Nutritional biomarkers associated with gynecological conditions among US women with or at risk of HIV infection[1–3]

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ABSTRACT

Background: Women infected with HIV face a combination of health threats that include compromised nutrition and adverse gynecological conditions. This relation among HIV, nutrition, and gynecological conditions is complex and has rarely been investigated.

Objective: Our objective was to investigate nutritional biomarkers associated with several gynecological conditions among US women with or at risk of HIV infection.

Design: Data on 369 HIV-infected and 184 HIV-uninfected women with both nutritional and gynecological outcomes were analyzed from a cross-sectional nutritional substudy of the HIV Epidemiology Research Study (HERS). We examined micronutrient distributions comparing HIV-infected with HIV-uninfected participants and both subgroups with the US population. We then modeled the relation of 16 micronutrient serum concentrations to various gynecological conditions, producing partially adjusted odds ratios, adjusted for study site, risk cohort, and HIV status.

Results: HIV-infected women's median antioxidant concentrations were lower than the medians of the US population. HERS women had lower median concentrations for vitamin A, selenium, and zinc irrespective of HIV status. Trichomoniasis prevalence was inversely related to serum α-carotene. Lower concentrations of vitamins A, C, and E and β-carotene were associated with an increased risk of bacterial vaginosis. Higher concentrations of serum zinc were associated with lower risk of human papillomavirus. *Candida* colonization was higher among women with higher concentrations of total-iron-binding capacity.

Conclusion: We identified several significant associations of micronutrient concentrations with the prevalence of gynecological conditions. These findings warrant further investigation into possible causal relations. *Am J Clin Nutr* 2007;85:1327–34.

KEY WORDS HIV, nutritional status, bacterial vaginosis, trichomoniasis, human papillomavirus, HPV, *Candida*

INTRODUCTION

Women infected with HIV face a combination of health threats along with immunodeficiency, including compromised nutrition and adverse gynecological conditions. The relation among HIV, nutrition, and adverse gynecological outcomes is complex and has rarely been investigated.

HIV and nutrition

People living with HIV, particularly those with AIDS, have compromised nutritional status, including low blood concentrations of micronutrients such as vitamin A (1–3), carotenoids (4–7), vitamin E (1, 4, 8), vitamin C (1, 4, 9, 10), vitamin B-12 (11–13), folic acid (2, 4, 9, 10), zinc (1, 14), and selenium (15–17). Anemia is also common in HIV infection and is associated with increased risk of mortality (18–21). HIV-associated malnutrition is often the result of several factors, including HIV-related conditions that impair intake of nutrients such as loss of appetite, nausea, oral lesions, and those that affect nutrient absorption such as persistent diarrhea, impaired nutrient storage, and altered nutrient metabolism (22).

Gynecological conditions and nutrition

Some nutritional deficiencies are themselves associated with adverse gynecological outcomes irrespective of HIV status. Low concentrations of folic acid are associated with cervical dysplasia (23–25), cervical cancer (26, 27), and human papillomavirus (HPV) (24). Low concentrations of vitamin C and β-carotene were associated with cervical dysplasia (28–30), cervical cancer (27, 31–33), HPV (34), and ovarian cancer (35).

HIV and gynecological conditions

HIV appears to affect the prevalence and persistence of gynecological conditions. HIV-infected persons have a higher prevalence and longer duration of sexually transmitted HPV infection than do HIV-uninfected persons (36–42). Bacterial vaginosis (BV) may also be more severe in HIV-infected women (43).

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Because of the complex relations among nutrition, gynecological health, and HIV disease, all 3 characteristics need to be investigated in concert. We are aware of only one study of the association of nutritional status and a gynecological condition among HIV-infected women (44), in which it was reported that retinol deficiency may contribute to the development of cervical squamous intraepithelial lesions (SILs). The present study examines the interrelated associations of various nutritional indexes with gynecological conditions among a cohort of HIV-infected and -uninfected women to examine whether the associations between nutrient concentrations and the gynecological conditions differ by HIV status.

SUBJECTS AND METHODS

We analyzed data from a cross-sectional nutritional substudy of the HIV Epidemiology Research Study (HERS). HERS enrolled 871 HIV-infected and 439 HIV-uninfected women at high risk of infection from 4 US communities (Boston, MA, New York, NY, Detroit, MI, and Providence, RI) and followed them semiannually for ≤7 y. Further details were published elsewhere (45). The nutrition substudy gathered data from 369 HIV-infected and 184 HIV-uninfected women participating at study sites in Baltimore, MD, New York, NY, and Providence, RI; data collection typically occurred 1–2 y after enrollment in the main study. The time frame spanned from June 15, 1994, through November 30, 1995. The women who participated in the nutritional substudy and had complete data on the gynecological outcomes were included in this analysis. There were 118 women on antiretroviral medications, of whom 106 were on monotherapy, 11 on dual therapy, and 1 on triple therapy. Institutional review boards approved the study protocol at each site and at the Centers for Disease Control and Prevention. All participants gave voluntary informed consent.

Nutritional substudy methods

HERS routinely collected data on women's height, weight, medical history, and sexual and drug-use behaviors. For the substudy, women were queried about their recent diet and use of nutritional supplements. Blood was drawn with the use of metal-free evacuated tubes and assayed for 16 measures of 13 different micronutrients, including antioxidants (vitamins C and E and the carotenoids, α-carotene, β-carotene, lycopene, β-cryptoxanthin, and lutein/zeaxanthin), vitamin A, vitamin B-12, serum folate, red blood cell (RBC) folate, and several minerals [ferritin, iron, total-iron-binding capacity (TIBC), selenium, and zinc]. Three indexes were used to assess iron status because the best measure of deficiency is the presence of 2 abnormal values (46). A low concentration of serum ferritin is the best indicator of inadequate iron storage in the body, whereas low serum iron concentrations and high TIBC values reflect lower amounts of iron in transit. Women were not required to fast before blood collection.

Standardized reference distributions do not exist for many of the micronutrients assayed. Therefore, we chose to develop our own reference standards with the use of nutritional data from the second and third National Health and Nutrition Examination Surveys (NHANES II and III), which are explained elsewhere (47, 48). These surveys, conducted by the National Center for Health Statistics in 1976–1980 and 1988–1994, used complex, multistage, stratified, clustered samples of civilian, noninstitutionalized US populations. Almost all of the micronutrients in the HERS were also measured in NHANES III. Vitamin B-12 was measured in NHANES III, but in only about half of the sample. Zinc was measured in NHANES II but not in NHANES III. We estimated the distribution of each of 16 micronutrients from the NHANES data, with the use of subset and weighting mechanisms to obtain population-level estimates of the distribution. The HERS age range for the main study was 16–60 y and for the substudy it was 20–57 y. We used the NHANES data for females aged 16–60 y to reflect the US population in approximately the same age range as the HERS. Thus, we derived reference distributions appropriate for our HERS subsample.

Gynecological methods

Our primary goal was to examine the association between various gynecological conditions and micronutrient levels for HIV-infected and -uninfected women. The gynecological data come from the core study, in which women received semiannual physical and gynecological examinations according to the core study protocol. The gynecological observations were made within 2 wk of the micronutrient measurements. The diagnosed conditions in this analysis are those that were concurrent with the micronutrient substudy visits. We focused on 5 common conditions among this population: trichomoniasis, BV, *Candida* colonization, HPV infection, and abnormal cervical cytology graded as SILs or worse.

Trichomoniasis was identified either by culture or potassium hydroxide-stained wet mount (49). We defined BV as a Nugent score of 7–10, which combines semiquantitative information on the presence of *Lactobacillus*, *Gardnerella*, and curved, gram-negative bacilli based on Gram stain (50, 51). *Candida* colonization was determined by culture or presence on Gram stain (52). HPV infection was determined by a positive result on polymerase chain reaction with the use of generic or any of several dozen type-specific primers (53). SIL was determined on regularly administered Papanicolaou tests, evaluated by a central laboratory where the technicians were blinded to the women's HIV status (54).

Statistical analysis

We examined the micronutrient distributions among the HERS nutrition subsample, comparing HIV-infected women with HIV-uninfected women and also comparing both subgroups with the US population. Because the distributions of most micronutrients are highly skewed, we used the nonparametric Wilcoxon's rank sum test to compare them.

We used logistic regression to model the associations of each binary gynecological condition with the 16 micronutrient measurements. Given the generally asymmetric distributions of the micronutrients, we used population concentration quartiles to estimate 4 discrete nutrient concentrations. This approach preserved epidemiologic interpretability, appealed to a robust standard, and gave more flexibility than merely dichotomizing the nutrient concentrations, although less than could have been achieved with the use of smoothing methods (such as generalized additive models). With the use of population quartiles in this way, our analysis produced an indirect standardization to population nutrient concentrations rather than an assessment of nutritional deficiency.

In addition to testing for an association between gynecological conditions and population micronutrient quartiles, we also tested

TABLE 1
Characteristics of the HIV-infected and HIV-uninfected women

	HIV-infected (n = 369)	HIV-uninfected (n = 184)	P[1]
Current age (y)	36.4 ± 6.6[2]	36.1 ± 7.2	0.6
Race or ethnicity [n (%)]			0.06
African American	229 (62.1)	100 (54.4)	
White	82 (22.2)	58 (31.5)	
Hispanic	58 (15.7)	26 (14.1)	
Baseline education [n (%)]			< 0.01
< High school graduate	171 (46.5)	61 (33.2)	
≥ High school graduate	197 (53.0)	123 (66.9)	
Live births [n (%)]			0.6
≥ 1	312 (84.5)	149 (80.9)	
0	57 (15.5)	35 (19.0)	
Albumin (g/dL)	4.0	4.2	< 0.01
Hemoglobin (g/dL)	12.6	13.3	< 0.01
Mean corpuscular volume (mm^3)	100	90	< 0.01
Current smoker [n (%)]	291 (78.9)	143 (77.7)	0.8
Ever had sex for drugs or money [n (%)]	148 (40.1)	89 (48.4)	0.06
Injection drug use in past 6 mo [n (%)]	109 (29.5)	42 (22.8)	0.10
Crack use in past 6 mo [n (%)]	50 (13.6)	32 (17.4)	0.2
Condom use in past 6 mo [n (%)][3]			< 0.01
No	46 (18.2)	55 (38.2)	
Yes	207 (81.9)	89 (61.8)	
Male sexual partners in past 6 mo [n (%)]			< 0.01
≥ 1	253 (68.8)	143 (78.6)	
0	115 (31.3)	39 (21.4)	

[1] P value for age is based on Student's t test (after verification that variances were equal); those for all categorical variables are based on Pearson's chi-square test of association.
[2] $\bar{x}$ ± SD (all such values).
[3] Results exclude women who did not have sex in that period.

for a linear trend against quartile scores. The first test establishes whether one might find any functional relation between condition prevalence and nutrient concentration, and the second test gives a sense for whether this relation is systematically increasing or decreasing.

Partially adjusted models accounted for study design parameters, including study site, risk category (sexual-only or injection drug use), and HIV status. We estimated model-based prevalence of each condition by HIV status and nutrient quartile as though each site and risk category were equally represented. We pursued further modeling by considering additional covariates that had observed associations with each condition in other published HERS analyses from the main study. These included race or ethnicity (black, white, Hispanic or Latina, or other), age, education level, cigarette use, crack use, consistency of condom use, frequency of vaginal sex, had a hysterectomy, recent menses, currently pregnant (urine test), sperm on Gram stain, ever traded sex for drugs or money, ever injected drugs, currently using hormonal contraceptives, antibacterial use, diabetes therapy, CD4 count, and HIV viral load (logarithmic scale). All analyses were performed in SAS version 8 (SAS Institute, Cary NC) and S-PLUS 6 (Insightful Corporation, Seattle WA).

RESULTS

Baseline characteristics of this subset of the HERS cohort (n = 553), by HIV infection status, show some expected differences between HIV-infected and -uninfected women. HIV-infected women had lower education, lower body mass index (BMI, in kg/m^2), lower concentrations of albumin and hemoglobin, higher mean corpuscular volume, used condoms more often in the past 6 mo, and had fewer male sexual partners in the past 6 mo than did the HIV-uninfected women (**Table 1**). A significantly higher prevalence of HPV, *Candida,* and SIL but not trichomoniasis or BV was found among the HIV-infected women than among the HIV-uninfected women (**Table 2**).

Comparisons of the population quartiles established from the NHANES data and the HERS median values for the 16 measurements of micronutrients in the HIV-infected and -uninfected women are shown in **Table 3**. For serum α-carotene, serum β-carotene, serum lycopene, serum β-cryptoxanthin, and TIBC,

TABLE 2
Prevalence of gynecological conditions among women of the nutrition substudy[1]

Condition	HIV^+	HIV^-	P[2]
	%	%	
Trichomoniasis (culture or wet mount)	18	15	0.40
Bacterial vaginosis (Gram stain)	47	40	0.10
Human papillomavirus (PCR)	68	33	< 0.01
Candida (culture)	37	27	< 0.02
SIL or worse (Papanicolaou test)	22	5	< 0.01

[1] Detection assay for condition included in parentheses. PCR, polymerase chain reaction; SIL, squamous intraepithelial lesion.
[2] Pearson chi-square test of association on 3 degrees of freedom for the marginal contribution of the micronutrient term in the model.

TABLE 3
Population medians and HIV Epidemiology Research Study (HERS) nutrition substudy medians and SEs of the 16 micronutrients[1]

			HERS				
	NHANES		HIV$^+$		HIV$^-$		
Micronutrient	Median	SE[2]	Median	SE[2]	Median	SE[2]	P[3]
Serum vitamin A (μg/dL)	49.9	0.2	42.1	1.0	43.3	1.4	0.28
Serum vitamin C (mg/dL)	0.777	0.009	0.592	0.044	0.410	0.067	0.068
Serum vitamin E (μg/dL)	966.8	4.7	856.0	13.4	850.5	25.7	0.68
Serum α-carotene (μg/dL)	3.3	0.0	0.7	0.0	1.0	0.1	0.003
Serum β-carotene (μg/dL)	14.7	0.2	7.1	0.3	8.6	0.5	0.031
Serum lycopene (μg/dL)	21.8	0.2	13.2	0.6	17.4	1.2	$<$ 0.001
Serum β-cryptoxanthin (μg/dL)	6.7	0.1	4.4	0.2	5.0	0.2	0.012
Serum lutein/zeaxanthin (μg/dL)	17.7	0.1	14.3	0.6	15.3	1.0	0.063
Serum vitamin β-12 (pg/mL)	429.6	4.0	456.0	18.9	500.0	11.6	0.016
Serum folate (ng/mL)	5.01	0.05	6.42	0.28	5.50	0.47	0.015
RBC folate (ng/mL)	166.1	1.5	180.7	5.6	157.3	11.3	0.10
Serum ferritin (ng/mL)	40.1	0.6	70.0	5.8	43.0	4.1	$<$ 0.001
Serum iron (μg/dL)	80.4	0.6	74.9	2.3	78.0	4.5	0.60
Serum TIBC (μg/dL)	363.6	0.8	334.3	3.6	351.5	5.8	$<$ 0.001
Serum selenium (ng/mL)	121.3	0.2	107.5	1.1	113.5	1.3	$<$ 0.001
Serum zinc (μg/dL)	82.6	0.2	67.9	0.9	72.0	1.1	$<$ 0.001

[1] NHANES, National Health and Nutrition Examination Survey; RBC, red blood cell; TIBC, total-iron-binding capacity.
[2] Bootstrap SE (percentile method, 2000 replicates, HERS SEs are bias-corrected and accelerated).
[3] P value for Wilcoxon rank-sum test.

the median values for HIV-infected women were lower than both the median values for the HIV-uninfected women and the first (lowest) quartile for the NHANES population. For all micronutrients except vitamin B-12, serum folate, RBC folate, and ferritin, the HIV-infected women had median antioxidant concentrations below the population medians (**Figures 1** and **2**). The mean BMI for the HERS women was 23.6 for the HIV-infected and 25.6 for the HIV-uninfected women; these values fell on either side of the population median BMI of 24.3.

We modeled with the various gynecological conditions and the serum measurements of the 16 micronutrients, producing odds ratios (ORs), adjusted for study site, risk cohort, and HIV status (**Table 4**). No significant associations were observed with SIL and any of the micronutrients; therefore, it is not reported in

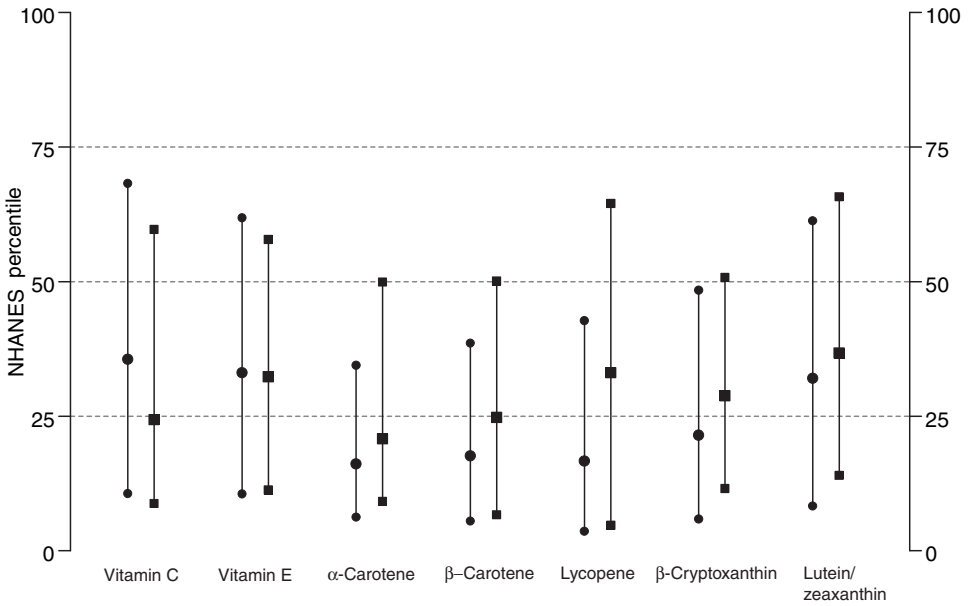

FIGURE 1. Antioxidant levels in the nutrition substudy of the HIV Epidemiology Research Study (HERS) are standardized to distributions in the National Health and Nutrition Examination Survey (NHANES). Each vertical element of the graph shows the first quartile, median, and third quartile for women in the HERS. The median antioxidant concentrations among HIV-infected (●; n = 369) and HIV-uninfected (■; n = 184) women in the HERS were below the population medians for each antioxidant. In addition, the median values of serum α-carotene, serum β-carotene, serum lycopene, and serum β-cryptoxanthin for the HIV-infected women were lower than both the median values for the HIV-uninfected women and the lowest quartile for the NHANES population.

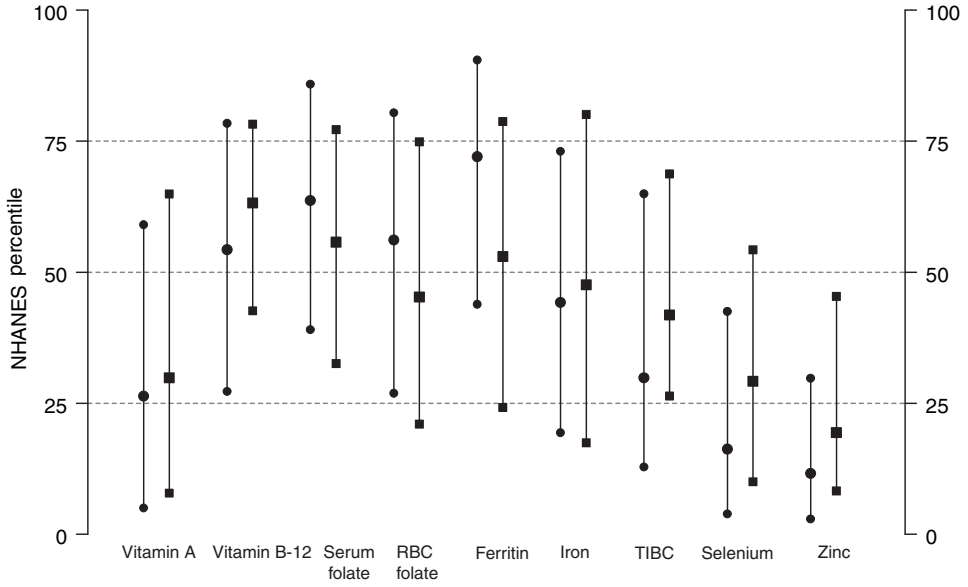

FIGURE 2. Vitamins A and B-12, folate, and mineral concentrations in the nutrition substudy of the HIV Epidemiology Research Study (HERS) are standardized to distributions in the National Health and Nutrition Examination Survey (NHANES). Each vertical element of the graph shows the first quartile, median, and third quartile for women in the HERS. The HIV-infected (●; $n = 369$) and HIV-uninfected (■; $n = 184$) women had median concentrations below the population medians for vitamin A, iron, total-iron-binding capacity (TIBC), selenium, and zinc. RBC, red blood cell.

the table. The reference group for all models was the HERS women who had nutrient concentrations below the first NHANES population quartile (Q1). The comparison groups were nutrient concentrations that fell between the first and second NHANES quartiles, between the second and third quartiles (Q3), and higher than the third population quartile (Q4). None of these models simultaneously considered >1 micronutrient or gynecological outcome.

Increasing concentrations of α-carotene were associated with lower prevalence of trichomoniasis, with adjusted ORs of 0.88, 0.63, and 0.12 for Q2, Q3, and Q4, respectively. The model of trichomoniasis and α-carotene considered race, crack use, cigarette use, and the presence of BV by Gram stain, but none of these variables remained in the final model.

Higher concentrations of 4 nutrients (vitamins A, C, and E and β-carotene) were associated with a lower risk of BV (Table 4). BV and these 4 nutrients were considered in 4 separate but common models, which considered race, education, presence of trichomonas infection, *Candida* colonization, the frequency of vaginal sex, and consistency of condom use. The final model included education, *Candida* colonization, and the frequency of vaginal sex.

Colonization of *Candida* was higher among women in the third quartile for TIBC values, but there was no suggestion of an overall monotonic relation (Table 4). The model of *Candida* colonization and TIBC considered age, presence of cervix, antibacterial use, diabetes therapy, recent menses, currently pregnant (by urine test), consistency of condom use, sperm on Gram stain, ever traded sex for drugs or money, ever injected drugs, and BV in the final model. No statistically significant interaction was observed between HIV status and the nutritional indexes within any of these models.

Women with higher concentrations of zinc appeared to be at lower risk of HPV than were women with lower concentrations of zinc (Table 4). For the relation between HPV and zinc, the model considered race, age, education, BV, *Candida* colonization, ever traded sex for drugs or money, current use of hormonal contraceptives, CD4 count, and HIV viral load (algorithmic scale).

DISCUSSION

The women who participated in this study, regardless of their HIV infection status, had nutritional indexes that were below the national average for many of the nutrients reported here. The exceptions were vitamin B-12, serum folate, RBC folate, ferritin, and iron, and observed median values were similar to the US population. In addition, the HIV-infected women had concentrations of albumin, hemoglobin, α-carotene, β-carotene, lycopene, β-cryptoxanthin, selenium, and zinc lower than the HIV-uninfected women in the same cohort. Our analysis produced an indirect standardization to population nutrient concentrations rather than an assessment of nutritional deficiency. There are few descriptions of the nutritional status of HIV-infected women in the United States, and this nutritional analysis is unique in the use of the US population-based NHANES data to establish reference distributions as a standard with which to compare with our specific cohort (women either infected with or at risk of infection of HIV).

In addition to the identification of low concentrations of several nutrients among HIV-infected women in this cohort, in some cases these low concentrations were found to be associated with adverse gynecological outcomes, including risk of BV and trichomonas, and HPV infections. Although the relation between *Candida* colonization and TIBC appears to be the opposite, it should be noted that elevated TIBC is an indication of low serum concentrations of iron. Note that the presence of inflammation and infection results in lower concentrations of serum iron. These

TABLE 4
Model-based estimates of prevalence and odds ratios relating gynecological conditions to micronutrient levels, adjusted for HIV status[1]

	Prevalance (95% CI)				
	HIV$^+$	HIV$^-$	Odds ratio (95% CI)	*P* for step[2]	*P* for trend[3]
	%				
Trichomonas					
α-Carotene					
Q1	16 (12, 22)	14 (9, 21)	Referent	0.044	0.024
Q2	15 (9, 24)	13 (7, 22)	0.88 (0.48, 1.63)		
Q3	11 (5, 23)	9 (4, 21)	0.63 (0.25, 1.60)		
Q4	2 (0, 15)	2 (0, 13)	0.12 (0.02, 0.92)		
BV				0.014	0.160
Vitamin A					
Q1	51 (43, 58)	45 (36, 54)	Referent		
Q2	38 (29, 48)	33 (23, 44)	0.60 (0.37, 0.96)		
Q3	32 (22, 43)	27 (18, 38)	0.45 (0.26, 0.79)		
Q4	47 (37, 57)	41 (30, 53)	0.87 (0.53, 1.41)		
Vitamin C				0.001	0.001
Q1	54 (46, 62)	45 (36, 55)	Referent		
Q2	45 (35, 55)	37 (26, 48)	0.70 (0.43, 1.12)		
Q3	33 (23, 44)	26 (17, 38)	0.42 (0.24, 0.73)		
Q4	33 (24, 44)	26 (17, 37)	0.42 (0.25, 0.72)		
Vitamin E				0.043	0.006
Q1	52 (44, 60)	45 (36, 54)	Referent		
Q2	43 (34, 53)	36 (27, 47)	0.70 (0.45, 1.09)		
Q3	39 (29, 49)	32 (23, 43)	0.58 (0.36, 0.94)		
Q4	36 (26, 48)	30 (19, 43)	0.52 (0.30, 0.91)		
β-Carotene				0.005	0.130
Q1	47 (41, 54)	41 (33, 50)	Referent		
Q2	39 (30, 49)	33 (25, 43)	0.72 (0.47, 1.10)		
Q3	57 (44, 69)	51 (37, 64)	1.46 (0.84, 2.56)		
Q4	26 (16, 41)	22 (12, 36)	0.40 (0.20, 0.81)		
Candida				0.010	0.850
TIBC					
Q1	32 (24, 40)	20 (13, 30)	Referent		
Q2	42 (32, 52)	28 (19, 38)	1.54 (0.90, 2.62)		
Q3	50 (38, 62)	35 (23, 48)	2.14 (1.20, 3.82)		
Q4	26 (16, 39)	16 (9, 26)	0.76 (0.39, 1.46)		
HPV				0.210	0.010
Zinc					
Q1	36 (31, 42)	26 (20, 34)	Referent		
Q2	37 (28, 48)	27 (18, 38)	0.85 (0.53, 1.35)		
Q3	40 (27, 54)	29 (19, 43)	0.38 (0.20, 0.72)		
Q4	41 (25, 60)	31 (17, 48)	0.64 (0.30, 1.38)		

[1] Variables included in the models were race/ethnicity (black, white, Hispanic or Latina, or other), age, education level, cigarette use, crack use, consistency of condom use, frequency of vaginal sex, had a hysterectomy, recent menses, currently pregnant (urine test), sperm on Gram stain, ever traded sex for drugs or money, ever injected drugs, current use of hormonal contraceptives, antibacterial use, diabetes therapy, CD4 count, and HIV viral load (logarithmic scale). Q1–Q4 were based on the National Health and Nutrition Examination Survey quartiles. BV, bacterial vaginosis; TIBC, total-iron-binding capacity; HPV, human papillomavirus; Q, quartile.

[2] *P* for step was determined by chi-square test of 4-category nutrient predictor (3 degrees of freedom).

[3] *P* for trend was determined by test for linear trend against quartile scores.

data do not imply that the association between nutrient concentrations and these gynecological conditions are modified by HIV status.

Our findings are similar to other reports of lower concentrations of antioxidants being associated with HPV infection in HIV-uninfected women (34). Most studies have reported an association of low antioxidant concentrations and cervical dysphasia, cancer, or both (27–31) with only one study reporting no association (54). No relation between antioxidant concentrations and cervical dysplasia was found in our cohort. French et al (44) reported a significant and independent association between lower retinol concentrations and cervical SILs among a cohort of HIV-infected women, similar to the HERS women, in a 6-site longitudinal study of women infected with or at risk of HIV infection in the United States. In our cohort, no associations were observed between SIL and any of the micronutrient measurements (Table 2), which may be due to the lower prevalence of SIL in our cohort. Belec et al (55) reported that among women in Central Africa vitamin A deficiency was associated with the number of genital tract infections diagnosed. Nutritional correlates of gynecological conditions such as BV have not been previously reported in the literature.

Several limitations of this study deserve mention. This was a cross-sectional study; therefore, a causal relation between nutritional status and risk of adverse gynecological conditions in the presence or absence of HIV cannot be inferred. Micronutrient concentrations in plasma can be affected by several factors. For example, in our analysis the women were not asked to fast before the collection of the blood samples, which may have affected concentrations of certain nutrients, especially zinc. In addition, the women in this cohort had a high prevalence of infection, potentially resulting in high levels of inflammation, which can alter plasma concentrations of several micronutrients, such as ferritin and retinol (56). In addition, data were not available for acute-phase reactants. A strength of the analysis is the breadth of these data, including the large sample size and the detailed data collected on the gynecological conditions and biochemical nutritional markers.

Others have indicated that better nutritional status might extend the time from infection with HIV to symptomatic AIDS (10, 57). This analysis highlights the importance of assessing nutritional status among persons with HIV infection in relation to potential opportunistic infections, specifically among HIV-infected women and gynecological conditions. Although this cross-sectional study did not show that nutritional therapy would alleviate these gynecological conditions, the results suggest that it may be beneficial. Therefore, further investigation with either well-designed nutritional interventional or longitudinal cohort studies is warranted.

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