Nutrition, an Under-Recognized Factor in Bacterial Vaginosis

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Suboptimal nutrition can alter immune function and increase susceptibility to infections. Previous research has focused on the association of nutrition, particularly micronutrient vitamins and minerals and, in more recent decades, dietary fats and fatty acids, with a spectrum of infections ranging from measles, diarrheal disease, acute and chronic respiratory tract infections, and more recently, with human papilloma virus (HPV)² and HIV (1). Little is known, however, about the association of nutrition with infections of the lower reproductive tract (LRTI), even though immune mechanisms in the lower reproductive tract are critically important for the prevention of LRTI and HIV infection (2). In this issue of The Journal of Nutrition, Neggers et al. (3) report on nutritional factors that may contribute to increased bacterial vaginosis in a study of 15- to 45-y-old non-pregnant women.

Genital tract infections are common in women. Organisms frequently considered responsible for symptomatic infections include group B Streptococi, Neisseria gonorrhoea, Chlamydia trachomatis, Candida albicans, Gardnerella vaginalis, and Trichomonas vaginalis (4). Bacterial vaginosis (BV) is the single most common LRTI in women of childbearing age. It involves a shift from the predominant hydrogen–peroxide producing bacteria to a polymicrobial flora that results in high vaginal pH. BV is associated not only with great discomfort, but in case of pregnant women, it is also associated with an increased risk of premature rupture of membranes and consequently premature birth (5) and reviewed in (4)). In addition, BV strongly increases the risk of acquiring other sexually-transmitted infections such as N. gonorrhoea, Chlamydia, and HIV in both pregnant and nonpregnant women (6) and reviewed in (7)).

The risk factors for BV comprise several sociodemographic factors, including race and lifestyle/behavorial factors such as smoking, IUD contraceptive use, douching, sexual behavior-related factors, and stress. In recent years, researchers have begun to hypothesize that nutrition is another putative risk factor for BV. This hypothesis, although biologically grounded, has been examined only in few cross-sectional studies across the world (4,7–9).

The study by Neggers et al. (3) is the first, to our knowledge, to report the association of BV with dietary intakes (energy, as well as macro and micro-nutrients) in 15- to 45-y-old nonpregnant women. This study is also unique because of its prospective design and follow-up with subjects over a number of visits to examine the evolution of the infection. Another interesting feature of this study is that, for statistical analyses purposes, BV was considered in 2 ways: BV (defined by Nugent score ≥7) and severe BV (Nugent score ≥9 and vaginal pH ≥5). For each nutrient, intakes were considered as quartiles and OR were obtained using the lowest quartile as the reference group.

Noteworthy findings from this study show that after adjusting for demographic and behavioral covariates, at baseline, the risk of BV was 40% higher in women who had a high energy intake (P = 0.05). Over follow-up, ~19% women who started the study without BV (n = 893), developed BV by the follow-up visit (visit 3). Interestingly, total energy intake was the only nutrient that remained marginally associated with incident BV (adjusted OR: 1.7; 95% CI: 1.0–2.9). Although this association was only marginally significant both for the entire study sample and for incident cases of BV, its consistency in the 2 situations suggests its importance and warrants further consideration in future investigations. Secondly, among all the macro- and micro-nutrients examined, only total fat was significantly associated with BV in the entire study sample; compared with Quartile 1 of fat intake, presence in Quartile 4 was associated with a 50% higher frequency of BV (95% CI: 1.1–2.4). When the relationship of nutrient intake with severe BV (Nugent score ≥9 and vaginal pH ≥5) was examined in adjusted models, the higher fat intake remained associated with higher frequency of BV. In addition, inverse associations were noted between severe BV and intake of protein, vitamin E, folic acid, and calcium: adjusted OR for each of these nutrients fell between 0.4 and 0.5 (P < 0.05). The findings of the study generally fit well with the roles of these nutrients in modulating immune function, which have been previously described (1). The strengths of the study include its large sample size covering a broad age range (15–45 y) and simultaneous adjustment for demographic and lifestyle factors, as well as energy intake, when appropriate, in the logistic regression models.

In summary, the findings by Neggers et al. (3) demonstrate the importance of optimal nutrition in BV infection. These results were obtained using the Block’s validated FFQ, which
estimates long-term nutrient intakes but is subject to some measurement error (10). This imprecision does not induce a bias that could create the observed significant associations (between BV and high intake of fat, as well as between BV and low intakes of vitamin E and folic acid). However, it could partly explain the lack of associations found between BV and other micronutrients (such as iron, zinc, and vitamins A, C, and D), for which immunomodulatory effects have been previously described (1). Furthermore, it is well-recognized that the absorption of many nutrients is affected by several dietary and physiologic factors. Thus, only nutrient levels in body fluids or tissues can provide a precise assessment of nutritional status. Indeed, by using blood-based tests, an association between elevated levels of serum transferrin receptors (considered a specific test for subclinical iron deficiency) and BV was shown (7). Moreover, in a recent large cross-sectional study of women with or at risk of HIV in the US, Tohill et al. (9) found that, in regression models adjusted for several potentially confounding variables, lower serum concentrations of vitamins A, C, and E, and β-carotene were associated with BV, and lower iron status (as measured by elevated serum total iron-binding capacity) was associated with increased prevalence of Candida colonization. Higher concentrations of serum zinc were also associated with lower risk of HPV in that study (9). Taken together, the findings of these two recent studies (3,9) for the first time provide ample critical evidence for the role of suboptimal nutrition in BV and other common gynecological infections in women of childbearing age.

These novel findings need to be confirmed in future prospective, and perhaps intervention, studies that could address a larger question pertaining to the relationship of LRTI, including BV, with nutrition. The latter should be assessed comprehensively via dietary intake and biochemical assessment whenever possible. In addition, because both studies (3,9) were conducted with primarily African American subjects, there is a need to address these questions in future studies with Caucasians, and with women in developing countries in whom LRTI are highly prevalent (6,11). Furthermore, because nutrient-nutrient interactions occur in the body, and nutrient imbalance usually occurs for multiple nutrients simultaneously, it may be of interest to examine several nutrients simultaneously in the statistical models (12). Such clinical studies need to be complemented with examination of the underlying biological mechanisms. The next steps ahead include sharing these findings with gynecologists, obstetricians, and general practitioners, as well as increasing the awareness of the general community to the importance of optimal nutrition, i.e., neither over- nor undernutrition, to prevent infections of the genital tract, reduce associated morbidity, and maintain reproductive health.

**Literature Cited**


