

# Bacterial Vaginosis Is Associated with Variation in Dietary Indices<sup>1,2</sup>

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## Abstract

Bacterial vaginosis (BV) is a common condition of unknown etiology and has been linked to adverse reproductive and obstetric health outcomes. Prior dietary research on BV has focused on specific macro- and micronutrients, but not dietary indices. We assessed the relationship between BV and selected dietary indicators among a cohort of 1735 nonpregnant women ages 15–44 y from Birmingham, Alabama. Annual intake was assessed with the Block98 FFQ, and the glycemic index, glycemic load (GL), and Healthy Eating Index were calculated by the Block Dietary Data System. The Naturally Nutrient Rich (NNR) score was also calculated. Vaginal flora was evaluated using Nugent Gram-stain criteria. Crude OR and adjusted OR were determined by multinomial and logistic regression in cross-sectional and prospective analyses, respectively. Participants were predominantly African American (85.5%) aged 25.3 ± 6.8 y (mean ± SD). Per 10-unit increase, GL was positively (adjusted OR = 1.01, 95% CI = 1.00–1.03) and NNR was negatively (adjusted OR = 0.93, 95% CI = 0.88–0.99) associated with BV compared to normal vaginal flora. In prospective analyses, only GL was associated with BV progression (adjusted OR = 1.03, 95% CI = 1.00–1.05) and persistence (adjusted OR = 1.02, 95% CI = 1.01–1.04) after adjustment. Both GL and NNR were associated with greater BV prevalence and GL was associated with an increase in BV persistence and acquisition. These results suggest that diet composition may contribute to vaginal flora imbalances and be important for elucidating the etiology of BV. *J. Nutr.* 141: 1698–1704, 2011.

## Introduction

BV<sup>8</sup> is the most frequent cause of vaginal complaints among reproductive-aged women and is characterized by an imbalance in the vaginal flora, with the replacement of *Lactobacillus species* by anaerobic bacteria and a corresponding increase in vaginal pH (>4.5) (1). In the United States, the prevalence of BV varies by ethnicity, with African American women having over 2 times higher prevalence of BV (51%) compared to white women (23%) (2). In addition, BV has considerable adverse reproductive and obstetric health consequences for women and their infants, including low birth weight, preterm birth, pelvic inflammatory disease, and HIV and other sexually transmitted infections (3). Despite the high prevalence of BV and adverse sequelae, its etiology remains poorly understood.

Although BV is related to sexual activity, its development may also depend on other nonsexual risk factors that make women more susceptible to vaginal flora imbalances. A growing body of evidence has emerged on the association between diet and nutritional status with BV (4–7), but the mechanisms remain unclear (8). Several studies have found associations between BV and poor micronutrient status, including vitamins A, C, E, and D and  $\beta$ -carotene (5,7) as well as low dietary intakes of folate, calcium, and vitamin E (4). LSVF previously assessed the association between macronutrient intake and BV in 1520 predominantly African American women 15–44 y of age and found an increased risk of BV among women with higher energy and total fat consumption (4). However, diets high in total energy and fat are often indicative of overall poorer diet quality; therefore, studying the relationship between individual nutrients and BV may be misleading due to the high correlations among nutrients within diets (9,10).

In recent years, the field of nutrition has shifted toward examining dietary indices as opposed to single nutrients, because it has become recognized that nutrients are not consumed in isolation, that individuals consuming one health-promoting nutrient also tend to consume many others, and that the specific source of nutrients may be of importance (11,12). In addition, dietary indices address the issue of multicollinearity of nutrients and may provide a better understanding of the relationship

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<sup>8</sup> Abbreviations used: BV, bacterial vaginosis; GI, glycemic index; GL, glycemic load; HEI, Healthy Eating Index; LSVF, Longitudinal Study of Vaginal Flora; NNR, Naturally Nutrient Rich.

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between diet and BV. A variety of dietary indices has been proposed, yet to date no one indicator has emerged as the gold standard. Indices that have shown utility in understanding the relationship of diet and disease outcomes include measures assessing the degree of conformance to dietary guidelines (13), measures of nutrient density, conceptualized as the concentration of micronutrients consumed per unit energy (14,15), and measures based on differing physiological response to carbohydrate-containing foods (16,17). Therefore, the objective of this paper was to examine the association between BV and several dietary indices among participants in the LSVF.

## Participants and Methods

**Study population and design.** Participants were enrolled in the LSVF between August 1999 and February 2002. Details of this study have been described previously (4,18). Briefly, the study population consisted of nonpregnant women aged 15–44 y presenting for routine care at health clinics in Birmingham, Alabama. Women were ineligible to participate if they were immunocompromised or postmenopausal or had major gynecologic surgery, were receiving antibiotics or immunosuppressive drugs, planned to move within the next 12 mo, or were nonfluent in English. The study was approved by the institutional review boards of the Jefferson County Department Health, the University of Alabama at Birmingham, and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development.

Participants were assessed at baseline and followed quarterly for 1 y. At each visit, a pelvic exam and detailed in-person interview were conducted. Vaginal flora was evaluated blinded to clinical data using Nugent Gram-stain criteria and defined as normal (Nugent score: 0–3), intermediate (Nugent score: 4–6), or BV (Nugent score: 7–10) (19). At the second study visit, the 110-item Block98 FFQ was administered (20) by trained interviewers who did not know the Gram-stain results. For administrative reasons, the Block FFQ was discontinued after the first 2005 participants completed their second visit. Demographic and behavioral characteristics did not differ between participants who completed the Block FFQ and those who did not (4).

**Dietary assessment.** The Block98 FFQ assessed annual intake and dietary data were analyzed by the Block Dietary Data System which uses the USDA Nutrient Database for Standard Reference for macro- and micronutrients (20). The dietary data were reanalyzed in 2010 for additional dietary variables, including mean daily GI, mean daily GL, and the HEI (13). Dietary data with serious errors (i.e. portions consumed were too few or many, identical serving sizes, etc.), as determined by the Block Dietary Data System, were excluded from further analyses ( $n = 265$ ).

The GI ranks carbohydrate-containing foods according to their effect on blood glucose concentration and is expressed as the percent increase in blood sugar relative to an equivalent quantity of glucose (i.e. GI of glucose = 100) (21). GI values for this analysis were obtained from the Clinical Nutrition Research Center at the University of North Carolina (22) or based on published values (21).

Both GI and GL are measures of carbohydrate quality, with the latter also representing quantity of carbohydrate consumed and applied frequently in epidemiologic studies (16). To calculate mean daily GI and GL, carbohydrate, fiber, and GI values were assigned to all food items in the questionnaire. A mean daily GL was calculated by multiplying the GI value of each food by its available carbohydrate (minus fiber) and summed across daily intake of all foods. A mean daily GI was calculated by dividing the mean daily GL by the total available daily carbohydrate and multiplied by 100.

The HEI is a measure of diet quality ranging from 0 to 100 that assesses conformance to federal dietary guidelines, with higher scores indicating greater conformance (13). The HEI was calculated using established methods of assigning scores based on adequacy of consumption of MyPyramid food groups as well as meeting guidelines for sodium, saturated fat, and cholesterol (23). An HEI score >80 implies a “good” diet, an HEI score between 51 and 80 implies a diet that “needs improvement,” and an HEI score <51 implies a “poor” diet (13).

An additional indicator of nutrient density of a diet was assessed using the NNR score (14). The NNR score was calculated from the FFQ as the unweighted arithmetic mean of percent daily values for 15 nutrients (protein, fiber, MUFA, vitamins A, C, D, E, and B-12, thiamin, riboflavin, folate, calcium, iron, zinc, and potassium) per 8370 kJ consumed.

**Statistical methods.** The association between dietary indices and BV was assessed in cross-sectional and prospective analyses. Demographic and behavioral characteristics expressed as mean  $\pm$  SD or  $n$  (%) across quartiles of dietary indices and correlations of dietary indices with total energy and fat intake were examined. Differences across quartiles were assessed using Kruskal-Wallis tests for continuous variables and chi-square tests for categorical variables. The association between dietary indices and the log odds of BV compared to normal was explored graphically using locally weighted least squares scatterplot smoothing techniques (24). Because intermediate vaginal flora represents a transitional state between normal and BV (25), cross-sectional analyses evaluated the association between different vaginal flora states (normal, intermediate, and BV) and dietary indices using multinomial logistic regression. Based on least squares scatterplot-smoothed curves, dietary indices were modeled as a continuous and a linear spline term for HEI at 70, which corresponds approximately to the 90th percentile of HEI in this population (there was no evidence of nonlinearity for other dietary indices). Models were adjusted for confounding factors chosen a priori, which included age, education, race, cigarette and alcohol use, number of sex partners since the previous visit, douching frequency, hormonal contraceptive use, and BMI. Interaction terms between the number of sex partners and dietary indices were assessed and were not significant. The high correlation of GL with total energy intake and total fat intake precluded adjustment for these variables in the model.

In the prospective analyses, BV status was classified into 4 groups based on BV status at the current visit (visit when FFQ was administered) and the subsequent follow-up visit only and defined as: 1) BV negative at both visits (non-BV maintenance); 2) BV negative at the current visit and positive at the next (BV progression); 3) BV positive at the current visit and negative at the next visit (BV resolution); and 4) BV positive at both visits (BV persistence). Logistic regression models were used to assess the association of dietary indices with BV progression, resolution, and persistence compared to maintenance of non-BV and BV resolution compared to persistence. Models were adjusted for the same confounding factors used in the cross-sectional analysis. A 2-sided  $P \leq 0.05$  was considered significant in all analyses. Data were analyzed using Stata/SE 10.1 for Windows (Stata).

## Results

The sample consisted of predominantly African American (85.5%) women ( $n = 1735$ ) aged  $25.3 \pm 6.8$  y, education of  $12.0 \pm 1.8$  y, and BMI of  $29.7 \pm 8.4$  kg/m<sup>2</sup>. The majority of women had not used alcohol (47.3%) or smoked since the prior visit (73.4%). The GI, GL, HEI, and NNR were  $55.1 \pm 3.5$ ,  $191.7 \pm 88.0$ ,  $54.2 \pm 11.1$ , and  $88.9 \pm 19.1$ , respectively. The correlation between GI and GL was 0.12 and between HEI and NNR was 0.46. The correlation of GI, GL, HEI, and NNR with total energy intake was 0.06, 0.93,  $-0.18$ , and  $-0.25$ , and with total fat was 0.14, 0.78,  $-0.38$ , and  $-0.30$ , respectively. All correlations were significant ( $P < 0.001$ ).

Quartiles of GI were associated with age, total energy intake, GL, HEI, NNR score, BMI, and alcohol use (Table 1). Quartiles of GL were associated with age, education, race, total energy intake, GI, NNR score, douching frequency, and vaginal flora (Table 1). Quartiles of HEI were associated with age, education, race, total energy intake, GI, and NNR score (Table 2). Quartiles of NNR were associated with age, education, race, total energy intake, GI, GL, HEI, smoking, number of sex partners, and vaginal flora (Table 2).

**TABLE 1** Characteristics of participants by quartiles of dietary glycemic index (GI) and glycemic load (GL)<sup>1,2</sup>

	Quartiles of dietary GI				Quartiles of dietary GL			
	1 (low)	2	3	4 (high)	1 (low)	2	3	4 (high)
<i>N</i>	435	433	434	433	434	434	434	433
Age, y	25.6 ± 7.04	24.2 ± 5.98	25.5 ± 6.77	25.9 ± 7.07*	26.3 ± 6.98	25.6 ± 7.06	25.3 ± 6.69	24.1 ± 6.07*
Education, <i>n</i> (%)								
<12 y	126 (29.0)	145 (33.3)	147 (33.7)	154 (36.0)	110 (24.7)	122 (28.5)	163 (37.8)	177 (41.0)*
12 y	188 (43.3)	162 (37.7)	166 (38.3)	174 (40.4)	174 (40.6)	177 (41.1)	174 (39.9)	165 (38.2)
>12 y	120 (27.7)	125 (28.9)	120 (17.9)	103 (23.7)	149 (34.6)	132 (30.4)	97 (22.4)	90 (20.8)
Race, <i>n</i> (%)								
Black	370 (85.7)	370 (85.7)	368 (84.8)	374 (86.3)	352 (81.1)	359 (82.9)	387 (89.2)	384 (88.9)*
White/other	65 (14.7)	62 (14.4)	66 (15.2)	58 (13.7)	82 (18.9)	74 (17.1)	47 (10.8)	48 (11.1)
Energy intake, kJ/d	11,800 ± 5980	12,900 ± 5940	12,500 ± 5100	12,700 ± 5400*	6800 ± 1800	10,100 ± 1780	13,400 ± 2340	19,600 ± 4910*
GI	50.6 ± 1.99	54.1 ± 0.70	56.4 ± 0.66	59.5 ± 1.66*	54.3 ± 3.90	55.3 ± 3.47	55.3 ± 3.38	55.7 ± 3.15*
GL	177 ± 88.8	194 ± 90.3	195 ± 79.7	201 ± 91.4*	96.5 ± 21.8	152 ± 13.8	205 ± 17.6	313 ± 67.0*
HEI	57.2 ± 11.8	54.4 ± 10.8	53.1 ± 10.9	52.1 ± 10.4*	54.8 ± 11.6	54.5 ± 11.8	53.0 ± 11.4	54.4 ± 9.61
NNR score	97.8 ± 23.1	88.5 ± 16.3	85.6 ± 18.1	83.8 ± 14.8*	96.4 ± 21.8	88.6 ± 17.7	87.5 ± 18.7	83.2 ± 15.3*
BMI, kg/m <sup>2</sup>	31.0 ± 8.42	29.6 ± 8.41	29.1 ± 8.62	29.1 ± 7.94*	29.9 ± 7.79	30.0 ± 8.04	29.9 ± 8.72	29.0 ± 8.89*
Cigarette use, <sup>3</sup> <i>n</i> (%)								
No	313 (71.9)	308 (71.7)	327 (76.6)	316 (73.3)	312 (72.6)	317 (73.2)	327 (76.4)	308 (71.5)
Yes	121 (28.1)	123 (28.3)	101 (23.4)	115 (26.7)	122 (27.4)	115 (26.9)	100 (23.7)	123 (28.5)
Alcohol use, <sup>3</sup> <i>n</i> (%)								
Never	177 (40.8)	203 (47.1)	205 (47.9)	231 (53.7)*	183 (41.9)	212 (49.1)	211 (49.4)	210 (48.7)
≤Once/mo	100 (23.3)	99 (23.0)	113 (26.4)	112 (26.0)	126 (29.3)	100 (23.2)	97 (22.7)	101 (23.4)
Once/wk – several times/mo	89 (20.3)	84 (19.3)	71 (16.6)	49 (12.1)	84 (19.4)	70 (16.2)	69 (16.4)	70 (16.2)
Several times/wk – every day	68 (15.7)	45 (10.7)	39 (9.1)	39 (8.9)	41 (9.5)	50 (11.6)	50 (11.5)	50 (11.6)
Vaginal flora, <i>n</i> (%)								
Normal	153 (35.1)	144 (33.4)	142 (33.3)	159 (37.6)	180 (41.9)	142 (33.0)	147 (34.1)	129 (30.3)*
Intermediate	91 (21.0)	94 (21.9)	90 (21.1)	104 (24.3)	89 (20.1)	93 (21.6)	98 (23.0)	99 (23.2)
BV	189 (43.8)	193 (45.0)	195 (45.7)	165 (38.1)	163 (38.0)	195 (45.4)	186 (42.9)	198 (46.5)
Number of sex partners, <sup>3</sup> <i>n</i> (%)								
0	93 (21.7)	83 (19.0)	89 (20.6)	100 (23.4)	90 (20.3)	93 (21.8)	83 (19.7)	99 (23.0)
1	308 (70.7)	310 (72.1)	315 (73.8)	311 (71.7)	322 (74.4)	312 (72.0)	307 (71.7)	303 (70.3)
2 or more	33 (7.6)	38 (8.8)	24 (5.6)	20 (4.9)	22 (5.3)	27 (6.3)	37 (8.7)	29 (6.7)
Douching frequency, <sup>3</sup> <i>n</i> (%)								
Never	243 (55.7)	255 (59.5)	236 (55.4)	233 (53.8)	251 (58.1)	249 (57.4)	235 (54.9)	232 (54.0)*
<Once/wk	139 (32.3)	139 (32.1)	133 (30.8)	150 (35.0)	147 (33.4)	142 (33.1)	139 (32.9)	133 (30.9)
Once/wk	37 (8.6)	23 (5.4)	43 (10.1)	25 (5.8)	32 (7.4)	24 (5.6)	34 (8.0)	38 (8.8)
Several times/wk – every day	14 (3.5)	13 (3.0)	16 (3.7)	23 (5.3)	4 (1.2)	17 (3.9)	18 (4.2)	27 (6.3)
Hormonal contraception, <sup>3</sup> <i>n</i> (%)								
No	207 (48.1)	199 (46.1)	199 (45.7)	206 (47.7)	197 (45.5)	203 (47.1)	195 (45.0)	216 (50.0)
Yes	227 (51.8)	233 (53.9)	234 (54.3)	226 (52.3)	236 (54.5)	230 (52.9)	238 (55.0)	216 (50.0)

<sup>1</sup> Values are *n* (%) or means ± SD. Asterisks indicate  $P \leq 0.05$  based on Kruskal-Wallis tests for continuous variables and chi-square tests for categorical variables.

<sup>2</sup> HEI, Healthy Eating Index; NNR, Naturally Nutrient Rich.

<sup>3</sup> Since the last visit.

Cross-sectional analyses assessed the association between dietary indices as continuous variables (per 10-unit increase) and vaginal flora (Table 3). In crude analyses, GL was positively and NNR inversely associated with BV compared to normal vaginal flora. After adjustment, the associations for GL and NNR remained significant ( $P = 0.037$  and  $0.025$ , respectively). BV was not associated with HEI values  $<70$ ; however, HEI values  $>70$  were associated with a reduction in BV that was significant in crude analyses and borderline significant after adjustment ( $P = 0.08$ ). Similar associations for dietary indices were found comparing intermediate to normal flora.

In prospective analyses, only GL was associated with BV progression and persistence (Table 4). The NNR score was significantly associated with BV progression in crude analyses but was borderline significant after adjustment ( $P = 0.11$ ). At HEI scores  $\geq 70$ , HEI was significantly associated with reduced

BV persistence in crude analyses, but not after adjustment for confounding factors. All significant estimates showed similar directions of associations to cross-sectional analyses. There was no association between dietary indices and women who resolved compared to those who persisted with or without BV (data not shown).

## Discussion

In this study population of predominantly African American women, dietary indices of carbohydrate quality (GI and GL) and overall diet quality (HEI and NNR) were associated with each other and with other demographic factors, including age, education, and race. Mean scores for HEI were below and for GI and GL were above means found in other U.S.-based sample populations (63.9, 50.0, and 100.2, respectively) (23,26), in-

**TABLE 2** Characteristics of participants by quartiles of the Healthy Eating Index (HEI) and Naturally Nutrient Rich (NNR) score<sup>1,2</sup>

	Quartiles of HEI				Quartiles of NNR			
	1 (low)	2	3	4 (high)	1 (low)	2	3	4 (high)
<i>n</i>	479	448	427	381	434	434	434	433
Age, y	25.0 ± 6.70	24.5 ± 6.34	25.5 ± 6.80	26.4 ± 7.09*	25.2 ± 6.40	24.6 ± 6.63	25.4 ± 7.00	26.0 ± 6.92*
Education, <i>n</i> (%)								
<12 y	175 (36.0)	168 (37.7)	133 (31.7)	96 (25.3)*	165 (37.8)	153 (35.0)	145 (33.5)	109 (25.7)*
12 y	201 (42.5)	170 (38.1)	176 (41.1)	143 (37.6)	181 (42.2)	179 (41.7)	154 (35.3)	176 (40.5)
>12 y	102 (21.5)	108 (24.2)	117 (27.2)	141 (37.1)	85 (20.0)	102 (23.3)	134 (31.2)	147 (33.8)
Race, <i>n</i> (%)								
Black	432 (90.2)	400 (89.5)	372 (87.1)	278 (73.2)*	364 (84.1)	381 (87.6)	383 (88.5)	354 (81.9)*
White/other	47 (9.8)	47 (10.5)	55 (12.9)	102 (26.8)	69 (15.9)	53 (12.4)	51 (11.5)	78 (18.1)
Energy intake, kJ/d	13,600 ± 5380	12,600 ± 5850	12,300 ± 5860	11,000 ± 4990	13,700 ± 5960	13,600 ± 5750	12,300 ± 5390	10,300 ± 4600
GI	55.9 ± 3.42	55.3 ± 3.47	55.2 ± 3.49	54.0 ± 3.45*	56.1 ± 3.24	55.7 ± 3.19	55.2 ± 3.25	53.5 ± 4.80*
GL	186 ± 79.1	194 ± 90.4	200 ± 93.9	187 ± 88.5	213 ± 93.2	205 ± 88.2	190 ± 84.8	159 ± 75.1*
HEI	40.5 ± 5.41	51.7 ± 2.26	59.1 ± 2.09	69.0 ± 5.13*	48.1 ± 9.50	51.2 ± 9.83	56.1 ± 9.85	61.4 ± 10.6*
NNR score	80.0 ± 13.9	85.6 ± 17.7	89.8 ± 17.6	103 ± 19.8*	67.9 ± 6.26	81.1 ± 2.92	92.3 ± 3.75	115 ± 15.1*
BMI, kg/m <sup>2</sup>	29.1 ± 8.04	29.5 ± 8.29	30.0 ± 8.31	30.3 ± 8.94	29.4 ± 8.36	29.6 ± 8.15	30.0 ± 8.28	29.8 ± 8.72
Cigarette use, <sup>3</sup> <i>n</i> (%)								
No	344 (72.9)	327 (73.0)	312 (73.5)	281 (74.3)	295 (68.4)	309 (72.1)	324 (75.4)	336 (77.7)*
Yes	132 (27.1)	121 (27.0)	110 (26.5)	97 (25.7)	138 (31.6)	121 (27.9)	107 (24.6)	94 (22.3)
Alcohol use, <sup>3</sup> <i>n</i> (%)								
Never	220 (46.2)	213 (47.5)	206 (48.8)	177 (46.8)	193 (44.3)	200 (46.3)	220 (51.3)	203 (47.2)
≤Once/mo	117 (24.8)	107 (23.9)	103 (24.4)	97 (25.7)	108 (25.2)	103 (24.0)	96 (22.3)	117 (27.2)
Once/wk – several times/mo	85 (17.9)	83 (18.5)	66 (15.9)	59 (15.6)	74 (17.1)	79 (18.4)	72 (16.7)	68 (16.1)
Several times/wk – every day	54 (11.3)	45 (10.0)	47 (10.9)	45 (11.9)	58 (13.4)	48 (11.4)	43 (9.7)	42 (9.5)
Vaginal flora, <i>n</i> (%)								
Normal	150 (31.7)	157 (35.6)	143 (34.0)	148 (39.0)	134 (31.0)	143 (33.7)	141 (32.9)	180 (41.7)*
Intermediate	97 (19.9)	104 (23.6)	96 (23.0)	82 (21.6)	103 (23.8)	99 (23.0)	98 (22.7)	79 (18.5)
BV	230 (48.4)	180 (40.8)	182 (43.0)	150 (39.5)	195 (45.1)	185 (43.3)	189 (44.4)	173 (39.8)
Number of sex partners, <sup>3</sup> <i>n</i> (%)								
0	99 (20.4)	96 (21.4)	83 (20.1)	87 (23.0)	78 (17.8)	97 (22.3)	93 (21.6)	97 (23.0)*
1	336 (70.8)	319 (71.2)	317 (74.6)	272 (72.0)	316 (73.0)	301 (70.0)	311 (72.4)	316 (73.0)
2 or more	41 (8.8)	33 (7.4)	22 (5.2)	19 (5.0)	39 (9.2)	32 (7.7)	27 (6.0)	17 (4.0)
Douching frequency, <sup>3</sup> <i>n</i> (%)								
Never	252 (53.4)	253 (56.5)	249 (58.5)	213 (56.4)	236 (54.5)	219 (51.3)	257 (59.8)	255 (58.8)
<Once/wk	162 (33.8)	145 (32.4)	127 (30.6)	127 (33.6)	144 (33.0)	155 (35.9)	124 (28.8)	138 (32.6)
Once/wk	43 (9.1)	25 (5.6)	33 (7.8)	27 (7.1)	32 (7.4)	38 (8.9)	31 (7.2)	27 (6.3)
Several times/wk – every day	17 (3.8)	25 (5.6)	13 (3.1)	11 (2.9)	21 (5.1)	17 (4.0)	18 (4.2)	10 (2.3)
Hormonal contraception, <sup>3</sup> <i>n</i> (%)								
No	246 (51.4)	197 (44.1)	190 (44.9)	178 (46.8)	214 (49.2)	208 (47.7)	187 (43.7)	202 (47.1)
Yes	233 (48.6)	250 (55.9)	235 (55.1)	202 (53.2)	219 (50.8)	226 (52.3)	246 (56.4)	229 (52.9)

<sup>1</sup> Values are *n* (%) or means ± SD. Asterisks indicate  $P \leq 0.05$  based on Kruskal-Wallis tests for continuous variables and chi-square tests for categorical variables.

<sup>2</sup> GI, glycemic index; GL, glycemic load.

<sup>3</sup> Since the last visit.

dicating a poorer diet among women in our study. A more healthful diet, as indicated by GL, NNR, and HEI indicating >70% conformance to dietary guidelines, was associated with a lower odds of BV compared to normal vaginal flora. However, only variation in GL remained significantly associated with BV in both cross-sectional and prospective analyses after adjustment for other covariates.

Our findings of a lower likelihood of BV among those consuming more healthful diets are consistent with other studies that report an association between nutritional status and BV (4–7). Unlike those studies, which were limited to assessing individual macro- or micronutrients, our study evaluated the effect of overall diet and carbohydrate quality on BV prevalence, progression, and persistence. Dietary indices have utility in epidemiologic studies and in demonstrating lowered risk of mortality and morbidity (11,16). With the exception of vitamin

D, which can be obtained from nondietary sources (i.e. UV-B exposure), intakes of nutrients are often correlated. Thus, dietary indices may be a more useful method of evaluation, because they address multicollinearity of nutrients and provide a useful target for nutritional interventions that capture the complexity of the human diet.

These results may be important for elucidating the etiology of BV. In particular, GL, but not GI, was consistently associated with BV prevalence, progression, and persistence. Both the source and amount of carbohydrate can influence an individual's glycemic response to a food or meal (27). Chronic exposure to postprandial rises in glucose may have adverse health effects and have been linked to diabetes, coronary heart disease, and cancer (28–35). Continual exposures to postprandial hyperglycemia may trigger oxidative damage through a reduction in plasma antioxidant defenses and increased inflammation due to free

**TABLE 3** Crude OR (cOR) and adjusted OR (aOR) for the relationship between dietary indices and vaginal flora assessed by Nugent Gram-stain criteria<sup>1-3</sup>

Dietary index	Intermediate flora (Nugent: 4-6)				BV (Nugent: 7-10)			
	cOR	95% CI	aOR <sup>4</sup>	95% CI	cOR	95% CI	aOR <sup>4</sup>	95% CI
Daily GI	1.28	0.89-1.85	1.26	0.86-1.87	0.92	0.68-1.25	0.99	0.71-1.38
Daily GL	1.02	1.00-1.03	1.01	1.00-1.03	1.02	1.01-1.03	1.01	1.00-1.03
HEI <sup>5</sup>								
<70	1.01	0.89-1.15	1.04	0.91-1.20	0.94	0.84-1.05	0.99	0.88-1.11
>70 <sup>6</sup>	0.44	0.19-1.02	0.49	0.21-1.15	0.38	0.19-0.78	0.48	0.23-1.04
NNR score	0.89	0.83-0.95	0.90	0.84-0.97	0.93	0.88-0.98	0.93	0.88-0.99

<sup>1</sup> Change in odds of intermediate flora or BV compared to normal flora (Nugent: 0-3) per 10-unit increase in corresponding dietary index value.

<sup>2</sup>  $n = 1719$  in crude analyses and  $n = 1644$  in adjusted analyses.

<sup>3</sup> aOR, adjusted OR; BV, bacterial vaginosis; cOR, crude OR; GI, glycemic index; GL, glycemic load; HEI, Healthy Eating Index; NNR, Naturally Nutrient Rich.

<sup>4</sup> Models adjusted for age, race, education, cigarette smoking, alcohol use, BMI, douching frequency, hormonal contraceptive use, and number of sex partners.

<sup>5</sup> Spline term with node at 70; OR correspond to the slopes < and > HEI = 70.

<sup>6</sup>  $P$  for the difference between slopes < and > HEI = 70 are 0.13 and 0.10 for crude and adjusted intermediate flora and 0.10 and 0.08 for crude and adjusted BV, respectively.

radical production (36,37). It is also known that women with diabetes, especially those with poor glycemic control, are more likely to be affected by genital tract infections (38,39). We could not distinguish the independent effects of GL and total energy or fat intake on BV given the high correlation between these variables in this study. Nevertheless, the biologic mechanism may be similar, given that even large amounts of low-GI foods may result in high spikes in postprandial glucose (40). Thus, it is plausible that chronic exposure to high-GL, energy-dense diets may affect host response to bacterial colonization and, in particular, the pathogenesis of BV through oxidative stress and impaired immune function.

Alternatively, diet may influence the microbial population of mucosal surfaces in the gastrointestinal and reproductive tracts. Studies conducted in mice suggest dietary factors, in particular high-fat diets, alter the composition of the gut microbiome (41). In turn, bacterial colonization of the gut may function as a reservoir for vaginal microbiota. A study by Antonio et al. (42) found concordance between *Lactobacillus* species in the rectum and vagina, suggesting that the rectum may serve as a potential source for vaginal colonization. The authors speculate that

adherence properties of specific bacteria in the rectum may determine what species adhere to vaginal epithelium.

There are several strengths of this study. Studies have validated the original Block FFQ in several populations, including ones similar to this study population (43,44), and the updated Block98 FFQ used in this study (45,46) but have not been specifically validated for the indices used in this study. Our outcome variable, the Nugent score, is currently the gold standard for assessment of vaginal flora in research settings (47). As previously mentioned, dietary indices have the advantage of accounting for multicollinearity and complexity of dietary nutrients. Finally, the association of BV with different dietary indicators was evaluated both cross-sectionally and prospectively after adjustment for several demographic and lifestyle factors among a large population of women with consistent results across different levels of vaginal flora disruption (i.e. intermediate and BV) and over time (BV progression and persistence).

Our ability to generalize these findings to other populations is limited given the geographic location and the majority of women in this sample were African American. In addition, there was

**TABLE 4** Crude OR (cOR) and adjusted OR (aOR) for the relationship between dietary indices and bacterial vaginosis (BV) progression and persistence<sup>1,2</sup>

Dietary index	BV progression <sup>3</sup>				BV persistence <sup>4</sup>			
	cOR	95% CI	aOR <sup>5</sup>	95% CI	cOR	95% CI	aOR <sup>5</sup>	95% CI
Daily GI	0.98	0.60-1.61	1.03	0.61-1.75	0.82	0.58-1.16	0.99	0.67-1.46
Daily GL	1.03	1.01-1.05	1.03	1.00-1.05	1.02	1.01-1.04	1.02	1.01-1.04
HEI <sup>6</sup>								
<70	0.88	0.74-1.04	0.93	0.77-1.13	0.91	0.80-1.04	0.94	0.82-1.08
>70	0.58	0.16-2.13	0.84	0.24-2.95	0.34	0.12-0.97	0.51	0.17-1.50
NNR score	0.90	0.82-0.99	0.92	0.83-1.02	0.95	0.89-1.01	0.94	0.87-1.01

<sup>1</sup> Change in odds of BV progression or persistence compared to non-BV maintenance per 10-unit increase in corresponding dietary index value.

<sup>2</sup> GI, glycemic index; GL, glycemic load; HEI, Healthy Eating Index; NNR, Naturally Nutrient Rich.

<sup>3</sup>  $n = 753$  in crude analyses and  $n = 738$  in adjusted analyses.

<sup>4</sup>  $n = 976$  in crude analyses and  $n = 962$  in adjusted analyses.

<sup>5</sup> Models adjusted for age, race, education, cigarette smoking, alcohol use, BMI, douching frequency, hormonal contraceptive use, and number of sex partners.

<sup>6</sup> Spline term with node at 70; OR correspond to the slopes < and > HEI = 70.

little variability in participants' diets compared to other U.S. populations (23,26). Unmeasured confounding may also be present if women who consume a particular diet also exhibit other health-related behaviors that increase their risk of BV, such as riskier sex, personal hygiene, or physical activity. To account for some of these factors, we adjusted for number of sex partners and douching frequency and found no change in inference. We controlled for BMI, but physical activity was not measured in this study and may also confound the association between BV and GL. We are not aware of any studies that have assessed the relationship between physical activity and BV and think this is an important area for future study.

Finally, it is generally recognized that associations between dietary indices and disease may be sensitive to slight differences in how those indices are calculated (11). The merits of the GI concept have been debated, without consensus, since its introduction, particularly owing to technical limitations in its calculation (48). A criticism of the GI is that the values can be imprecise, because they are significantly altered by factors including processing, ripeness, and cooking methods and that it does not account for the effect of carbohydrate quantity on the glycemic response. GL addresses this latter limitation by quantifying the overall glycemic effect of the diet but is still limited by imprecision from its calculation based on the GI. Output from the Block98 FFQ did not enable us to calculate an updated HEI (HEI-2005) in our study. In addition, the most currently proposed nutrient density measure is the Nutrient Rich Foods index (49); however, there are numerous nutrient density measures with no clear gold standard. Calculation of the Nutrient Rich Foods index required information on added sugars, which was not provided in the Block98 FFQ analysis. Therefore, we calculated another measure of nutrient density, the NNR, to assess this concept in our study (14). Despite these limitations, the consistency of associations across several dietary indices and vaginal flora measures demonstrates the robustness of our findings.

Our results suggest that BV is associated with dietary indices. Because this study included primarily African American women in the South, epidemiologic studies should be conducted to explore whether this relationship is consistent in other populations. Future studies investigating dietary and biochemical indicators of nutritional status, physical activity, and the role of diet in changes to gut and vaginal microbiome may further elucidate biologic mechanisms for these findings.

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W.A., M.K., Y.N., and J.S. designed research; W.A., Y.N., and J.S. conducted research; M.E.T. analyzed data; M.E.T., M.K., A.R., T.N., Y.N., W.A., and J.S. wrote the paper; and M.E.T. had primary responsibility for final content. All authors read and approved the final manuscript.

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