The quality of the diet in Malawian children with kwashiorkor and marasmus

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Abstract

Nutritionists have suggested that kwashiorkor is related to low dietary protein and/or antioxidant intake. This study explored the hypothesis that among Malawian children with severe malnutrition, those with kwashiorkor consume a diet with less micronutrient- and antioxidant-rich foods, such as fish, eggs, tomatoes and orange fruits (mango, pumpkin and papaya), than those with marasmus. A case-control method with a food frequency questionnaire was used to assess the habitual diet. Children with severe childhood malnutrition presenting to the central hospital in Blantyre, Malawi during a 3-month period in 2001 were eligible to participate. The food frequency questionnaire collected data about foods consumed by siblings <60 months of age in the home. It was assumed that the habitual diet of all siblings 1–5 years old in the same home was similar. Dietary diversity was assessed using a validated method, with scores that ranged from 0 to 7. Regression modelling was used to control for demographic and disease covariates. A total of 145 children with kwashiorkor and 46 with marasmus were enrolled. Children with kwashiorkor consumed less egg and tomato than those with marasmus: 17 (15) vs. 24 (31) servings per month for egg, mean (SD), $P < 0.01$ and 27 (17) vs. 32 (19) servings per month for tomato, $P < 0.05$. Children with kwashiorkor had a similar dietary diversity score as those with marasmus, 5.06 (0.99) vs. 5.02 (1.10), mean (SD). Further research is needed to determine what role consumption of egg and tomato may play in the development of kwashiorkor.

Keywords: malnutrition, kwashiorkor, diet.

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Severe childhood malnutrition is manifest by one of two distinct clinical syndromes: kwashiorkor (including marasmic-kwashiorkor), which is defined by the presence of oedema, and marasmus which is characterized by wasting. Traditionally, nutritionists have

hypothesized that kwashiorkor develops in conjunction with dietary protein deficiency (Waterlow 1984). This hypothesis has been challenged by data showing that oedema resolves long before any change in serum albumin concentration occurs (Golden *et al.* 1980), children with kwashiorkor do not ingest any less protein on average than those without kwashiorkor (Gopalan 1968), and oedema dissipates while being fed a very low protein diet (Golden 1982).

Alternatively, it has been proposed that kwashiorkor results from an imbalance between the production of free radicals and their safe disposal, and that relative dietary deficiency of antioxidants plays a role in the development of kwashiorkor (Golden & Ramdath 1987). This hypothesis is supported by the observation that in Nigeria, serum concentrations of vitamin E derivatives were lower in children with kwashiorkor than in marasmic or well-nourished children (Becker *et al.* 1994). The amount and synthesis rate of glutathione, the principal intracellular antioxidant, was less in Jamaican children with kwashiorkor than in marasmus or well-nourished children, which suggests that dietary intake of sulphur-containing amino acids may be related to the development of kwashiorkor (Badaloo *et al.* 2002). In addition, red blood cell selenium dependent antioxidant enzyme concentrations were lower in South African children with kwashiorkor when compared with those with marasmus (Sive *et al.* 1993). However, a large prospective randomized, double-blind placebo controlled trial of supplementation with vitamin E, n-acetyl cysteine, and selenium did not prevent kwashiorkor in a vulnerable population of children (Ciliberto *et al.* 2005). The aetiology of kwashiorkor and its relationship to dietary quality remains an enigma.

Dietary surveys among malnourished children comparing marasmus and kwashiorkor have not been reported, presumably because of the difficulty in assessing the habitual diet of a child after he/she presents to a healthcare facility for treatment. This study explored the hypothesis that among Malawian children with severe malnutrition, those with kwashiorkor consume a diet with less micronutrient- and antioxidant-rich foods, such as fish, eggs, tomatoes and orange fruits (mango, pumpkin and papaya), than those with marasmus.

Methods

Participants

The study was conducted with children and their caretakers presenting for treatment of marasmus or kwashiorkor at the Queen Elizabeth Central Hospital in Blantyre, Malawi from February 2001 to May 2001. Eligible caretakers had a child with either clinical kwashiorkor (including marasmic-kwashiorkor), defined by oedema, irritability, anorexia and dermatosis; or marasmus, defined as a weight-for-age <60% of the National Center for Health Statistics (NCHS) standard (Wellcome Trust Working Party 1970). These caretakers were housed in the same ward and received the same nutrition counselling during their child's hospitalization. In addition to having a child with severe malnutrition, to be eligible, caretakers must also have had a healthy child older than the malnourished child who was <60 months of age; caretakers of children where the firstborn was being treated for malnutrition or all older siblings had died were not eligible. The caretakers gave their informed consent to participate. The study was approved by the College of Medicine Research Committee of the University of Malawi and the Human Studies Committee of Washington University in St Louis.

Study design

This was a case-control study, where children with kwashiorkor were cases and those with marasmus were controls, conducted in the population of children presenting with severe malnutrition during a 3-month period. Their habitual diet was assessed using a 47-item food frequency questionnaire administered to caretakers 4 weeks after therapy was initiated. We chose to survey the diets of siblings in the home as an indirect way of assessing the diet of the malnourished child, in an effort to control for methodological problems and bias present in more direct assessment methods. If ill, severely malnourished children are surveyed upon admission to the hospital, most caretakers report the child has been anorexic and has consumed very little food of any kind. A minority of caretakers report that their malnourished child has been eating very generous quantities of healthy food,

which seems unlikely given his/her clinical state. Surveying caretakers about dietary consumption of the malnourished child 1 month prior to admission is unreliable because their recall after 1 month is likely to be poor. The treatment of severe malnutrition involves therapeutic feeding, so dietary surveys of the malnourished child after therapy has begun are likely to reflect these interventions, not the habitual diet which led to malnutrition.

The study was conducted during the pre-harvest rainy season in Malawi, when most cases of severe malnutrition occur. In general, fruits and vegetables are more available during this season than other times of the year. During the 4-month period when the surveys were conducted and the children developed malnutrition, the availability of different foods did not vary much.

Upon admission to the hospital, weight, length and mid-upper arm circumference were measured using standard methods (WHO 1995). Information about family size, marital, educational and employment status of parents, physical structure of the house, source of water and ownership of radios/bicycles was collected using a questionnaire.

The primary outcomes for the study were the servings consumed of fish, eggs, tomatoes and orange fruits by children with kwashiorkor and marasmus. These foods were chosen because they had the greatest micronutrient and antioxidant content among those identified through the focus group discussions. The secondary outcome was the dietary diversity of the two groups of severely malnourished children.

The estimated sample size was 200 children. It was assumed that 75% of malnourished children presenting to this unit would have kwashiorkor, based on previous survey data. The sample size was chosen to detect differences in intakes of fish, eggs, tomatoes, papaya, mango and pumpkin of 20% between the two groups with 95% sensitivity and 80% power, assuming that the SD of the intake frequencies would be one-half the mean, and that demographic and clinical status of the two groups would not be significantly different. In making this sample size estimation, we understood that the demographic and clinical status of the two groups were likely to be different, but we

did not have an estimate as to the magnitude of the effect of these factors in the regression modelling.

Food frequency questionnaires

Prior to the enrolment of participants, 47 foods were identified as principal constituents of the diet by mothers of children hospitalized for severe malnutrition at the Queen Elizabeth Central Hospital. These foods were identified during standardized focus group discussions designed to ascertain this information (Greenwood & Parsons 2000; Parsons & Greenwood 2000; Mansell *et al.* 2004). A total of 75% of the mothers who participated in the focus groups had a child with kwashiorkor, a similar fraction to the study population. The diet of rural Malawians is monotonous and maize-based diet, devoid of processed foods. About 50% of the dietary energy is derived from maize, and animal-derived foods constitute a very small part of the diet (Ferguson *et al.* 1995; Hotz & Gibson 2001).

The food frequency questionnaire asked how often the older sibling closest in age to the malnourished child consumed each of the 47 foods over the last 2 months. There were nine possible food frequency answers for each food: 1, 2 or 3 times per day; 1, 2 or 3 times per week; or 0, 1 or 2 times per month. In addition to the food frequency information, the age and sex of the older child surveyed was determined.

Dietary diversity score

Dietary diversity was assessed using a standard 7-point score, which categorizes foods into the following groups: starchy staples, legumes, dairy, meat–fish–eggs, vitamin A-rich foods, other fruits and vegetables and foods rich in fats (Arimond & Ruel 2004). Each subject receives a score from 0 to 7, with 7 indicating the greatest dietary diversity. This has been used and validated extensively in the developing world. Each of the 47 foods identified in this study was categorized into one of the seven groups. The score for each category was determined by adding servings per day of each food in the category. Thus the score for each category ranged from 0 to over 20, with the number representing the estimated number of servings per

day in that category. All category scores that were greater than 1, were reduced to 1. The sum of all seven categories was the child's dietary diversity score.

Data analyses

The demographic and anthropometric characteristics of the children with kwashiorkor and marasmus were summarized and expressed as mean (SD) for continuous characteristics and number (%) for dichotomous characteristics. The food frequency data were expressed as servings per month (25 percentile, 75 percentile). Comparisons were made using the Wilcoxon rank sum test for continuous characteristics and by chi-squared test for dichotomous characteristics. All statistical analyses for this study were performed with SPSS 13.0 for Windows (SPSS Inc., Chicago, IL, USA).

Nine of the foods were different forms of cooked maize; these foods were considered as a single food item. Six of the foods were cooked leaves, such as sweet potato leaf, cassava leaf and turnaposi (Swiss chard), which are consumed in very small quantities and have similar nutrient compositions; these were also considered as a single food. Therefore the original 47 food items were collapsed into 34 foods prior to analyses. Nutrient composition of cooked maize foods and cooked leaves was assessed using local food tables developed during a previous study (Hotz & Gibson 2001).

A binary logistic regression model was created using the enter mode to predict the type of malnutrition (kwashiorkor or marasmus) and included the four most significant demographic, clinical or anthropometric characteristics and 15 different foods, expressed as servings per month. The number of foods included in the model was based on the sample size and the standard statistical guideline that there should be at least 10 subjects for every term included in the regression model (Neter *et al.* 1996). All foods included in the model were those consumed by at least 20% of those children surveyed, because the paucity of data provided by infrequently consumed foods was unlikely to identify meaningful associations in regression modelling. The predictive value of the

model was determined by the Cox and Snell correlation coefficient r (Neter *et al.* 1996). Foods excluded from the regression model were those that were consumed with a similar frequency by children in families with kwashiorkor or marasmus (mean servings per month differed by <10%) and were not particularly rich in protein or micronutrients. A $P < 0.05$ of any food term in the model was considered to be significant.

Dietary diversity scores were tabulated. The total dietary diversity score, and the mean score in each of the seven categories were compared using Student's t -test.

Results

Data from 191 food frequency questionnaires were collected: 46 from caretakers with marasmic children and 145 from those with children with kwashiorkor; a total of 239 eligible children were hospitalized during the study period. Table 1 describes the demographic and anthropometric characteristics of the malnourished children.

Table 1. The demographic and anthropometric characteristics of the study children

Characteristic	Kwashiorkor	Marasmus
	Male = 88 Female = 57	Male = 24 Female = 22
Age (months)	31 (15)	26 (14)
Weight-for-age, z-score	-3.4 (1.1)	-3.7 (0.9)
Height-for-age, z-score	-3.6 (1.5)	-3.8 (1.3)
Weight-for-height, z-score	-1.8 (1.0)	-1.9 (0.9)
Mid-upper arm circumference (cm)	11.9 (1.6)	11.4 (1.7)
Mother alive	135 (93%)	46 (100%)
Father alive	131 (90%)	40 (87%)
Age weaned from the breastmilk (months)	20 (8)	19 (9)
Time since being breastfed (months)	11 (14)	8 (11)
Unprotected source of water	26 (18%)	7 (15%)
Grass used as roofing material	78/143 (55%) [†]	29 (63%)
Number with HIV	22 (15%)	22 (48%)*

Data expressed as number (%) for dichotomous characteristics and mean (SD) for continuous characteristics. * $P < 0.01$ by chi-squared test. [†]Two caretakers provided no data for this item.

The 48 children who did not enrol were on average 29 (15) months old and 35/48 (73%) had kwashiorkor, which was similar to the participants. The participants that did not enrol offered the explanation that they lived far from the hospital and could not return to complete the questionnaire. A total of 44 children were not eligible for the study because they did not have an older sibling, and 35 (80%) of these children had kwashiorkor, a similar fraction as our study population.

The caretakers of children with kwashiorkor surveyed gave food frequency information about children who were on average 49 (14) months in age, and 79 (55%) of these children were boys; the caretakers of children with marasmus gave food frequency information about children who were 45 (15) months in age and 23 (50%) of them were boys.

Regression modelling using only the demographic, clinical (HIV status and breastfeeding status), socio-economic and height to predict the type of malnutrition (kwashiorkor or marasmus) yielded a model with

Cox and Snell $r = 0.37$, with HIV status being highly significant ($P < 0.01$). The variables related to the socio-economic status were not significant predictors in this model. Regression modelling using the four most significant variables (age, HIV status, height, the age that the child was weaned from the breastmilk) to predict the type of malnutrition yielded a model with Cox and Snell $r = 0.35$.

Table 2 shows the food frequency data for the foods consumed by more than 20% of the children surveyed, considering the nine maize foods and the six cooked leaves as single entities. Thirteen foods were found to be consumed by less than 20% of children surveyed, including liver and meat of any kind (Table 3).

Twenty-one foods were candidates for inclusion in the regression model. Six foods were excluded from the regression model: wheat bread, rice, guava, okra, banana and cabbage. Adding 15 foods to the model improved its ability to predict the type of malnutrition (Cox and Snell $r = 0.46$). Children with kwashiorkor consumed less egg and tomato than those with marasmus: 17 (15) vs. 24 (31) servings per month for egg ($P < 0.01$) and 27 (17) vs. 32 (19) servings per month for tomato ($P < 0.05$) (see Table 4).

The dietary diversity score in children with kwashiorkor and marasmus was similar, as was the fre-

Table 2. Frequency of consumption of foods in siblings of children with kwashiorkor and marasmus

Food	Kwashiorkor <i>n</i> = 145	Marasmus <i>n</i> = 46
Cooked maize	61 (9, 61)	61 (30, 61)
Orange	30 (13, 61)	30 (13, 61)
Mango	30 (9, 61)	30 (0, 61)
Cooked leaves	30 (9, 61)	30 (9, 61)
Tomato	30 (9, 30)	30 (30, 30)
Banana	30 (4, 30)	30 (9, 30)
Sweet potato	30 (4, 30)	13 (0, 30)
Egg	9 (5, 13)	13 (9, 30)
Cow's milk	2 (0, 30)	1 (0, 30)
Cabbage	4 (0, 9)	4 (1, 9)
Avocado	4 (1, 13)	4 (1, 13)
Papaya	4 (1, 30)	4 (1, 30)
Potato chips	4 (0, 30)	4 (0, 30)
Okra	4 (0, 9)	4 (1, 9)
Fish	9 (4, 9)	9 (9, 9)
Wheat bread	1 (0, 30)	0 (0, 9)
Ants	0 (0, 9)	0 (0, 13)
Pumpkin/gourd	4 (1, 9)	4 (2, 13)
Beans	4 (0, 9)	4 (0, 13)
Guava	0 (0, 4)	0 (0, 1)
Rice	1 (0, 4)	1 (0, 4)

Values expressed as median number of times food was eaten per month (25 percentile, 75 percentile).

Table 3. Infrequently consumed foods of the siblings of malnourished children

Food	Kwashiorkor <i>n</i> = 145	Marasmus <i>n</i> = 46
Millet	4 (3)	0 (0)
Cucumber	26 (18)	7 (15)
Liver	3 (2)	0 (0)
Locust	3 (2)	0 (0)
Carrot	23 (16)	3 (6)
Pineapple	6 (4)	3 (6)
Carbonated soda pop	9 (6)	4 (9)
Sugarcane	17 (12)	4 (9)
Plums	26 (18)	5 (10)
Beef	1 (1)	0 (0)
Chicken	19 (13)	8 (17)
Goat	16 (11)	4 (9)
Eggplant	28 (19)	8 (17)

Values expressed as number of children that consumed the food at least once per month (%).

Table 4. Foods and other factors in regression model used to predict the type of malnutrition

Food	Estimated odds ratio Kwashiorkor/marasmus	95% confidence interval
HIV status	0.17	0.00–0.90
Age	1.04	0.99–1.09
Height	1.29	1.01–1.57
Time since weaned from breastmilk	1.00	0.94–1.06
Cooked maize	1.00	0.98–1.02
Potato/bean leaves	0.99	0.97–1.01
Beans	1.01	0.98–1.04
Tomato	0.98	0.97–0.99*
Fish	1.02	0.98–1.06
Ants	0.98	0.95–1.01
Mango	1.00	0.98–1.02
Avocado	1.01	0.98–1.04
Potato chips	1.00	0.97–1.03
Eggs	0.97	0.95–0.99*
Papaya	1.01	0.98–1.04
Oranges	1.00	0.98–1.02
Cow's milk	1.01	0.99–1.03
Sweet Potato	1.01	0.98–1.04
Pumpkin/gourd	0.96	0.91–1.01

*Siblings of children with kwashiorkor consumed these foods less frequently, $P < 0.05$.

quency of intake of each of the food categories (Table 5).

Discussion

The results of the food frequency questionnaires from siblings of severely malnourished children indicate that eggs and tomatoes are consumed less frequently by children with kwashiorkor than those with marasmus. The limitations of the study render the results preliminary and these results should be used only for the generation of hypotheses for further research.

The indirect method used to obtain dietary information, surveying a sibling under 5 years of age in the household, is a limitation of this study. The study design, a case-control method which assessed dietary intake once severe malnutrition has already developed, precluded the collection of data about the malnourished children themselves, since at the time of presentation these anorexic children uniformly had very poor dietary intakes. Feeding practices in south-

Table 5. Dietary diversity of siblings of children with kwashiorkor and marasmus

Food group	Kwashiorkor	Marasmus
Grains, roots, tubers	1.00 (0.02)	1.00 (0.01)
Legumes and nuts	0.79 (0.29)	0.81 (0.28)
Vitamin A-rich fruits and vegetables	0.98 (0.09)	0.98 (0.14)
Other fruits and vegetables	0.99 (0.09)	0.99 (0.09)
Dairy	0.35 (0.42)	0.35 (0.45)
Meat, poultry, fish and egg	0.56 (0.38)	0.54 (0.35)
Foods cooked with fat or oil	0.39 (0.45)	0.37 (0.44)
Dietary diversity score	5.06 (0.99)	5.02 (1.10)

Values expressed as mean number of servings from each food group consumed daily (SD). Dietary diversity score is the sum of the seven food groups.

ern Malawi during this season are such that families gather together as a large group and share food from a common pot 1–2 times per day. Children are not fed separately from adults, nor are they given different foods. Boys are not fed differently from girls at this age. The research team has extensive experience over the last 20 years in residing in villages in southern Malawi, observing food preparation and observing child feeding practices (Hotz & Gibson 2001). No practices have been noted to suggest that siblings in the same household between the ages of 1–5 years would receive different foods. In addition, it has been shown that the results of food frequency questionnaires from Nepalese siblings under the age of 5 years in the same household are 'remarkably consistent' for 21 common foods, with correlation coefficients that are on average 0.40 (Shankar *et al.* 1996; Gittelsohn *et al.* 1997). Among Mexican siblings, the correlation coefficient of dietary intake from a food frequency questionnaire was found to be 0.62 (Patterson *et al.* 1988). While we acknowledge that the choice of study design is an important limitation, the standard practices in Malawi and data from other studies indicate that food frequency data from siblings under the age of 5 years in a rural setting in the developing world do coincide. This is not surprising in light of the monotony of the diets.

Another limitation is that this study was conducted at one centre that treats only severe malnutrition in southern Malawi, thus these data do not reflect the diet of children with less severe malnutrition, nor

should the results be generalized to children living where there are different habitual diets. We used children with marasmus as a control for those with kwashiorkor, but the use of additional control groups, such as healthy children, might have been useful to determine what associations exist between foods consumed very infrequently and the type of childhood malnutrition. This study identifies an association between dietary intake of certain foods and the type of severe malnutrition, and provides no evidence that there is a causal link underlying this association.

While the assessment methods used here are simple, there have been no other reports of food frequency questionnaires used to characterize the diet of children with kwashiorkor. Gopalan (1968) performed a careful assessment of nutrient consumption in southern India among a healthy population of children with and without kwashiorkor, and found very similar intakes of protein and energy; however, micronutrient and antioxidant intakes were not reported in his study.

A diet that is lacking tomatoes and eggs is certainly lower in micronutrients than a maize-based diet that includes these foods. Tomatoes are an important source of antioxidant micronutrients, including vitamin C, lycopene and carotenoids. Eggs are rich in iron, zinc and other minerals. It has been observed that increased frequency of tomato consumption by Sudanese children was related to decreased morbidity due to diarrhoea and fever-related deaths, and the authors suggest that the micronutrients and antioxidants in tomatoes might enhance a child's immune system (Fawzi *et al.* 2000).

This study focused on consumption of antioxidant foods, rather than specific antioxidant nutrients. The negative results from the recent randomized, blinded, prospective trial of supplementary cysteine, selenium, vitamin E and riboflavin to prevent kwashiorkor in Malawi (Ciliberto *et al.* 2005) make it unlikely that these antioxidant nutrients alone are the differences that distinguish the diet of children with kwashiorkor from those with marasmus. However, foods are much more than mixtures of nutrients; it is the interactions of all the components of food with the human body that determines how diet affects the development of a disease. Even though kwashiorkor is a classic nutri-

tional disease, very little is yet known about how foods and nutrients affect the pathogenesis of this condition.

No differences in the frequency of consumption of fish or orange fruits were found in this survey; however, the variation in the frequencies of food consumption and the actual sample size of the study were such that only differences of about 25% in consumption frequency would achieve statistical significance. Indeed, the intersubject variation in the data collected was greater than anticipated, and to give the study the statistical power that we originally intended would have required about 300 participants. However, examination of the data in Tables 2 and 3, which quantified the servings of food consumed by children who developed kwashiorkor and marasmus, does not suggest that these diets differed very much.

This study was not designed to determine quantitative nutrient intake. The average portion size of egg in 3–5-year-old Malawian children in the same geographic area was reported to be 49 g (Hotz & Gibson 2001). Assuming that these portion sizes are the same in this population, our data indicate that the children with marasmus on average consume seven additional servings of egg per month, or about 84 g of additional protein per month, which is $0.16 \text{ g protein kg}^{-1} \text{ day}^{-1}$. While this is not a large amount of dietary protein, the staple food of these children, maize, consumed more than once a day, provides only about $0.3 \text{ g protein kg}^{-1} \text{ day}^{-1}$. Therefore one cannot dismiss the notion that eggs provide a significant amount of dietary protein for these children. However, the other foods available to these children that are relatively rich in protein, such as milk, fish or legumes, are not consumed less frequently by children with kwashiorkor.

It is unusual, almost unheard of, for kwashiorkor to simultaneously occur in an older and younger sibling both under the age of 5 years living in the same home in Malawi (Ciliberto *et al.* 2005). While these siblings receive the same foods from their caretakers, their diet may not be the same. Older children are more mobile and independent than younger children and spend several hours each day in their neighbour's homes. In the course of a day, these older children will receive small amounts of food from their neighbours. While the foods they receive outside of their

home are unlikely to be very different from the foods that their caretaker offers to them, the quantity of food and nutrients consumed by these children is likely to be greater than if they were fed exclusively at home.

The results of our preliminary study suggest topics for future research. Prospective studies to characterize the diets of children who go on to develop kwashiorkor need to be conducted to better understand the role of diet in this enigmatic clinical condition. Dietary surveys from other parts of the world are needed to verify or refute our findings. Further investigation of the role of dietary protein intake in the pathogenesis of kwashiorkor is needed to understand what role protein may play in preventing kwashiorkor. Intervention studies with egg or tomato might be useful in preventing kwashiorkor.

Acknowledgements

This work was supported by the Allen Foundation. We thank Rosemary Godwa and Chrissie Khoriyo for collecting the food frequency data, and Per Ashorn and Sarah Boslaugh for their advice with the data analyses.

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