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SCREENING OF BACTERIAL VAGINOSIS IN PRETERM LABOR AND PREGNANT

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ABSTRACT

The polymicrobial ecosystem of the vagina complicates the determination of the microbial etiology of BV. Using culture-independent techniques, attempts have been made to differentiate the diversity of vaginal microbiota in BV-positive and BV-negative women. Several trials discovered a decrease in the incidence of preterm labor when BV was treated, but most of those trials were performed on women with a history of preterm labor. However, the majority of trials reviewed advise against the treatment of a general low-risk obstetric population, as there was no significant decrease in preterm labor. Conclusions: Therefore, based on the above studies and the current guidelines of the Centers for Disease Control and Prevention (CDC), treating pregnant women in high-risk populations who are diagnosed with BV provides the clinician with an opportunity to possibly prevent preterm labor in this population. In nulliparous women without a history of preterm birth, treatment is recommended if other risk factors are present (e.g. gonorrhea or chlamydia).

KEYWORDS: Bacterial vaginosis, preterm labor.

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 malodor. It has been associated with a significant number of obstetric and gynecologic complications, such as preterm labor and delivery, preterm premature rupture of membranes, spontaneous abortion, chorioamnionitis, postpartum endometritis, post-Caesarean delivery wound infections, post-surgical infections, and subclinical pelvic inflammatory disease.[1]

Premature births remain a serious problem in the USA, occurring in 11% of all pregnancies. Preterm birth, defined as delivery of an infant before 37 weeks' gestation, is also the leading cause of neonatal mortality and morbidity in the developed world.

Causes of preterm labor vary, but infection is highly suspect. Up to 80% of early premature births are associated with an intrauterine infection prior to the rupture of membranes. Asymptomatic bacteriuria, Neisseria gonorrhea, Chlamydia trachomatis, Trichomonas vaginalis and bacterial vaginosis (BV) have all been associated with an increased risk of preterm birth. The exception is vaginal yeast infections.[2]

Multiple studies suggest that BV is a cause of preterm labor, yet its routine treatment remains controversial.[3] In conjunction with preterm delivery, BV in pregnant patients is associated with premature rupture of membranes, infection of the amnion and chorion, histologic chorioamnionitis and infection of amniotic fluid. Flynn et al. noted a 60% increase in the risk of preterm delivery in the presence of BV. Another study by Hillier et al.[4] associated BV with the risk of spontaneous preterm birth by a factor of 1.5 to 3 in high-risk women, while other studies suggest that BV almost doubles the risk of spontaneous preterm delivery. Although BV is present in almost 20% of pregnant women, most cases remain asymptomatic, and not all women with the condition will deliver prematurely8. It is postulated that there exists a subgroup of high-risk women (e.g. those who have vaginal colonization with Mycoplasma hominids). African–American women may also exhibit 200–300% more BV than white populations. The exact conditions under which BV directly correlates with preterm labor are unknown.[5]

The purpose of this paper is to review the recent literature addressing the association between BV and preterm birth, Preterm labor is a challenging issue for the obstetricians even today. It is the largest contributor to the perinatal morbidity and mortality throughout the world. With the improvement of neonatal care, there has been a dramatic improvement in the neonatal survival rates of preterm infants. But Neonatal Intensive Care Unit (NICU) care is expensive and a preterm baby is at an increased risk of many complications like respiratory distress syndrome (RDS), hyperbilirubinemia, etc.[6]

So preterm labor is not only a medical and social problem but also an economic burden. Hence, all efforts should be directed towards the prevention of preterm labor and preterm birth. The etiology of preterm labor is multifactorial, but there is a piece of overwhelming

evidence to implicate infection as a major cause, accounting for about 40% of all cases of spontaneous preterm labor and preterm birth. Horcoff M. Ryan, et al have shown that bacterial vaginosis diagnosed in the second trimester of pregnancy plays a major role as a risk factor for preterm delivery.[7] Bacterial vaginosis (BV) is the most common cause of vaginal discharge in the reproductive age group with the prevalence rate of 10-15%. The rate of complications resulting from bacterial vaginosis is higher in ascending infection cases such as those using intrauterine device (IUD).

Background

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. Lactobacilli are believed to provide defense 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.[8]

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 gynecology clinics (with a higher proportion of low income and uninsured women) it has been 23%.[9] 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. In pregnant women, studies have documented similar prevalence rates to those seen in non-pregnant populations, ranging from 6% to 32%.[10] 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 of 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 vaginosis is made if three of the four following signs are present 19: • 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 a 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 labor 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 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 the 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.[11]

In oral treatment trials, cure rates have consistently been greater than 70%. Hauth et al showed resolution of bacterial vaginosis in 70% of women two to four weeks after treatment with oral metronidazole and erythromycin. McDonald et al found cure rates of 76% four weeks following two 2-day courses of metronidazole 400 mg twice daily. Carey et al. demonstrated normalization of vaginal flora on Gram stain in 78% of women after two 2-gram doses of oral metronidazole.[12]

Klebanoff and colleagues reported a cure in 78% of patients following two 2-gram doses of oral metronidazole. In studies using oral clindamycin, McGregor et al. 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%.[13] 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, Josef et al. 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. found a range of cure rates (71% to 78%) using several different criteria for a 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.[14]

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.[15]

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).[16]

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 labor, or low birth weight between the two groups, despite adequate treatment and eradication of bacterial vaginosis. Similarly, Josef et al. found no difference in preterm delivery rates between women with bacterial vaginosis at 14 to 26 weeks' randomized to topical clindamycin or placebo.[17] 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, 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.

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. 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 colleagues 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.[18]

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.[19]

Women in the treatment group had a significantly decreased incidence of hospital admissions for preterm labor, premature births, infants with low birth weights, and preterm premature rupture of membranes compared with those in the placebo group. Hauth et al. 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.[20] and Carey et al. described above, two groups of women have enrolled: those at average (not increased) risk for preterm birth, and those with 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. 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. 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.[21]

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. 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.[22]

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. 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.[23]

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. 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.[24]

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 preterm birth. 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.

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.[25] 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 labor and delivery.[26]

Hauth et al. (Level I study in 1995) treated pregnant women with a history of preterm birth or weight < 50 kg and a positive diagnosis of BV7. Treatment consisted of metronidazole (250 mg three times a day for 7 days) and erythromycin (333 mg three times a day for 14 days). The results of this 2:1double-blind randomization trial revealed a decreased incidence of preterm delivery (< 37 weeks) for the entire study population (odds ratio, OR, 0.48; 95% confidence interval, CI 0.28–0.81), as well as for a subset of patients with a previous preterm delivery (OR, 0.48; 95% CI, 0.25–0.90). Women who were diagnosed with BV at the initial visit (24 weeks) and who received antibiotics rather than placebo presented with fewer preterm deliveries. Since this treatment benefit was only observed at the initial examination, the overall results do not support mid-trimester treatment with metronidazole and erythromycin in women at risk for preterm delivery without BV.[27]

There are no data to suggest that treatment of low-risk pregnant women with BV decreases the rates of prematurity. Over a period of 3 years, Morales et al. (level I study in 1994) screened for BV in women between 13 and 20 weeks with a singleton gestation and a history of preterm birth via a double-blind randomized trial. The 80 women with a positive screen received either metronidazole (250 mg three times a day) or a placebo for 7 days. The study showed a significant decrease in delivery prior to 37 weeks among women taking metronidazole (18%) compared with those on placebo (39%) ($p < 0.05$). In the metronidazole group, there were significantly fewer hospital admissions for preterm labor, cases of premature rupture of membranes, and low birth weights9. In 1995, McGregor et al. (level I study) performed a prospective, controlled treatment trial of 1260 subjects to study the effect of clindamycin on pregnant women with BV. Women who were treated with 300 mg of clindamycin orally twice daily for 7 days showed a reduction in preterm birth (relative risk 0.5; 95% CI, 0.3–0.9), and the authors recommended that women at risk for preterm birth with BV should be screened and treated1. In 1997, McDonald et al. 10 conducted a multicenter, randomized, placebo-controlled trial of 879 women at 19 weeks' gestation, but failed to demonstrate a reduced preterm birth rate among pregnant women with BV or those with a heavy growth of Gardnerella vaginalis (level I). The intention-to-treat analysis showed no difference between the treatment and placebo groups in overall preterm birth (31/429

[7.2%] vs. 32/428 [7.5%]) or spontaneous preterm birth rate (20/429 [4.7%] vs. 24/428 [5.6%]).[28]

However, among women with a previous preterm birth, those treated with oral metronidazole (400 mg twice daily for 2 days at 24 weeks' gestation, and again at 29 weeks) demonstrated a marked reduction in spontaneous preterm birth rate (OR, 0.14; 95% CI, 0.01–0.84)10. A meta-analysis from the Cochrane database determined that preterm birth rates did not differ significantly between treated and non-treated pregnant patients with BV (OR, 0.78; 95% CI, 0.60–1.02), yet a subgroup of women with a previous preterm birth demonstrated a significant decrease in the incidence of preterm birth, with an odds ratio of 0.37 (95% CI, 0.23–0.60).

This meta-analysis of 1504 women from a total of five trials using amoxicillin, clindamycin, and metronidazole did not recommend screening and treating all pregnant women for BV in order to prevent preterm birth. Carey et al. recently conducted a randomized, double-blind clinical trial of the use of metronidazole to treat asymptomatic BV. Treatment did not reduce the frequency of delivery before 37 weeks' gestation (relative risk in the metronidazole group, 1.0; 95% CI, 0.8–1.2). This clinical trial differed from previous attempts because it was larger (1953 subjects) and it studied the general obstetrical population, not just women with a history of preterm delivery. Treatment involved a shorter course of metronidazole therapy with two 2 g doses during a 48-hour period, and a second treatment of the women between 24- and 30-weeks' gestation. These researchers recommended the longer course of therapy to eradicate upper genital tract organisms.[29]

RESULTS AND DISCUSSION

The vaginal ecosystem is established over a number of years. The dynamic environment of the vagina is influenced by factors such as hormonal fluctuations, menstruation, douching, hygiene, pregnancy, breastfeeding, and sexual practices. Skin commensals and microbiota normally inhabiting the bowel are the original colonizers of the young, healthy female vagina. Aerobic lactobacilli persist in the vagina for weeks after birth while the vaginal pH remains acidic. The pH of the vagina converts to neutral during early childhood, remaining so until puberty. A plethora of different microbial species co-exist in this vaginal ecosystem, 70%–90% of which are lactobacilli. During puberty and menarche, dramatic hormonal and physical changes occur in the vaginal environment favoring the colonization of lactobacilli.[30]

Although identified in both BV-positive and BV-negative women, H_2O producing lactobacilli numbers are reported to be significantly increased in BV-negative females. Their population dominance is considered to be beneficial in maintaining the health of the female, through their production of hydroxyl radicals, lactic acid, bacteriocins, hydrogen peroxide, and probiotics.[31] After menopause, or when the vaginal lactobacilli are depressed or removed, hydrogen peroxide is no longer produced and the pH of the environment increases, thus facilitating the establishment of BV-associated microbial communities in the vaginal biofilm. However, not all healthy females have vaginal microbiota dominated by lactobacilli, and other lactic acid producers such as *Atopobium vaginae, Leptotrichia* and *Megasphaera* have also been suggested to assist in maintaining the acidity of the vagina. With BV considered a non-specific (predominantly anaerobic) polymicrobial infection and the identities of many of the vaginal microflora remaining elusive, determining the health of the vaginal ecosystem appears to be subjective.

Two species of lactobacilli have frequently been found to colonize the healthy vagina, namely, *Lactobacillus gasseri and Lactobacillus crispatus* both members of the *Lactobacillus acidophilus* complex.[32] While *L. crispatus* and *L. jensenii* have a better ability to adhere to vaginal cells, *in vitro*studies have reported that acid and hydrogen peroxide production by *L. acidophilus* and *L. casei* are able to inhibit the growth of BV-associated microbes such as *Gardnerella vaginalis*, *Mobiluncus*, *Bacteroides* and species of anaerobic cocci, while decreased production of bacteriocins and hydrogen-peroxide by lactobacilli enhances the growth of *G. vaginalis*, *Prevotella bivia*, *Mobiluncus*, *Peptococcus* species, and *Peptostreptococcus anaerobius* by the production of ammonia, acetic, succinic acids and amino acids respectively.[33]

Lactobacillus iners has been recommended as a marker of the imbalance of the vaginal microflora leading to BV and its presence correlated with the colonization of other BV-associated bacteria such as *Megasphaera, Leptotrichia,* and *Eggerthella.*[34] Thus the significance of the relative ratio of *Lactobacillus iners, Atopobium vaginae* and other anaerobes in BV provides substantial information for its diagnosis.[38] *L. gasses* and *L. crispatus*, have been associated with health, while a negative correlation has been reported between *L. gasseri* and *L. in*; *L. gasseri* and *Atopobium*, *Prevotella* and *G. vaginalis*all of which are associated with BV. *L. iners* is dominant after treatment for BV and has been reported together with *L. crispatus* in women without BV[34] suggesting that *L. in* may be an

opportunistic pathogen whose prevalence and pathogenic potential is enhanced by *L. gasses*, an assumed later colonizer than *L. crispatus*.[35]

Several mechanisms have been proposed for the establishment of the BV biofilm, namely, stress, sexual practices, microbial synergism (one organism inducing the ideal growing environment for another) or antagonism (inhibition or killing of one organism by another). Because of the polymicrobial nature of infection, growing resistance to metronidazole and other antimicrobial treatments have been reported.[36] The outcome of any infection is usually determined by the initial response of the host to invasion by an infective agent, followed by chemotaxis (the migration of polymorphonuclear neutrophils (PMNs) towards the locus of infection). This initial response to the recognition of chemotactic factors results in phagocytosis. In an effort to fully understand BV, clinicians made a distinction between vaginitis and vaginosis by defining bacterial vaginitis as an infection of the vagina associated with inflammation of the vulva, while vaginosis was defined as the degradation of the normal flora of the vagina in the absence of an associated inflammatory response.[37] The inhibition of PMN chemotaxis by virulence factors expressed by certain of the BV-associated organisms may explain the absence of inflammation.

In order to be implicated in the etiology of BV, a specific bacterium should demonstrate an increase in BV and be reduced or eliminated in the healthy vagina. BV has been attributed to an imbalance of the normal vaginal microbiota with many of the anaerobic bacteria detected in BV showing great pathogenic potential either individually or as a consortium. Symbiotic relationships appear to play an important role in the pathogenesis of BV, thereby implicating several species in its etiology. They are examined below in the light of their effect on host defenses, provision of essential nutrients for growth and survival, alteration of the environment and expression of virulence factors.[38]

Diagnosis of BV includes clinical examination and microscopy, using Amsel criteria and Nugent scoring. BV is characterized by a discharge (often white or yellow) with a fishy odor following the addition of 10% potassium hydroxide to the vaginal fluid, vaginal pH > 4.5 and the microscopic scoring of bacterial morphotypes along with the presence of “clue cells”, vaginal epithelial cells with boarders coated with bacteria.[39]

It may also be asymptomatic which explains why it is often misdiagnosed. It may be differentiated from aerobic vaginitis, which is characterized by the absence of succinate,

increased sialidase activity and a host response resulting in the increased production of cytokines such as interleukin-1, -6 and -8.[40]

Laboratory-based diagnostic methods for BV include culture and anaerobic metabolic activity analysis such as the assessment of the production of short-chain volatile and non-volatile fatty acids as end products of anaerobic metabolism, and the production of specific enzymes, Detection of fatty acids in vaginal fluid can differentiate between health (major lactic acid) and BV (major succinic and acetic acids) as well as monitor the effects of treatment for BV. Culture-based and molecular approaches have identified several anaerobic species in BV[41] with molecular methods have overcome many of the problems associated with culture and revealing species not previously reported.

Preterm labor may be classified as either physiologic or pathologic. Physiologic preterm labor describes a normal initiating factor that occurs too early in pregnancy, while pathologic preterm labor results from an abnormal initiating factor with timing being a distinguishing factor.

There is disruption of the vaginal ecosystem that results in increased levels of anaerobes. BV alters the vaginal flora by decreasing the number of hydrogen-peroxide-producing Lactobacillus acidophilus organisms. Consequently, the levels of G. vaginalis, M. hominids, and Mobiluncus species increase rather than remaining in their normal state of suppression. The metabolic by-products of these organisms include amines, which increase the vaginal pH, and exfoliation of vaginal epithelial cells results.[42] Although the exact mechanism is not known, studies have shown that BV can cause infection of the upper genital tract, which acts as a premature birth trigger6. BV and T. vaginalis are also associated with many microorganisms that produce phospholipase A2 and C or phospholipase-like activity, and affected patients show increased levels of sialidase, phospholipase A2, prostaglandin E2, and interleukin–1(beta). The rise in levels of these enzymes may result in the decidual or fetal membrane cell fatty acid tissue stores releasing arachidonic acid2, a precursor of the uterotonic prostaglandins. Other explanations of an association between BV and preterm labor include activation of fetal and/or maternal inflammatory responses or proteolytic enzymes. Elevated vaginal or cervical levels of endotoxin, mucinous, sialidase, and interleukin-1(alpha) are found in women with BV, which suggests that the microorganisms produce cytokines6. These cytokines and the release of interleukin-1(beta) and tumor necrosis factor induce cyclooxygenase II, an enzyme that produces prostaglandins involved in

parturition. Proteolytic enzymes that may overcome maternal mucous membrane defenses and impair fetal membrane strength and elasticity include collagenases, immunoglobulin A proteases, elastases, mucinases and/or sialidases.[43]

CONCLUSION

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.

- 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).
- 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).
- Asymptomatic women and women without identified risk factors for preterm birth should not undergo routine screening for or treatment of bacterial vaginosis. (I-B).
- Women at increased risk for preterm birth may benefit from routine screening for and treatment of bacterial vaginosis. (I-B).
- 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)

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