Low and deficient niacin status and pellagra are endemic in postwar Angola[1–3]

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ABSTRACT

Background: Outbreaks of pellagra were documented during the civil war in Angola, but no contemporary data on the incidence of pellagra or the prevalence of niacin deficiency were available.

Objective: The objective was to investigate the incidence of pellagra and the prevalence of niacin deficiency in postwar Angola and their relation with dietary intake, poverty, and anthropometric status.

Design: Admissions data from 1999 to 2004 from the pellagra treatment clinic in Kuito, Angola, were analyzed. New patients admitted over 1 wk were examined, and urine and blood samples were collected. A multistage cluster population survey collected data on anthropometric measures, household dietary intakes, socioeconomic status, and clinical signs of pellagra for women and children. Urinary excretion of 1-methylnicotinamide, 1-methyl-2-pyridone-5-carboxymide, and creatinine was measured and hemoglobin concentrations were measured with a portable photometer.

Results: The incidence of clinical pellagra has not decreased since the end of the civil war in 2002. Low excretion of niacin metabolites was confirmed in 10 of 11 new clinic patients. Survey data were collected for 723 women aged 15–49 y and for 690 children aged 6–59 mo. Excretion of niacin metabolites was low in 29.4% of the women and 6.0% of the children, and the creatinine-adjusted concentrations were significantly lower in the women than in the children ($P < 0.001$, t test). In children, niacin status was positively correlated with the household consumption of peanuts ($r = 0.374$, $P = 0.001$) and eggs ($r = 0.290$, $P = 0.012$) but negatively correlated with socioeconomic status ($r = -0.228$, $P = 0.037$).

Conclusions: The expected decrease in pellagra incidence after the end of the civil war has not occurred. The identification of niacin deficiency as a public health problem should refocus attention on this nutritional deficiency in Angola and other areas of Africa where maize is the staple. *Am J Clin Nutr* 2007;85:218–24.

KEY WORDS Pellagra, niacin, Angola, urine metabolites

INTRODUCTION

First described in 1762, pellagra is a nutritional deficiency disease that continues to affect vulnerable groups in both developing and developed countries (1). The primary cause of pellagra is a lack of niacin, tryptophan, or both, and this condition classically manifests as a triad of dermatitis, diarrhea, and dementia that can lead to death. Sporadic cases continue to be seen globally and are associated with monotonous diets of untreated maize, food faddism, tuberculosis treatment, malabsorption states, and alcoholism (2–7). Recent major outbreaks have been described in association with humanitarian emergencies in Malawi, Mozambique, Angola, Zimbabwe, and Nepal (8–11).

The pellagra outbreak in Angola was described in 2000, after recognition of the first case in 1999 (8), and was centered in the provincial capital of Kuito in Bie Province, central Angola. Since 1999, the Medecins Sans Frontieres (MSF)–Belgium/Ministry of Health (MINSA) pellagra treatment clinic in Kuito has recorded admissions and diagnoses, which has allowed the tracking of the evolution of the epidemic during the transition from war to peace and rehabilitation. Although the general nutritional situation has much improved after the end of the civil war in 2002, access for humanitarian agencies to many areas of Bie Province remains limited because of the persistence of land-mine contamination and poor road and bridge conditions (12).

Although certain stages of the outbreak have been documented in terms of facility admissions and attack rates, no survey to determine the prevalence of niacin deficiency has been carried out to determine the extent and severity of biochemical deficiency within the population (8, 9, 13).

Interest in the epidemiology of niacin deficiency in the context of the HIV pandemic has reemerged because of evidence that tryptophan metabolism, and thereby niacin status, may be particularly vulnerable during HIV infection and play a role in the pathogenesis of AIDS (14, 15). There is also some evidence that maintaining niacin status may play a role in reducing the risk of carcinogenesis (16).

The current study was initiated by the World Food Programme as a collaboration between the government of Angola and various implementing partners. Having been involved in attempts to address the pellagra outbreak at the end of the 90s via the provision of groundnuts, canned fish, or both, the United Nations agency was interested in finding out whether pellagra and niacin

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deficiency were still problems of public health importance because this would affect its intervention planning.

Little or no representative biochemical data has been published on niacin status in populations affected by endemic pellagra. We describe the niacin status of newly admitted patients to a pellagra-treatment clinic and examine the relations between niacin status and household dietary intake, poverty, geographic location, and anthropometric status.

SUBJECTS AND METHODS

Study sites

For the first part of the study, the subjects were recruited from the MSF-Belgium/MINSA Pellagra Clinic in Kuito City; for the second part of the study, the subjects were recruited via survey from the population of the Municipality of Kuito in Bie Province, Angola. The Municipality had an estimated population of 310 000 at the time of the survey and lies in the central highlands of Angola at an altitude of ≈1700 m. It was one of the most active areas of conflict during the civil war. Residual land mine contamination of roads and other areas means that access to some areas was problematic and had to be undertaken with caution. Of the 5 submunicipality administrative areas (Communes), Kuito, Kunje, and Trumba were included in the survey. Chicala was excluded because of insecure access, and Cambandua was excluded because of an ongoing food aid distribution of fortified maize meal. The surveyed area included the provincial capital of Kuito City.

Subjects

All new patients attending the weekly MSF-Belgium/MINSA Pellagra Clinic in Kuito City were sampled on the day of registration (13 December 2004). The patients received a diagnosis of pellagra if they met the case definition of bilateral dermatitis on sun-exposed areas, a facial "butterfly" sign, or a Casal necklace. The diagnosis was made by local medical officers and followed established local procedures. A questionnaire was administered to the pellagrins, and urine and blood samples were collected (*see* below). The patients were treated according to the standard local clinical protocol and received a 100-mg nicotinamide supplement and a B complex tablet 3 times daily for 17 d if an adult or a 50-mg nicotinamide supplement and a B complex tablet 3 times daily for 15 d if aged <15 y. In addition, all patients received a weekly food supplement—400 g of a fortified blended food (corn soy blend, oil, and sugar)—for 3 wk. Families of the pellagra patients were also eligible for a food ration from the World Food Programme, which was distributed monthly for 3 mo.

Ethical approval for the surveys was obtained from the Angolan Ministry of Health, and a letter of support was issued by the ethical review board of the Institute of Child Health, London. The procedures followed were in accordance with the ethical standards of the respective institutions. Before the survey began, community leaders were consulted to discuss any questions and reservations that they had concerning the process of surveying the population. Individual informed consent was obtained from all participants before the samples were collected. No material benefits, other than feedback on their nutritional and health situation, were offered to encourage participation. Any subjects with infections or who were malnourished were referred to the national health facilities using local referral criteria.

Population sampling method

Multistage cluster sampling was performed with cluster allocation to sections made proportional to population size. The target population for the assessment was children (ages 24–59 mo) and nonpregnant women (ages 15–49 y) who were resident in the selected households at the time of the survey. Men and children of other ages were excluded from the sampling frame because of resource limitations and the desire to target the population groups that were most vulnerable and could be feasibly accessed through a household survey.

Sample sizes were calculated for biochemical niacin deficiency with the use of EPIINFO 6.04 (Centers for Disease Control and Prevention, Atlanta, GA) based on an estimated prevalence of 15% in women and children and a desired relative precision of 50% and assuming a design effect of 1. This resulted in a required sample size of 88. To allow for refusals and to ensure even sampling coverage, the objective was to recruit the first 4 women and 4 children sampled in each of 30 clusters to yield a target sample size of 120 for each age group. Because children aged <2 y would not be asked to donate urine, it was anticipated that the actual sample size for children would be reduced to ≈90. For other variables, a standard nutrition survey design using 30 clusters of 30 households was used (17).

Cluster and household selection was performed by using standard World Health Organization (WHO) procedures (17). Within each household, all eligible subjects were selected for inclusion. A household was defined as a group of people who had slept under the same roof (shelter) during the previous week. Any subject who refused to take part in the survey was not replaced. Age data were based, when possible, on vaccination or health records or subject or parental recall. For the anthropometric assessment of children whose age could not be determined, a height range of 65–110 cm was used to identify children aged 6–59 mo (17).

Staff training

Three separate survey teams were used, each of which consisted of 3–4 local medical and nutrition staff. All team members received 3 d of training on how to select subjects to be sampled, on how to administer questionnaires, on the importance of universal safety precautions, on how to collect blood samples, on how to use the Hemocue (HemoCue AB, Ángelgolm, Sweden), and on how to identify the clinical signs of micronutrient deficiency diseases.

Questionnaire data collection

Information on the frequency of consumption of 18 food items, during the previous 7 d, was collected by interviewing the head of household. The 18 food items were selected for inclusion in the questionnaire after interviews with key informants and focus groups discussions. The average consumption of each item and a food variety score (FVS) were calculated for each household from the number of unique food items consumed during the recall period. Socioeconomic status (SES) was estimated by combining observations about house roofing material and the years of schooling of the household head. A scoring system based on these variables was designed after key informant interviews and focus group discussions were undertaken. Pellagra was identified, as at the pellagra clinic, on the basis of one or more of the following signs: visible bilateral dermatitis, Casal necklace, or

the facial "butterfly" sign. Survey staff involved in screening for pellagra were familiarized with these clinical signs with the use of laminated photocards and by attendance and observation of patients at the weekly pellagra clinic. An initial diagnosis of pellagra was made by the team leader and was subsequently confirmed by the survey supervisor. The all-cause crude mortality rate was estimated by using a current census retrospective household questionnaire, with a recall period of 105 d (18). The previous mass polio vaccination campaign (21–23 August 2004) was used as the memorable date to define the recall period.

Anthropometric measures

Anthropometric measurements were made in children (ages 6–59 mo) and nonpregnant women (ages 15–49 y) from each household by using standard anthropometric equipment and methods (17). Weight was measured to the nearest 100 g and height or length to the nearest 1 mm. Children aged <24 mo were measured while supine, whereas children aged 24–59 mo were measured while standing. Global acute malnutrition was defined as a weight-for-height <-2 *z* scores of the National Center for Health Statistics/WHO growth reference curves (19), the presence of edema, or both; severe acute malnutrition was defined as a weight-for-height <-3 *z* scores, edema, or both. Chronic malnutrition (stunting) was defined by using the same *z* score cutoffs for the height-for-age index.

Hemoglobin measurement

Measurement of hemoglobin in children was performed in the household by using a portable Hemocue Photometer (HemoCue AB, Angelholm, Sweden) according to the azidemethemoglobin principle. Peripheral blood was collected from a finger prick made with a safety lancet (Hemocue). The women's hemoglobin concentration was measured in venous blood collected into lithium heparin–coated 2-mL Vacutainer tubes (Becton Dickinson Diagnostics, Preanalytical Systems, Oxford, United Kingdom). Blood tubes were kept in vaccine boxes at 4–8 °C until the end of each day. Altitude-adjusted cutoffs were calculated based on the average altitude of the cluster start points (1701 m) and were used to calculate anemia prevalence (20). The altitude of cluster start points was determined by using an eTrex Summit GPS handset (Garmin International Inc, Kansas City, KS).

Collection of urine samples and biochemical analysis

Urine was collected from consenting children (>2 y of age) and from nonpregnant women (15–49 y of age) in 100-mL collection cups. The urine was transferred into 10-mL Monovette urine collection tubes (Sarstedt AG & Co, Nümbrecht, Germany) and labeled with the identification number of the child or woman. Urine tubes were stored at 0–8 °C until the end of the day, when they were transferred into 2-mL Nalgene cryovials and frozen at −20 °C. The samples were transported from Angola to London on dry ice.

The urinary niacin metabolites *n*-methyl nicotinamide (1-MN) and 2-pyridone 5-carboxymide (2-PYR) were measured by ion-pairing reversed-phase HPLC with ultraviolet diode array detection (21). The limits of detection for 1-MN and 2-PYR were 0.5 and 0.1 μmol/L respectively. The CV for the purification and analysis of a urine quality-control sample was 3.0% for 2-PYR (mean concentration: 37.0 μmol/L) and 6.6% for 1-MN (31.3 μmol/L). Urinary creatinine was analyzed by Camelia Botna Laboratories (London, United Kingdom) with the use of Vitros CREA slides (Ortho Clinical Diagnostics, Rochester, NY).

The cutoffs for metabolite excretion used to define low and deficient niacin status were <4 mg/g creatinine (<3.0 μmol/mmol creatinine) and <2 mg/g creatinine (<1.5 μmol/mmol creatinine) for 1-MN and <1.6 mg/g creatinine (<1.32 μmol/mmol creatinine) and <0.5 mg/g creatinine (<0.4 μmol/mmol creatinine) for 2-PYR (22). The subjects were defined as having a low or deficient status if the excretion of either metabolite fell below the appropriate cutoff.

Data entry and analysis

Data were entered and analyzed by using EPIINFO 6.04d, EXCEL 2000 (Microsoft, Redmond, WA), STATA version 8.0 (StataCorp, College Station, TX), and SPSS version 12.0.1 (SPSS Inc, Chicago, IL). CIs for proportions and means were calculated by using the Complex Samples module within SPSS, which allows for the design effect of cluster sampling. Correlations between continuous variables were tested by using Pearson's test. A P value <0.05 indicated significance.

RESULTS

Admission figures from the MSF/MINSA Pellagra Clinic in Kuito were collated and are presented in **Figure 1**. The data illustrate that pellagra is endemic in the Kuito region and that the recording of new cases has continued with no evidence of a decrease since the end of the civil war in 2002. A comparison of the same annual period (weeks 1–32) between 2001 and 2004 indicates the occurrence of 836, 696, 836, and 807 incident cases, respectively.

Although the number of new, positively identified cases of pellagra at the clinic does not appear to be decreasing, the shape of the epidemic curve has changed with a broadening and diminution of the seasonal peak since 2002. Important changes in the population structure were occurring during this time period. These included an increased mobility of residents in outlying areas because of the end in hostilities, a resultant increase in the effective catchment area of the clinic, and the return of internally displaced people (IDP) from Kuito City to rural areas. Such movements would make the denominator for the expression of an incident rate unstable, so the results are expressed as a simple count rate. The proportion of patients that were residents rather than IDPs increased from 60% in 2000 to 92% in 2004 (weeks 1–31). A review of the patients admitted between 1999 and 2002 showed that most of the patients were women (72%) and that only 11.6% of the patients were aged <15 y. The overall mean age was 33 y (range: 1–90 y).

To biochemically confirm the clinical diagnosis used in the pellagra treatment clinic, all patients attending the clinic over 1 wk were interviewed and urine samples were collected. The characteristics of the 11 new patients admitted to the clinic are given in **Table 1**. Most of the new patients were male, and the average age was 33 y. General malnutrition was not evident, although 3 subjects had a body mass index (BMI; in kg/m^2) of <18.5 and in one of these subjects had a midupper arm circumference of <22.0 cm. None of the patients had edema. Anemia was present in 1 female and 1 male subject, whereas diarrhea was reported by 8 of the 11 patients and headache by 7 of the 11 patients. Almost all of the subjects reported depression, and all

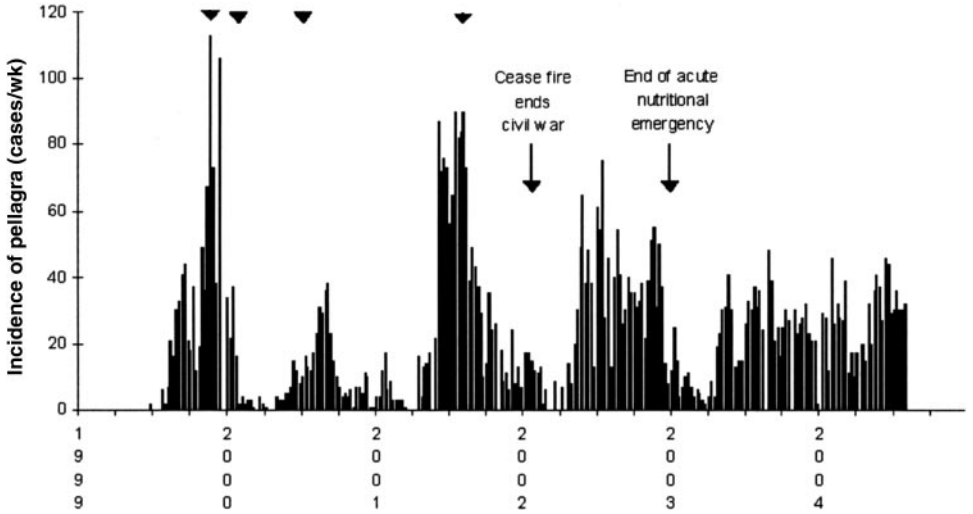

FIGURE 1. Persistence of clinical pellagra after the end of the civil war and after the acute nutritional emergency. Triangles indicate the timing of mass vitamin B tablet distributions that were undertaken by the Medecins Sans Frontieres–Belgium as an emergency measure. The data cover the period July 1999 to August 2004.

new patients complained of insomnia. Dermatitis was most commonly observed on the arms; only one patient exhibited signs on the hands or legs. Two patients had a Casal necklace and one showed facial dermatitis in the form of a "butterfly" sign. At admission, 9 of 11 patients had low or deficient excretion of 2-PYR concentrations, and 9 of 11 patients had low or deficient excretion of 1-MN concentrations. Overall, 10 of 11 patients were classified as having a low or deficient niacin status on the basis of metabolite excretion (**Table 2**).

To investigate the prevalence of niacin deficiency in the Kuito area, a multistage population cluster survey was conducted. A total of 900 households were sampled, of which 8 refused to participate and 68 were absent at the time of the survey. Two households were excluded from the analysis because of missing data. Therefore, data from 822 households were analyzed. A total of 788 eligible women were sampled, of whom 49 refused to participate or were absent from the household at the time of the survey. Data were therefore collected for 739 women; however, after the ages were calculated from reported birth dates during the analysis, 723 women fell within the desired age range of 15–49 y. A total of 725 eligible children were sampled; 2 of these children were found to be outside of the desired age range and their data were therefore excluded from the analysis. Thirty-one subjects were absent from the household at the time of the survey, and the caregivers refused consent for 2 to participate. Therefore, 690 children participated in the questionnaire and anthropometric data collection portions of the study, and complete data were obtained for 629 of these subjects.

The demographic characteristics of the population samples are shown in **Table 3**. The crude mortality rate was within the normal range for sub-Saharan Africa (23). Anthropometric indicators showed moderate levels of wasting and stunting, which were indicative of a population under nutritional stress but not affected by an acute emergency (23). Anemia was assessed in subsamples of the population and was evident in 25% of the women and in 67% of the children. Severe anemia was present in only 2.0% of

TABLE 1
Characteristics of the pellagra patients at admission

										Bilateral dermatitis				
Subject	Age	Sex	BMI	MUAC[1]	Hemoglobin	Diarrhea	Headache	Depression	Insomnia	Hands	Arms	Legs	"Butterfly" sign	Casal necklace
	y		*kg/m²*	*mm*	*g/dL*									
1	23	F	21.18	288	9.4		■	■	■					■
2	29	M	19.19	244	19.3				■					■
3	35	F	17.80	242	12.8	■	■	■	■	■				
4	41	F	21.73	266	17.5		■	■	■		■			
5	36	M	22.72	256	15.8	■		■	■			■		
6	42	M	20.84	254	21.5	■		■	■		■			
7	33	M	19.15	260	13.5	■		■	■		■			
8	38	F	16.99	240	16.6	■	■	■	■		■			
9	38	M	18.90	250	22.6	■	■	■	■		■			
10	23	M	16.36	214	12.9	■	■	■	■		■		■	
11	21	M	21.75	274	16.9	■	■	■	■		■			

[1] Midupper arm circumference.

TABLE 2
Niacin metabolite excretion in patients newly diagnosed with pellagra[1]

	New patients (n = 11)
Low or deficient niacin status (%)	91
2-PYR/creatinine (mg/g)	2.36 (1.04, 3.69)
<4 mg 2-PYR/g creatinine (%)	82
<2 mg 2-PYR/g creatinine (%)	55
1-MN/creatinine (mg/g)	1.19 (0.27, 2.11)
<1.6 mg 1-MN/g creatinine (%)	82
<0.5 mg 1-MN/g creatinine (%)	46

[1] 95% CI in parentheses. 2-PYR, 2-pyridone 5-carboxymide; 1-MN, *n*-methyl nicotinamide.

the women and in 0.0% of the children. The high level of anemia in children suggested a high prevalence of iron deficiency. Clinical signs of pellagra were assessed in the children and the women. The low prevalence detected in both groups indicated that pellagra was a mild public health problem; the CIs indicated that the sample size was inadequate to ensure a reliable estimate in children (24).

The niacin status of a subsample of women and children was biochemically assessed by determining the urinary concentration of 2-PYR and 1-MN expressed relative to creatinine (22). As shown in **Table 4**, when standardized in this way, the concentrations of niacin metabolites are markedly lower in the urine of

TABLE 3
Sample characteristics of the population sample and the prevalence of clinical pellagra[1]

Population data	No. of subjects	Value
Households		
Household size	822	5.15 (4.98, 5.33)
Crude mortality (all cause) rate[2]	822	0.23 (0.07, 0.38)
Displaced within past 3 y (%)	822	30.9 (19.0, 46.1)
Education of head of household (%)	753	
None		10.4
Initiation		19.5
1st to 10th grade		66.5
≥11th grade		3.5
Women		
Age (y)	723	27.6 (26.68, 28.44)
BMI (kg/m^2)	118	21.2 (20.4, 21.9)
<18.5 (%)	118	11.9 (7.0, 19.3)
<16.0 (%)	118	2.5 (0.8, 7.6)
Hemoglobin (g/dL)	107	13.5 (13.0, 13.9)
Anemia, <12.5 g/dL (%)	107	25.2 (17.8, 34.4)
Clinical signs of pellagra (%)	709	0.3 (0.1, 1.2)
Children		
Age (mo)	639	28.9 (27.5, 30.2)
Sex (% male)	639	50.1 (45.6, 54.6)
Weight-for-height z score	629	−0.51 (−0.61, −0.42)
<−2 z scores (%)	629	6.5 (4.5, 9.3)
Height-for-age z score	629	−1.52 (−1.70, −1.34)
<−2 z scores (%)	629	41.5 (36.7, 46.5)
Hemoglobin (g/dL)	233	10.8 (10.5, 11.0)
Anemia, <11.5 g Hb/dL (%)	233	67.0 (59.2, 73.9)
Clinical signs of pellagra (%)	639	0.2 (0.0, 1.2)

[1] 95% CI in parentheses.
[2] 10 000 p/d.

TABLE 4
Categorization of niacin status in women and children by measurement of urine metabolites[1]

	Women (n = 102)	Children (n = 84)
Low or deficient niacin status (%)	29.4 (20.4, 40.3)	6.0 (2.5, 13.6)
2-PYR/creatinine (mg/g)	7.59 (6.31, 8.88)	15.70 (13.22, 18.07)
<4 mg 2-PYR/g creatinine (%)	23.5	2.4
<2 mg 2-PYR/g creatinine (%)	5.9	0.0
1-MN/creatinine (mg/g)	3.06 (2.58–3.54)	5.63 (4.80–6.46)
<1.6 mg 1-MN/g creatinine (%)	22.5	6.0
<0.5 mg 1-MN/g creatinine (%)	2.9	0.0

[1] 95% CI in parentheses. 2-PYR, 2-pyridone 5-carboxymide; 1-MN, *n*-methyl nicotinamide.

women than of children and the prevalence of deficiency much higher. Twenty-nine percent of the women and 6% of the children had low or deficient niacin status [relative risk (RR) = 1.89; 95% CI: 1.62, 2.21]. According to WHO guidelines, the extent of niacin deficiency in women should be considered a public health problem (11).

To assess whether creatinine excretion may have been affected by malnutrition, excretion in women with a BMI < 18.5 (n = 15) was compared with those with a BMI ≥ 18.5 (n = 86). There was no significant difference between the 2 groups (9.1 compared with 8.6 mmol/L; P = 0.711). In children, only 2 subjects who were assessed for urine metabolite excretion had a weight-for-height z score <−2. There was no significant difference in the mean excretion of 1-MN (6.0 compared with 5.2 mg/g creatinine; P = 0.29) or 2-PYR (17.7 compared with 13.5 mg/g creatinine; P = 0.07) between the boys and girls, respectively.

Correlation analysis was performed to investigate the relation of age, BMI, midupper arm circumference, weight-for-height z score, height-for-age z score, hemoglobin, SES, household food variety, and household consumption of individual food items with niacin status. For the purposes of this analysis, the urinary concentrations of 2-PYR and MN-1 were summed, because this approximates most closely to total niacin intake. In women, no significant correlation with any of the potential predictors was observed. In children, a positive correlation was only found for 2 individual food items: peanuts (r = 0.374, P = 0.001) and eggs (r = 0.290, P = 0.012). However, SES was negatively correlated with niacin excretion (r = −0.228, P = 0.037). This apparent anomaly can probably be explained by the fact that the food variety scores for peanut consumption were higher (2.12 compared with 1.39; P = 0.086) in rural households, whereas the SES scores were significantly lower than in urban households (2.8 compared with 4.4; P < 0.001). Knowledge of pellagra was low: 95.0% and 98.9% of the heads of households did not recognize any of the symptoms or causes of pellagra.

DISCUSSION

The data indicated the persistence of clinical pellagra in this area of Angola after the end of the war and after the recovery from the acute nutritional emergency. The main nutritional emergency

that occurred after the cessation of hostilities started early in 2002, when humanitarian access to areas of the province previously inaccessible was allowed, and continued through the end of that year. From 2003 until the time of the survey, conditions had been improving, yet, surprisingly, the incidence rate of pellagra did not decrease.

The validity of pellagra case identification at the pellagra treatment clinic was confirmed by a clinical audit conducted in 2001 (13) and by the biochemical analysis of patients reported here. However, with the opening up of the region, more people with pellagra may have been able to access the pellagra clinic than before, which may have led to a possible measurement or ascertainment bias.

This is the first report of a household population survey of niacin status in a region with a pellagra endemic and has brought to light a serious prevalence of low and deficient niacin status in women. Biochemical surveys in other areas have targeted schoolchildren or hospital admissions (25–28). These previous studies have assessed niacin status by quantifying the major urinary metabolites 1-MN and 2-PYR and sometimes the less abundant metabolite 1-methyl-4-pyridone-3-carboxamide. Status is usually expressed as the ratio of 2-PYR to 1-MN or as the concentrations of the individual metabolites relative to creatinine (22). Both 2- and 24-h urine collections have been used; however, such collections are often not practical in field studies because of compliance issues, the difficulty of refinding individuals and households, and the costs associated with solving these problems.

Random spot urine sampling, together with the measurement of 1-MN and 2-PYR concentrations, has been suggested as an alternative because it avoids these issues and would provide a guide to status (22). However, the ratio of these metabolites has been shown to vary according to the time after the last meal because they are sequential intermediates on the same catabolic pathway (21). This makes the ratio an intrinsically unstable variable for use in population surveys; in the present study we chose to use cutoffs previously established for the excretion of individual metabolites expressed relative to creatinine. The subjects whose excretion fell below the established cutoffs for either metabolite were considered to be deficient.

The validity of expressing metabolite concentrations relative to creatinine in a population in which malnutrition is prevalent should be assessed in each situation. Malnutrition may lead to a decrease in creatinine excretion and thereby lead to a spurious increase in the ratio of metabolite to creatinine. In the data reported herein, no difference in creatinine excretion was observed by anthropometric status of the subjects; therefore, malnutrition will not have affected the prevalence estimates for low and deficient niacin status. It is worth noting that the urinary creatinine concentrations of the children in the present study were significantly lower than those of the adults (data not shown), whereas niacin metabolite concentrations were comparable between the 2 groups. The significance of this difference between children and adults in the assessment of niacin status deserves further attention.

Many constraints to the implementation of the population survey were encountered. The population figures had not been reviewed in the past 2 y, over which time there had been substantial population movements and resettlement of previously displaced persons. This led to some discrepancies between the best available information and the situation as actually encountered on the ground, which may have led to some loss of proportionality in cluster allocation. However, it is unlikely to have directly affected our prevalence estimations. Land mine contamination of roads and other areas meant that access to certain selected sampling areas was problematic. Certain areas were excluded from the survey area because access was impossible.

The overall nutritional and health situation of the surveyed population was consistent with a sub-Saharan postemergency African country. The mortality rate and prevalence of malnutrition were within expected ranges, and the population was not under any particular acute stress at the time of the survey. The prevalence of anemia in children, however, was very high. Nearly 1 in 3 women was found to be niacin deficient, which indicated that urgent action is required to tackle this important nutritional deficiency in the population studied and probably in similar African maize-dependent populations. The much higher niacin metabolite excretion in the children than in the adults was consistent with the lower recorded pellagra incidence rates seen in this population group at the pellagra treatment clinic.

Given the low prevalence that was found, the sample size obtained was inadequate to reliably assess the clinical signs of pellagra in children. However, the presence of clinical pellagra in women indicates that the widespread biochemical deficiency detected can progress into clinical disease. These data agree with the continued admissions reported at the pellagra clinic.

Correlation analysis failed to identify any risk factors for low or deficient niacin status in women but did identify household consumption of individual food items that were considered to be protective in children. Because peanuts and eggs are known to be rich sources of niacin, the protective effect of these foods was not unexpected. The consumption of alcoholic beverages was assessed, but no association with niacin status was found. Alcohol consumption is very difficult to determine accurately from a food-frequency questionnaire, and the questionnaire that was used in this survey was only designed to capture household rather than individual levels of consumption. Therefore, although no evidence that alcohol consumption was a risk factor for low or deficient niacin status was found in this survey, it cannot be ruled out and further investigation may be warranted.

The lack of knowledge about pellagra was slightly surprising given the endemic nature of the disease. However, it may be that the symptoms of severe niacin deficiency are so diverse that people do not understand them as a single disease and account for them separately using other terminology. Certainly, this lack of knowledge makes the inclusion of information on pellagra in public health information and communications a high priority.

While WFP is now providing fortified maize flour to vulnerable groups in Bie province, this study suggests that there may be a need for a national flour fortification initiative and other locally targeted interventions.

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AJS designed the study and was lead author on the manuscript. PIC conducted the laboratory analysis of niacin status. FD managed the fieldwork and undertook the data analysis. EC assisted with the study design and management of the fieldwork. TvdB and PS contributed to the study design and writing of the paper. None of the authors had any conflicts of interest to declare.

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