

TABLE 4. *Comparisons of neurological data between malnourished people with epilepsy (PWE) and not malnourished PWE, Benin, 2005*

	Malnourished people with epilepsy (%)	Not malnourished people with epilepsy (%)	p (chi^2 test)
Age at onset			0.47
≤20 years	86.2	80.4	
>20 years	13.8	19.6	
Type of seizure			
Tonic–clonic seizure	67.9	71.3	0.73
Other generalized seizure	7.1	10.2	0.63
Focal seizure	10.7	4.9	0.26
Focal seizure with secondary generalization	10.7	8.9	0.77
Status epilepticus	3.6	4.7	1.00
Antiepileptic treatment			0.18
None	64.3	58.8	
Modern treatment	28.6	19.7	
Traditional or combined (modern and traditional) treatment	7.1	21.5	

higher than expected malnutrition prevalence odds ratio. In fact, malnutrition was found to be significantly more frequent in people with epilepsy than in controls in Djidja Centre (crude pOR = 2.9; 95%CI: 1.6–7.4).

One of the strengths of this study is the use of a population-based sample because, in this kind of population (rural sub-Saharan people), access to medical services is often limited by the fact that cases prefer to rely on traditional healers (Danesi and Adetunji, 1994). Although concealment is likely in an unsolicited survey due to stigmatization, none of the people with epilepsy refused to participate. Only two randomly selected controls refused to participate and were replaced. A selection bias in the control group compared to the general population is unlikely: variables such as ethnic groups and religion were not significantly different in controls from the rest of the population. Potentially confusing factors were controlled by matching cases and controls based on age, sex, and village of residence. These factors could affect nutritional status: age and sex can influence the nutritional status of subjects in developing countries and as the different villages are far from each other the feeding habits could be different (FAO, 1996; Nube and Van Den Boom, 2003; Kherwaja et al., 2005; Quet, 2005). In addition, some epilepsy risk factors linked to poor sanitary conditions such as cysticercosis could be partially controlled (Preux and Druet-Cabanac, 2005) by residence matching. Because of difficulties (such as a lack of a census with names) inherent in rural areas of developing countries, a formal random selection among all potential controls was not possible. This is a potential limitation in our study even though we tried to select controls as randomly as possible.

Only one trained operator performed measurements, avoiding interoperator variability. Blindness against case or control status was not done; which could result in a differential measurement according to case or control status. However, we think that a bias, if it exists, is limited because of validated quantitative data measurements being done by only one investigator.

Because problems relating to malnutrition might be secondary to feeding difficulties due to cerebral palsy, cognitive impairment, head injuries, or a history of cerebral malaria, it would have been interesting to take these comorbidities into account. A neurological impairment was found in 26% of the cases, but this has probably not influenced the results as most had benign or mild troubles that could not impacted on their nutrition.

In developing African countries, people with epilepsy are often stigmatized (Jilek-Aall et al., 1979; Bernet-Bernady et al., 1997; Traore et al., 1998; Birbeck and Kalichi, 2003; Nubukpo et al., 2003; Ndour et al, 2004). Because of social constraints, people with epilepsy could sometimes not answer surveys directly. In our survey, the intervention of a surrogate respondent was more frequent in cases than in controls. This could possibly have led to a social desirability bias (because of social burden). Analysis into the group of cases showed that subgroups of people with epilepsy could be more stigmatized and had an increased risk of being malnourished (people with epilepsy with tonic–clonic seizures, people with epilepsy on treatment, etc.).

The food questionnaire could have been subject to a recollection bias. We tried to reduce the impact of this bias by using different formulations and indirect questions in the sociodemographic and food questionnaire. This allowed verification of the answers. Moreover, we think that a 3-day recollection also limited any bias.

We found an association between epilepsy and nutritional status but no inference can be made about the direction of this association because of the study design (cross-sectional study sampling on prevalent epilepsy status and correlating with prevalent malnutrition).

On one hand, malnutrition may contribute to the high prevalence of epilepsy in such countries (Hackett and Iype, 2001). There are several hypotheses about the possible mechanisms involved like the reduction of the seizure threshold or an immunological vulnerability (Smith et al., 1974; Bennish et al., 1990; Andrade and Paula-Barbosa, 1996; Chandra, 1997; Bushinsky and Monk, 1998; Kumar and Berl, 1998). Biochemical variations due to malnutrition like electrolyte abnormalities and hypoglycemia could affect seizure threshold (Bennish et al., 1990; Bushinsky and Monk, 1998; Kumar and Berl, 1998). A decreased availability of inhibitory amino acid neurotransmitters in the brain combined with a low dietary intake of amino acids or precursors (Smith et al., 1974) and hippocampal damage associated with low protein diet are also

TABLE 5. *Factors linked to epilepsy in univariate and multivariate analysis, Benin, 2005*

	Number of subjects		Univariate analysis		Multivariate analysis		
Factors	Cases	Controls	Crude prevalence odds ratio	p	Adjusted prevalence odds ratio	p	95% CI
Sociodemographic factors							
Surrogate respondent yes/no	131	262	7.6	0.0003	16.8	0.001	3.1–90.3
Ethnic group: Fon/others	131	262	1.4	0.13			
Religion: Christian or Muslim/animist	131	262	0.9	0.55			
Marital status							
Live with parents/being married	131	262	4.2	0.0002			
Live alone/being married	131	262	7.9	0.004			
Education status							
Primary school/illiterate	131	262	0.4	0.001			
Secondary school/illiterate	131	262	0.5	0.2			
Occupation:	131	262					
Shopkeeper, salaried employee, artisan/farmer			0.9	0.72			
Pupil, student/farmer			0.4	0.40			
Other occupation/farmer			0.5	0.26			
None/farmer			3.2	0.02			
Second job: yes/no	131	262	0.2	<0.0001	0.1	0.0008	0.04–0.4
Tobacco: yes/no	131	261	1.5	0.38			
Alcohol: yes/no	131	262	0.3	0.0015			
Anthropometric factors							
Malnutrition: yes/no	131	262	2.9	0.006			
Skinfold thickness	131	262	0.9	0.039			
Mid arm upper circumference	131	262	0.7	<0.0001	0.7	0.002	0.6–0.9
Nutritional factors							
Alimentary difficulties: yes/no	129	260	2.0	0.02			
Consumption of all type of food: yes/no	129	262	0.2	<0.0001			
Food taboos: yes/no	130	262	7.1	0.0001	25.0	<0.0001	8.3–100.0
Number of meals/day: <3 per day/≥3 per day	131	262	2.5	0.0005	4.2	0.0037	1.6–10.9
Meal taken with family: yes/no	131	262	0.5	0.35			
Meal portion different from the rest of family: yes/no	131	262	1.9	0.07			
Varied feeding: yes/no	131	262	1.4	0.19			
Consumption of milk-based product: yes/no	129	262	1.3	0.32			
Fruits: yes/no	131	262	0.7	0.12			
Vegetables: yes/no	131	262	0.8	0.49			
Cereals: <3 times during the 3 days before the study/≥ 3 times during the 3 days before the study	131	262	2.0	0.015	4.2	0.001	1.8–10.0
Tubers: yes/no	131	262	0.6	0.01			
Leguminous plants: yes/no	131	261	0.6	0.03			
Oleaginous plant: yes/no	131	262	0.9	0.64			
Meat/fish: yes/no	131	262	0.5	0.02			
Eggs: yes/no	131	262	1.3	0.45			
Sweets: yes/no	131	262	0.6	0.02			
Clinical signs of malnutrition							
General health status	131	262					
Correct/good			2.7	0.012			
Bad/good			5.0	0.026			
Hair depigmentation: yes/no	131	262	2.3	0.01			
Curly hair: yes/no	130	262	2.6	0.0007			
Conjunctive pallor: yes/no	131	260	1.3	0.61			
Glossitis: yes/no	131	262	0.8	0.79			
Cheilitis: yes/no	131	262	2.0	0.17			
Gum bleeding: yes/no	131	262	0.9	0.57			
Tooth decay: yes/no	130	262	2.2	0.003	2.9	0.028	1.1–7.4
Gingival hypertrophy: yes/no	131	262	1.0	0.86			
Dry skin: yes/no	131	262	2.8	0.0004			
Leg edema: yes/no	130	262	0.6	0.68			
Curved legs: yes/no	130	262	1.4	0.57			

suspected (Kumar and Berl, 1998). Studies show that malnutrition reduces resistance to infection (Chandra, 1997); this can make malnourished people more vulnerable to a range of infections including neurotropic infections that cause epilepsy and which are prevalent in developing countries (Preux and Druet-Cabanac, 2005).

On the other hand, because of attitudes toward epilepsy in sub-Saharan Africa, epilepsy may also contribute to malnutrition. Dike (1999) suggests that in children with epilepsy, a neurological disorder may impair the children's ability to feed or they could be the victims of a "conscious selective neglect." Epilepsy imposes a social and cultural burden, with a high stigma (Jilek-Aall et al., 1979; Bernet-Bernady et al., 1997; Traore et al., 1998; Birbeck and Kalichi, 2003; Nubukpo et al., 2003). People with epilepsy, in sub-Saharan Africa, often have a lot of food taboos. Nubukpo et al. (2003) show that 64% of people with epilepsy from Benin and 44% of people with epilepsy from Togo had food taboos. These customs could be responsible for nutritional deficiencies.

As we only found a difference in the prevalence of malnutrition between people with epilepsy and controls in adults and adolescents, one might consider epilepsy a more probable risk factor for malnutrition. However, the low number of children could also explain this result as there was far more malnutrition in control children than in cases, albeit this difference was not statistically significant. The best design for the study would have been a cohort study in order to test one direction of the hypothesis (malnutrition as the exposure factor or epilepsy as the exposure factor) but this kind of study is very difficult to carry out in a developing country where there is a lack of good quality medical records measuring past exposure, which would be necessary to perform such a real case–control study (furthermore people with epilepsy do not usually go through the modern medical system in Africa).

It is difficult to establish the link between epilepsy and malnutrition in developing countries because although a few studies on this relationship have been published, conflicting methodologies, and conclusions have engendered disagreement on the direction of this link (Hackett et al., 1997; Pal et al., 1998, Nkwetngam Ndam, 2004).

Two out of the three studies did not use WHO criteria to define malnutrition and contrary to our study, the definition used for epilepsy was sometimes different from the ILAE definition. The number of controls and the way of selection were also not clearly described. Hackett et al. (1997) found a significant difference in mean BMI in a sample of Indian children aged between 8 and 12. The mean BMI of children with active epilepsy was lower than other children (13.2 ± 1.9 vs. 14.0 ± 1.7 kg/m^2) ($p = 0.02$). The adjusted OR was 0.75 per unit of BMI ($p = 0.01$). The second Indian study included children and adolescents from 2 to 18 years (Pal et al., 1998). The design was a case–control study including 61 people with epilepsy and 59 controls. No link between BMI and epilepsy was found (adjusted OR = 31.3 95% CI = 0.8–1203.0), but this study was clearly subject to a lack of power due to the small number of participants as was a third survey conducted in the same area as our study (Djidja, Benin) with only 39 people with epilepsy and 39 controls (Nkwetngam Ndam, 2004).

In a database consolidating results from 13 epidemiologic studies on epilepsy in sub-Saharan Africa, Quet (2005) found a prevalence of malnutrition of 25.4% in people with epilepsy (257/1013 people with epilepsy). This prevalence is similar to ours (22.1%). The prevalence of malnutrition in the control group (9.2%) was lower than that provided by FAO in Benin for underfeeding: 15% (FAO, 2006). These data are however hardly comparable because of the difference between definitions of malnutrition and underfeeding (dietary intakes <2,100 kcal/day according to FAO). Moreover, nutritional status, specifically in rural areas, usually depends on seasons (lean and postharvest season) and as sub-Saharan Africa nutritional assessment studies are usually done on young children, comparisons with other data are difficult.

In conclusion, although our results support the hypothesis that epilepsy and nutritional status are associated in Benin, additional differently designed studies, such as a cohort study, need to be done to further clarify the direction of this association. Moreover, our results suggest that it is important to pay attention to the nutritional status of people with epilepsy and to implement global programs to fight against this condition taking into account nutritional factors.

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