

Screening and Management of Bacterial Vaginosis in Pregnancy

This guideline has been prepared by the Infectious Diseases Committee and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Disclosure statements have been received from all members of the committee.

Values: The evidence obtained was rated using the criteria developed by the Canadian Task Force on Preventive Health Care.

Benefits, Harms, and Costs: Guideline implementation will assist the practitioner in developing an approach to the diagnosis and treatment of bacterial vaginosis in pregnant women. Patients will benefit from appropriate management of this condition.

Validation: These guidelines have been prepared by the Infectious Diseases Committee of the SOGC, and approved by the Executive and Council of the SOGC.

Sponsors: The Society of Obstetricians and Gynaecologists of Canada.

Recommendations

There is currently no consensus as to whether to screen for or treat bacterial vaginosis in the general pregnant population in order to prevent adverse outcomes, such as preterm birth.

1. In symptomatic pregnant women, testing for and treatment of bacterial vaginosis is recommended for symptom resolution. Diagnostic criteria are the same for pregnant and non-pregnant women. (I-A)
2. Treatment with either oral or vaginal antibiotics is acceptable for achieving a cure in pregnant women with symptomatic bacterial vaginosis who are at low risk of adverse obstetric outcomes. (I-A)
3. Asymptomatic women and women without identified risk factors for preterm birth should not undergo routine screening for or treatment of bacterial vaginosis. (I-B)
4. Women at increased risk for preterm birth may benefit from routine screening for and treatment of bacterial vaginosis. (I-B)
5. If treatment for the prevention of adverse pregnancy outcomes is undertaken, it should be with metronidazole 500 mg orally twice daily for seven days or clindamycin 300 mg orally twice daily for seven days. Topical (vaginal) therapy is not recommended for this indication. (I-B)
6. Testing should be repeated one month after treatment to ensure that cure was achieved. (III-L)

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INTRODUCTION

Bacterial vaginosis is the most common lower genital tract disorder among women of reproductive age (pregnant and non-pregnant) and the most prevalent cause of vaginal discharge and malodour.^{1,2} It has been associated

Abstract

Objective: To review the evidence and provide recommendations on screening for and management of bacterial vaginosis in pregnancy.

Options: The clinical practice options considered in formulating the guideline.

Outcomes: Outcomes evaluated include antibiotic treatment efficacy and cure rates, and the influence of the treatment of bacterial vaginosis on the rates of adverse pregnancy outcomes such as preterm labour and delivery and preterm premature rupture of membranes.

Evidence: Medline, EMBASE, CINAHL, and Cochrane databases were searched for articles, published in English before the end of June 2007 on the topic of bacterial vaginosis in pregnancy.

Key Words: Bacterial vaginosis, pregnancy, screening, treatment

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Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of Evidence Assessment*	Classification of Recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action
	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.¹²

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with a significant number of obstetric and gynaecologic complications, such as preterm labour and delivery, preterm premature rupture of membranes, spontaneous abortion, chorioamnionitis, postpartum endometritis, post-Caesarean delivery wound infections, postsurgical infections, and subclinical pelvic inflammatory disease.³⁻¹¹ The purpose of this guideline is to review the literature and evidence for approaches to the screening and management of bacterial vaginosis in pregnancy. The quality of evidence reported in these guidelines has been described using the criteria of the Canadian Task Force on Preventive Health Care¹² (Table 1).

MICROBIOLOGY

Normal vaginal flora consists of both aerobic and anaerobic bacteria, with *Lactobacillus* species being the predominant microorganisms and accounting for greater than 95% of all bacteria present.^{13,14} Lactobacilli are believed to provide defence against infection, in part by maintaining an acidic pH in the vagina and ensuring hydrogen peroxide is present in the genital environment. In contrast, bacterial vaginosis is a polymicrobial syndrome resulting in a decreased concentration of lactobacilli and an increase in pathogenic bacteria, mainly anaerobic or microaerophiles. These organisms include *Gardnerella vaginalis*, *Mobiluncus* species, *Bacteroides* and *Prevotella* species, and *Mycoplasma* species.^{15,16}

PREVALENCE AND EPIDEMIOLOGY

Bacterial vaginosis is very common, with the exact prevalence varying widely depending on the patient population. In studies of private office patients, the prevalence has ranged from 4% to 17%, while in gynaecology clinics (with a higher proportion of low income and uninsured women) it has been 23%.^{17,18} In college students, the prevalence has ranged from 4% to 25%, while it has been as high as 61% in women attending sexually transmitted disease clinics.^{13,19-21} In pregnant women, studies have documented similar prevalence rates to those seen in non-pregnant populations, ranging from 6% to 32%.^{3,22-25} A Canadian study of maternity patients reported an overall prevalence of bacterial vaginosis of 14%.²⁶

There are several risk factors for the acquisition of bacterial vaginosis. It has been associated with racial origin, smoking, sexual activity, and vaginal douching. Bacterial vaginosis is more common in black women,²⁷ women who smoke,²⁸ women who are sexually active compared with virginal women,²⁹ and those who use vaginal douches.³⁰

DIAGNOSIS

Bacterial vaginosis is a syndrome that can be diagnosed both clinically and microbiologically. Diagnostic criteria are the same for pregnant and non-pregnant women. Amsel et al.¹⁹ published clinical diagnostic criteria in 1983, and these are still in use today. The clinical diagnosis of bacterial

Table 2. Scoring system (0–10) for Gram-stained vaginal smears

Score	Lactobacillus morphotypes	Gardnerella and Bacteroides spp. morphotypes	Curved Gram-variable rods
0	4+	0	0
1	3+	1+	1+ or 2+
2	2+	2+	3+ or 4+
3	1+	3+	
4	0	4+	

vaginosis is made if three of the four following signs are present¹⁹:

- An adherent and homogenous vaginal discharge
- Vaginal pH greater than 4.5
- Detection of clue cells (vaginal epithelial cells with such a heavy coating of bacteria that the peripheral borders are obscured) on saline wet mount
- An amine odour after the addition of potassium hydroxide (positive whiff test)

Gram stain of vaginal fluid is the most widely used and evaluated microbiologic diagnostic method for bacterial vaginosis. To perform a Gram stain, vaginal discharge is collected on a glass slide, allowed to air dry, stained in the laboratory, and examined under oil immersion for the presence of bacteria. Most laboratories use an objective diagnostic scheme that quantifies the number of *Lactobacillus* morphotypes and pathogenic bacteria, resulting in a score that is used to determine whether the infection is present. The most commonly used system is the Nugent score (Table 2).³¹ The criterion for bacterial vaginosis is a score of seven or higher. A score of four to six is considered intermediate, and a score of zero to three is considered normal.

SCREENING AND MANAGEMENT

Vaginal discharge is common in pregnancy and may be physiologic. In women with persistent and bothersome discharge, screening for lower genital tract infections (vaginal and cervical) is recommended. If bacterial vaginosis is diagnosed, treatment is indicated. The 2006 Canadian Guidelines on Sexually Transmitted Infections published by the Public Health Agency of Canada recommends using either metronidazole 500 mg orally twice daily for seven days or clindamycin 300 mg orally twice daily for seven days.³² There is no evidence that metronidazole is teratogenic or mutagenic, and it is considered safe for use in pregnancy.^{33,34} Topical agents are not recommended because, although cure rates are similar to those observed with oral treatment, they have not been shown to be effective for preterm birth prevention (discussed below). Repeat testing should be performed one month after treatment to ensure

that cure was achieved.³⁵ Treatment has relatively moderate rates of success with high rates of recurrence in some women.

The presence of bacterial vaginosis has consistently been shown to be a risk factor for adverse obstetric outcomes, such as preterm labour and delivery, preterm premature rupture of membranes, spontaneous abortion, chorioamnionitis, and postpartum infections such as endometritis and Caesarean section wound infections.^{3–8} Despite these proven associations, screening and treatment in large-scale studies of women at low risk of adverse outcomes were unable to demonstrate a reduction in the incidence of prematurity. The United States Preventive Services Task Force published a statement in 2001, concluding that the available evidence was insufficient to recommend for or against routinely screening women at high risk for preterm birth for bacterial vaginosis, and recommending against screening average-risk asymptomatic pregnant women.³⁶ The Health Canada Guidelines on Sexually Transmitted Infections recommends against screening or treatment of asymptomatic or low-risk women, but states that there is evidence to support screening and treatment at 12 to 16 weeks' gestation for high-risk women.^{32,35}

Several trials have explored screening for and treatment of bacterial vaginosis in pregnant women. These trials have evaluated the efficacy of various treatment regimens—including oral and vaginal metronidazole and clindamycin—in achieving and maintaining cure. The studies have also investigated whether the treatment of disturbed vaginal flora can reduce the incidence of prematurity and the other bacterial vaginosis-associated adverse pregnancy outcomes. The varying and sometimes conflicting results of these trials can be difficult to interpret.

The Effect of Treatment on Cure Rates in Pregnant Women

Because the definition of cure has varied widely among published trials on treatment of bacterial vaginosis, there is a large variation in reported treatment efficacy rates. As well, studies of the natural history of this condition have shown that it gradually recurs with longer follow-up in

pregnant and non-pregnant women, and rates of cure depend on the timing of follow-up evaluations.^{17,24,37,38}

In oral treatment trials, cure rates have consistently been greater than 70%. Hauth et al.³⁸ showed resolution of bacterial vaginosis in 70% of women two to four weeks after treatment with oral metronidazole and erythromycin. McDonald et al.³⁹ found cure rates of 76% four weeks following two 2-day courses of metronidazole 400 mg twice daily. Carey et al.⁴⁰ demonstrated normalization of vaginal flora on Gram stain in 78% of women after two 2-gram doses of oral metronidazole. Klebanoff and colleagues⁴¹ reported cure in 78% of patients following two 2-gram doses of oral metronidazole. In studies using oral clindamycin, McGregor et al.⁴² published cure rates of 92.5% two to four weeks after treatment. Ugwumadu et al. found that using oral clindamycin 300 mg twice daily for five days resulted in cure rates of 90%.⁴³

In addition to oral treatment trials there have been many studies using vaginal preparations, most commonly clindamycin cream, with cure rates ranging from 33% to 86%. In randomized controlled trials of clindamycin cream versus placebo, Joesef et al.⁴⁴ showed a cure rate among 340 pregnant women of 85.5% two weeks after treatment. Kekki and colleagues⁴⁵ demonstrated normalization of vaginal flora in 66% of 187 patients one week following treatment. Kurkinen-Räty et al.⁴⁶ reported cure rates of 33% among 51 women two weeks after treatment. Lamont et al.⁴⁷ found a range of cure rates (71% to 78%) using several different criteria for cure in over 200 pregnant women three and six weeks post-treatment. A study by McGregor et al. clearly demonstrated that cure depends on the timing of follow-up, with rates of 90% at one week but dropping to 60% to 70% at four weeks post-treatment.³⁷

There are very few studies comparing oral and vaginal treatment. In a study by Yudin and colleagues,⁴⁸ pregnant women with bacterial vaginosis were randomized to receive either oral metronidazole 500 mg twice daily for seven days or vaginal metronidazole gel for five days. The results demonstrated that, at four weeks after treatment, cure rates were greater than 70%, and were equivalent for oral and vaginal therapy.

The Effect of Treatment on Obstetric Complications

Multiple studies have examined whether treatment of bacterial vaginosis in pregnancy can affect the frequency of adverse pregnancy outcomes, especially premature delivery. Despite the consistent association between bacterial vaginosis and preterm birth, the results of these treatment trials have been inconsistent. The reason for this lack of clarity in the literature may be that studies have used mixed populations (women at both low and high risk for preterm

birth) and different treatment modalities (systemic and local therapy). In addition, definitions of bacterial vaginosis and cure are not very precise.

Women at Low Risk for Preterm Birth

In trials enrolling women from the general population who are not at increased risk (i.e., who have the background population risk) for preterm birth, there does not seem to be any benefit to screening for and treating bacterial vaginosis. McGregor et al. randomized women with bacterial vaginosis from 16 to 27 weeks' gestation to receive intravaginal clindamycin or placebo. There were no significant differences in adverse outcomes such as preterm birth, preterm labour, or low birth weight between the two groups, despite adequate treatment and eradication of bacterial vaginosis.³⁷ Similarly, Joesef et al. found no difference in preterm delivery rates between women with bacterial vaginosis at 14 to 26 weeks' gestation randomized to topical clindamycin or placebo.⁴⁴ A study from Finland found no difference in rates of preterm birth or puerperal infections among women enrolled at 12 weeks' gestation and receiving vaginal clindamycin versus placebo,⁴⁶ and an Italian group showed no difference in the frequencies of preterm delivery, gestational age at birth, or low birth weight in women enrolled between 14 and 25 weeks' gestation and randomized to topical clindamycin or placebo.⁴⁹ Oral treatment trials in women at low risk for preterm birth have had similar results. In two trials with large numbers of women, McDonald et al.³⁹ found no difference in preterm delivery rates in 879 women randomized to oral metronidazole or placebo at 24 and 29 weeks' gestation, and Carey and colleagues⁴⁰ reported no difference in rates of preterm birth, low birth weight, or preterm premature rupture of membranes among 1953 pregnant women randomized to oral metronidazole or placebo from eight to 22 weeks' gestation.

Women at Increased Risk for Preterm Birth

Although trials of women at low risk for preterm delivery have not demonstrated benefit in treating bacterial vaginosis in pregnancy with respect to adverse outcomes, studies enrolling women who are at higher risk for premature birth have had more promising results. Morales et al. published results on a cohort of 80 women at 13 to 20 weeks' gestation with bacterial vaginosis and a history of preterm delivery who were randomized to oral metronidazole or placebo.⁵⁰ Women in the treatment group had a significantly decreased incidence of hospital admissions for preterm labour, premature births, infants with low birth weights, and preterm premature rupture of membranes compared with those in the placebo group. Hauth et al.³⁸ showed that women with bacterial vaginosis and either a history of preterm birth or low pre-pregnancy

weight who were treated with oral metronidazole and erythromycin had a lower incidence of preterm birth than those receiving placebo. In the trials by McDonald et al.³⁹ and Carey et al.⁴⁰ described above, two groups of women were enrolled: those at average (not increased) risk for preterm birth, and those with a higher risk because of a history of premature delivery in the past. As already noted, women at low risk did not benefit from treatment. In the trial by Carey et al., there was no benefit of treatment for either the low-risk or high-risk population of women.⁴⁰ However, in the study by McDonald and colleagues, the subgroup of women with a history of preterm delivery that was randomized to oral metronidazole had an approximate 50% reduction in premature birth.³⁹ In a Cochrane Collaboration review of 15 treatment trials involving 5888 women, there was a statistically significant decrease in the rate of preterm prelabour rupture of membranes and low birth weight in treated women with a history of previous preterm birth, but no effect on preterm delivery rates.⁵¹ However, in the same review, there was a statistically significant decreased risk of preterm birth in five trials of 2387 women treated before 20 weeks' gestation.⁵¹ Finally, a meta-analysis of 14 randomized controlled trials of treatment of bacterial vaginosis in pregnancy found no decrease in the risk of preterm delivery or any other adverse outcome for either the general population or for any subgroup that received antibiotics.⁵²

In contrast to these promising results, a small number of studies have indicated that treatment with metronidazole may in fact increase preterm birth rates. Shennan et al. reported significantly more preterm deliveries in women positive for fetal fibronectin randomized to metronidazole therapy than in those who received placebo.⁵³ However, only a small proportion of women in both groups had bacterial vaginosis. A meta-analysis of treatment trials for preterm birth prevention showed that women who received mid-trimester metronidazole had a higher rate of premature delivery than those who received placebo.⁵⁴

Route of Treatment and Preterm Birth Prevention

Although vaginal treatment regimens have been shown to be efficacious in eradicating bacterial vaginosis in pregnancy, they are ineffective in preventing preterm birth.^{37,44-46,49,51,55} The one published exception to this is a trial by Lamont et al. that shows a statistically significant reduction in preterm birth (4% vs. 10%) in women randomized to clindamycin vaginal cream at 13 to 20 weeks' gestation compared with placebo.⁵⁶ As noted above, some oral treatment trials have been successful in showing a decreased rate of prematurity in women treated for bacterial vaginosis, but only in those with a previous history of a preterm birth.^{38,39,50,51} A meta-analysis exploring the issue of

oral or vaginal treatment in women at low risk versus those at high risk found no significant reduction in preterm delivery by treatment of all women, women with a previous preterm birth, or women at low risk for preterm birth.⁵⁷ However, in the subgroup of women who had a previous preterm delivery and who had received oral treatment for at least seven days, there was a highly significant decrease in preterm delivery (OR, 0.42; 95% CI 0.27, 0.67). There was no benefit seen in the group of women receiving vaginal treatment. Similarly, in the Cochrane review there was no effect of vaginal antibiotics on any measure of preterm birth.⁵¹ It is still unclear why vaginal treatment might not offer the same benefit for preterm birth prevention as systemic therapy, although it has been hypothesized by some authors that systemic treatment might be required to fully eradicate bacterial vaginosis-associated organisms from both the lower and the upper genital tract, thereby preventing preterm labour and delivery.^{37,45}

Recommendations

There is currently no consensus as to whether to screen for or treat bacterial vaginosis in the general pregnant population in order to prevent adverse outcomes, such as preterm birth.

1. In symptomatic pregnant women, testing for and treatment of bacterial vaginosis is recommended for symptom resolution. Diagnostic criteria are the same for pregnant and non-pregnant women. (I-A)
2. Treatment with either oral or vaginal antibiotics is acceptable for achieving a cure in pregnant women with symptomatic bacterial vaginosis who are at low risk of adverse obstetric outcomes. (I-A)
3. Asymptomatic women and women without identified risk factors for preterm birth should not undergo routine screening for or treatment of bacterial vaginosis. (I-B)
4. Women at increased risk for preterm birth may benefit from routine screening for and treatment of bacterial vaginosis. (I-B)
5. If treatment for the prevention of adverse pregnancy outcomes is undertaken, it should be with metronidazole 500 mg orally twice daily for seven days or clindamycin 300 mg orally twice daily for seven days. Topical (vaginal) therapy is not recommended for this indication. (I-B)
6. Testing should be repeated one month after treatment to ensure that cure was achieved. (III-L)

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