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The Role of Bacterial Vaginosis in Infection After Major Gynecologic Surgery

L. Lin,[1]* J. Song,[1] N. Kimber,[1] S. Shott,[2] J. Tangora,[1]
A. Aroutcheva,[1] M.B. Mazees,[1] A. Wells,[1] A. Cohen,[1] and S. Faro[1]

[1]*Department of Obstetrics and Gynecology, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL*
[2]*Biostatistics Unit, Department of Neurosurgery, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL*

Abstract

Purpose: Previous studies have reported an association between bacterial vaginosis (BV) and postoperative fever and infection. This prospective study investigated whether the intermediate or definite stages of BV are risk factors for postoperative infection after major gynecologic surgery.

Methods: Vaginal cultures were obtained preoperatively from 175 women undergoing gynecologic surgery. The diagnostic criteria for BV were based on Nugent's standardized method of Gram stain interpretation. Postoperative fever was defined as at least one temperature equal to 101.0°F or greater, or two or more temperatures more than 6 hours apart equal to 100.4°F or greater.

Results: Thirty-six percent of the positive-BV group developed a postoperative fever, compared with 20% of the *Lactobacillus*-predominant group and 12% of the intermediate-BV group (P = 0.017). The differences between the positive-BV group and the *Lactobacillus*-predominant group, and between the positive-BV group and the intermediate-BV group, with respect to postoperative fever, were statistically significant (P = 0.045 and P = 0.007, respectively). The difference between the intermediate-BV group and the *Lactobacillus*-predominant group was not statistically significant (P = 0.28).

Conclusions: Although the association between BV and postoperative febrile morbidity could be a spurious result of confounding with other variables, it may be prudent for the surgeon to identify patients with BV and treat them preoperatively. Infect. Dis. Obstet. Gynecol. 7:169–174, 1999.

Key words
postoperative fever; vaginal microflora; lactobacilli

Postoperative fever and infection continue to be significant complications of major gynecologic surgery. The reported incidence of postoperative infection in women without antibiotic prophylaxis ranges from 9 to 50%.[1,2] Factors related to infection include age, obesity, indication for surgery, type of surgery, duration of procedure, and amount of perioperative bleeding.[3,4] Soper et al.[5,6] and Larsson et al.[7] have reported an association between bacterial vaginosis and vaginal cuff cellulitis after abdominal hysterectomy. Person et al.[8] found that infection after gynecologic surgery was associated with bacterial vaginosis (BV).

One of the major challenges in the evaluation of BV is the widely varying and subjective clinical criteria used for diagnosis. The literature describes BV in a variety of ways. The most widely accepted clinical method of evaluation requires any three of the following four criteria to establish a diagnosis: a vaginal pH greater than 4.5, the presence of clue cells in the vaginal fluid, a milky homogenous discharge, and the release of an amine (fishy) odor

*Correspondence to: Dr. Larry Lin, 1540 W. Harrison, Apt. 3D, Chicago, IL 60612.

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after the addition of 10% hydrogen peroxide to the vaginal fluid.[9] The subjective interpretation of these signs can be very different, particularly with respect to the recognition of clue cells in the wet mount preparation of the vaginal fluid. This often leads to discrepant diagnoses.[10]

A more objective and reproducible measure than the direct wet-mount exam is the Gram-stained vaginal smear, which has 62 to 100% sensitivity and a positive-predictive value of 76 to 100%.[10,11,12,13] Nugent's criteria for interpreting Gram-stained smears for the diagnosis of BV have good to excellent intraobserver reproducibility[14] and correlate well with clinical signs and vaginal culture results.[15] This scoring system also allows for gradation of the severity of BV, from normal flora (*Lactobacillus* predominant) to intermediate (mixed flora) to BV. This allows the inclusion of patterns that are a combination of normal flora and BV. Nugent's criteria appear well suited for evaluating the vaginal ecosystem since the process of the development of BV is an evolution from a healthy vaginal ecosystem to a disrupted ecosystem.

Bacterial vaginosis has a complex microbiology. The development of BV is not an all-or-none phenomenon but rather a continuum of events and changes in the vaginal ecosystem. By examining the progression of BV from normal to intermediate to a predominance of BV, a better understanding of the possible impact of each stage on postsurgical infection may be achieved. Previous studies have examined BV as either present or absent. Our study looks at the significance of the intermediate stage of BV, characterized by reduced *Lactobacilli.* Few studies have prospectively examined the characteristics of these three vaginal flora patterns in the obstetric population,[15] and no studies have investigated them in the gynecologic population. The aim of this study was to investigate whether the intermediate or definite stages of BV are risk factors for postoperative infection after major gynecologic surgery.

MATERIALS AND METHODS

A total of 175 women were consecutively chosen and followed prospectively in this study. Vaginal cultures were obtained preoperatively for nonpregnant patients undergoing major gynecologic surgery, which included benign gynecologic, urogynecologic, and gynecologic oncology cases. All women who presented for such surgery from July 1997 through October 1997 were candidates for this study. Data were obtained for the following variables: age, gravidity, parity, diagnosis, surgical procedure, preoperative and postoperative antibiotic use, preoperative and postoperative complete blood count, length of surgery, estimated blood loss, complications, and postoperative fever. Each patient was identified only by a code to ensure confidentiality.

Specimens were obtained in a uniform fashion from the lower third of the vagina using a Culturette II transport medium (Becton-Dickinson, MD). Specimens were taken prior to any preoperative povidone iodine preparation and were transported to the laboratory at ambient temperature for analysis within 1 hour of collection. The vaginal smear was air-dried and Gram stained using safranin as the counterstain.

The diagnostic criteria for BV were based on Nugent's standardized method of Gram-stain interpretation. Each Gram-stained smear was evaluated under oil immersion (1,000 magnification) for the following three bacterial morphotypes: large gram-positive rods (*Lactobacilli*), small gram-negative or small gram-variable rods (bacteroides or *Gardnerella vaginalis*), and curved gram-negative to gram-variable rods (Mobiluncus).[1] Each morphotype was quantitated from 1+ to 4+ with respect to the number of morphotypes per oil immersion field (0 = no morphotypes; 1+ = less than 1 morphotype; 2+ = 1 to 4 morphotypes; 3+ = 5 to 30 morphotypes; 4+ = 30 or more morphotypes).[16] The weighted quantitative sum of the morphotypes was then used to develop a 0- to 10-point scoring system for the diagnosis of BV.[16] The criterion for BV was a score of 7 or higher; a score of 4 to 6 was considered intermediate (mixed flora), and a score of 0 to 3 was considered normal vaginal flora (*Lactobacillus* predominant).[16]

The surgical procedures were classified into four types with respect to invasiveness: 1) peritoneum not entered vaginally or abdominally (e.g., Burch procedure); 2) peritoneum entered vaginally but not abdominally (e.g., vaginal hysterectomy); 3) peritoneum entered abdominally but not vaginally (e.g., exploratory laparotomy); and 4) peritoneum

TABLE 1. Characteristics of study sample (mean ± standard deviation of % within BV group)

Characteristic	Total sample (n = 175)	Bacterial vaginosis: *Lactobacillus*-predominant (n = 80)	Bacterial vaginosis: Intermediate (n = 48)	Bacterial vaginosis: Positive (n = 47)	*P* value
Age (y)	48.7 ± 12.5	48.6 ± 12.8	50.5 ± 13.2	47.0 ± 11.2	0.43
Gravidity	2.8 ± 2.4	2.7 ± 2.1	3.0 ± 2.9	3.0 ± 2.4	0.86
Parity	2.1 ± 2.0	2.0 ± 1.6	2.3 ± 2.6	2.0 ± 1.7	0.95
Race					
African-American	45	38	44	61	0.34
White	50	58	51	33	
Hispanic	4	3	5	6	
Other	1	2	0	0	
Duration of surgery (h)	2.8 ± 1.2	2.4 ± 1.0	3.0 ± 1.3	2.9 ± 1.3	0.16
Preoperative WBC	7.3 ± 2.6	7.1 ± 2.3	7.2 ± 2.6	7.5 ± 3.1	0.77
Postoperative WBC	11.6 ± 3.7	11.7 ± 3.8	11.5 ± 3.8	11.4 ± 3.6	0.99
Peritoneum entry					0.086
Neither vaginal nor abdominal	5	6	0	2	
Vaginal only	11	8	6	6	
Abdominal only	39	38	13	17	
Vaginal and abdominal	45	39	28	22	
Pre/perioperative antibiotics given	89	88	92	89	0.76
Antibotic type					
Cefazolin only	41	46	38	34	0.42[a]
Cefoxitin only	33	25	40	38	
Clindamycin only	6	6	2	8	
Gentamycin + ampicillin	6	9	4	2	
Gentamycin + clindamycin	2	0	4	2	
Ciprofloxacin + metronidazole	1	1	0	2	
Ampicillin only	1	0	0	2	
Gentamycin + cefoxitin	1	0	2	0	
Gentamycin + vancomycin	1	0	2	0	
None	11	12	8	11	

[a]P value for comparison of BV groups with respect to % receiving cefazolin only, % receiving cefoxitin only, and % receiving other antibiotics.

entered both vaginally and abdominally (e.g., total abdominal hysterectomy). Postoperative fever was defined as at least one temperature equal to 101.0°F or greater or two or more temperatures more than 6 hours apart equal to 100.4°F or greater.

Preoperative antibiotics were given based on risk factors, according to physician discretion. Most patients (86%) received preoperative antibiotics. When given, antibiotics were administered within an hour of incision time. The specific antibiotic administered was at the discretion of the patient's surgeon.

SPSS for Windows (version 7.5) was used for data management and statistical analysis. The chi-square test of association was used to compare groups with respect to nominal variables, and the nonparametric Mann-Whitney test was done to compare groups with respect to non-nominal variables that were statistically non-normal. A 0.05 significance level was used for all statistical tests. Means are presented as mean standard deviation.

RESULTS

A total of 199 women had major gynecologic surgery during the 4 months of study. Twenty-four women were excluded from the analysis because of missing data, leaving a total sample of 175 women. Characteristics of the study sample are summarized in Table 1. Most women (89%) received preoperative or perioperative antibiotics, with cefazolin alone (41%) and cefoxitin alone (33%) the most commonly given antibiotics.

Forty-six percent of the patients had *Lactobacillus*-predominant vaginal microflora, 27% had an intermediate BV vaginal microflora, and 27% had a BV vaginal microflora. There were no statistically significant differences between the three BV groups with respect to age, gravidity, parity, race,

TABLE 2. Preoperative and operative characteristics and postoperative fever

Characteristic	Postoperative fever (%)	χ^2 test *P* value
Vagina entered during procedure		0.16
No	18	
Yes	26	
Pre-/perioperative antibiotics given		0.19
No	10	
Yes	24	
BV		0.017
Lactobacillus predominant	20	
Intermediate	12	
Positive	36	
Pre-/perioperative antibiotic type (for patients given antibiotics)		0.72
Cefazolin only	21	
Cefoxitin only	25	
Other antibiotic(s)	29	
Vagina not entered during procedure (n = 74)		0.11
Lactobacillus predominant	14	
Intermediate BV	8	
Positive BV	33	
Vagina entered during procedure (n = 98)		0.09
Lactobacillus predominant	28	
Intermediate BV	15	
Positive BV	39	
Preoperative antibiotics not given (n = 19)		—[a]
Lactobacillus predominant	10	
Intermediate BV	0	
Positive BV	20	
Preoperative antibiotics given (n = 156)		0.024
Lactobacillus predominant	21	
Intermediate BV	14	
Positive BV	38	

[a]Sample size too small for χ^2 test.

duration of surgery, preoperative or postoperative WBC, invasiveness of the surgery, or use of preoperative antibiotics (Table 1).

Table 2 describes relationships between preoperative and operative characteristics and postoperative fever. Although the percentage of patients with postoperative fever was higher for procedures in which the vagina was entered than for other procedures (26% versus 18%), this difference was not statistically significant. Postoperative fever was also more common in patients who received preoperative or perioperative antibiotics (24% versus 10%), but this difference was not statistically significant. The higher rate of postoperative fever associated with pre/perioperative antibiotic use may reflect a tendency to use antibiotics in patients who are at higher risk of postoperative infection. No statistically significant difference was found between cefazolin alone, cefoxitin alone, and other antibiotics with respect to the postoperative fever rate.

There was a statistically significant difference between the three BV groups with respect to postoperative fever ($P = 0.017$): 36% of the positive-BV group developed postoperative fever, compared with 20% of the *Lactobacillus*-predominant group and 12% of the intermediate-BV group (Table 2). Further significance testing found that the differences between the positive-BV group and the *Lactobacillus*-predominant group, and between the positive-BV group and the intermediate-BV group, with respect to postoperative fever, were statistically significant ($P = 0.045$ and $P = 0.007$, respectively). The difference between the intermediate-BV group and the *Lactobacillus*-predominant group was not statistically significant ($P = 0.28$).

The relationship between BV and postoperative fever was further evaluated by separately analyzing patients with procedures in which the vagina was entered versus other patients, as well as patients who were given preoperative antibiotics versus other patients (Table 2). For procedures in which the vagina was entered, the postoperative fever rate was higher in the positive-BV group (39%) than in the *Lactobacillus*-predominant group (28%) and the intermediate-BV group (15%). For procedures in which the vagina was not entered, the postoperative fever rate remained higher in the positive-BV group (33%) than in the *Lactobacillus*-predominant group (14%) and the intermediate-BV group (8%). Although these differences were not statistically significant, this may be due to the loss of statistical power when the sample was subdivided for these analyses.

Only 19 patients did not receive preoperative or perioperative antibiotics, an insufficient sample size for comparison of the BV groups within this subgroup. For the 156 patients who received pre/perioperative antibiotics, the postoperative fever rate was higher in the positive-BV group (38%) than in the *Lactobacillus*-predominant group (21%) and the intermediate-BV group (14%), a statistically significant difference ($P = 0.024$). Further significance testing found that the difference between the positive-BV group and the intermediate-BV group with respect to postoperative fever was sta-

tistically significant (P = 0.009). The differences between the *Lactobacillus*-predominant group and the positive-BV group and the intermediate-BV group were not statistically significant (P = 0.056 and P = 0.30, respectively).

DISCUSSION

Bacterial vaginosis comprises many different species, each with a different impact on the vaginal flora. *Lactobacillus* exerts a protective effect in the vagina by producing hydrogen peroxide and bacteriocins and by lowering the pH, thereby inhibiting the colonization of the vagina by BV-associated organisms.[17,18,19,20] However, when the host defenses are impaired, the patient is at higher risk of pelvic infection. Opportunistic pathogens such as Prevotella, Peptostreptococcus, *Bacteroides*, and *Gardnerella vaginalis* can grow in higher concentrations in the lower genital tract, leading to pelvic complications such as chorioamnionitis, postpartum endometritis, pelvic inflammatory disease, postoperative gynecologic infections, and increased risk of preterm labor.[5,7,8,20–25] In this prospective study, positive BV was associated with a statistically significant increased risk of postoperative fever, compared with *Lactobacillus* predominant and intermediate BV.

Intermediate BV may play an important role in the vaginal ecosystem, even though it was not associated with an increased risk of postoperative fever in our study. As the ecosystem changes from healthy vaginal flora that is *Lactobacillus* predominant to one with a decreasing number of lactobacilli and an increasing number of anaerobes, the protective ability of the vaginal flora is weakened. Hillier et al.[15] reported an association between intermediate BV and an increased risk of infection in pregnant women. Group B streptococci and yeast were associated with normal flora, while *Neisseria gonorrhoeae* and *Chlamydia trachomatis* were recovered more frequently in women who were intermediate or positive for BV. *Trichomonas vaginalis* was associated with intermediate BV. The use of antibiotics was significantly linked with intermediate BV, suggesting that intermediate BV may result from incomplete treatment of BV or the killing of *Lactobacilli* by antibiotic therapy.

The serious morbidity of pelvic infection associated with gynecologic surgery makes identification of risk factors a high priority in reducing the patient's risk for adverse outcome. This study found a statistically significant, positive association between the presence of BV at the time of surgery and the incidence of postoperative febrile morbidity. Although we cannot rule out the possibility that this finding may be a spurious result of confounding with other variables, it may be prudent for the surgeon to identify patients with BV and treat them preoperatively. An effort to return the vaginal ecosystem to one that is dominated by *Lactobacillus* at the time of surgery may decrease the incidence of postoperative febrile and infectious morbidity. The questions that remain to be studied are: (1) Does BV really expose the patient to significant risk of developing postoperative pelvic infection? (2) Is the patient with BV undergoing gynecologic surgery and receiving standard cephalosporin prophylaxis likely to fail antibiotic prophylaxis? and (3) Would the patient with BV undergoing gynecologic surgery benefit from receiving metronidazole rather than a first-generation cephalosporin for antibiotic prophylaxis?

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