

# Adverse obstetric sequelae of bacterial vaginosis

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**Bacterial vaginosis is increasingly associated with adverse sequelae in obstetrics such as preterm prelabour rupture of membranes, preterm labour and preterm birth. It is important to diagnose the condition early in pregnancy where appropriate treatment can be administered to women who are symptomatic or who are at high risk of adverse sequelae.**

Normal vaginal flora is dominated by *Lactobacillus* spp which, by producing lactic acid from glycogen in vaginal secretions, maintain an acidic environment (pH <4.5) in which the growth of potentially pathogenic organisms is suppressed. In bacterial vaginosis (BV), the *Lactobacillus*-dominated flora is replaced by a 1000-fold increase in other organisms, particularly anaerobes. BV is the commonest cause of a vaginal discharge in young women, although 50% may be asymptomatic.

## EPIDEMIOLOGY

The prevalence of BV in a given population varies widely. In the UK, between 10% and 15% of women in a general gynaecology clinic (Hay et al, 1992) and an unselected antenatal population (Hay et al, 1994) were found to have BV. In contrast, 64% of women attending a sexually transmitted disease (STD) clinic were found to have BV (Embree et al, 1984). In a female college population in the USA, BV was found in 4% of asymptomatic women and 16% of symptomatic women (Eschenbach et al, 1988). In a group of asymptomatic women attending their general practitioners for routine cervical cytology examination, BV was found twice as often as candidiasis (Lamont et al, 2000).

## PATHOGENESIS, MICROBIOLOGY AND BIOCHEMISTRY

The aetiology of BV remains unclear and the polymicrobial nature of the condition makes it difficult to implicate one specific organism. BV may be the result of antibiotic usage or of a change in endocrine status, and there is some evidence that phage viruses may be involved (Tao and Pavlova, 1998).

Under circumstances where there is an increase in vaginal pH, such as with douching or during menstruation, lactobacilli become less efficient at producing hydrogen peroxide, a substance that is toxic to other bacteria. This results in a 1000-fold increase in other organisms such as anaerobes, *Mobiluncus* spp, *Gardnerella vaginalis*, *Mycoplasma hominis* and *Ureaplasma urealyticum*. These organisms produce ketoacids which blunt the chemotactic response of polymorphs and also reduce their killing ability. This results in a further increase in anaerobes which produce enzymes such as aminopeptidases and decarboxylases which break down peptides to amino acids and then to amines.

At low pH, these amines are stable but at high pH they are volatile and give off a characteristic malodour. This also explains why BV results in large numbers of potentially pathogenic organisms and yet no cellular inflammatory response. This is an ideal way for a condition to establish itself unnoticed within the host, and is why the condition is known as vaginosis rather than vaginitis.

## DIAGNOSIS

The accepted 'gold standard' for the diagnosis of BV was devised by Amsel et al in 1983. They proposed that a diagnosis of BV made on the basis of composite criteria required the presence of three out of four of the following:

1. A homogeneous white vaginal discharge
2. A vaginal pH greater than 4.5
3. A positive 'whiff' test (a characteristic amine odour) on addition of a 10% solution of the alkali potassium hydroxide to a sample of vaginal secretions
4. The presence of clue cells on a wet mount. Clue cells are defined as vaginal epithelial

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cells which are covered by so many adherent coccobacilli that their borders are indistinct on microscopy. This method of diagnosis can be clumsy and unpleasant in the clinical setting.

An alternative method of diagnosis makes use of the Gram staining of vaginal secretions and quantifying the bacterial morphotypes (Speigel et al, 1983). The detection of BV by Gram stain is now the preferred method in many centres and is cheap to perform as well as being less subjective. It also allows samples to be stored and re-examined and has a high sensitivity and specificity.

### **ADVERSE OBSTETRIC SEQUELAE OF BV**

Pregnant women with BV are known to have an increased risk of late miscarriage, chorioamnionitis, preterm prelabour rupture of membranes (PPROM), spontaneous preterm labour and delivery, and postpartum endometritis.

#### **Late miscarriage**

Hay et al (1994) showed that there was a five-fold increased risk of late miscarriage in women with BV compared to those without BV and Llahi-Camp et al (1996) showed a significant association between women who had had at least one second trimester miscarriage and BV compared to those women who had a history of only early miscarriages.

#### **Chorioamnionitis**

BV-related organisms such as *G. vaginalis*, *M. hominis* and *Bacteroides* spp. are commonly found in amniotic fluid cultures in women in preterm labour with intact membranes who subsequently deliver preterm, and BV is an independent risk factor for chorioamnionitis. Higher rates of amniotic fluid infection and histological chorioamnionitis were linked to an increase in low birthweight babies and preterm birth (Hillier et al, 1988). Silver et al (1989) showed that women with BV were more likely to develop chorioamnionitis than women without BV, and *M. hominis* and *G. vaginalis* were commonly isolated.

#### **Preterm prelabour rupture of membranes**

PPROM remains a major cause of perinatal morbidity and mortality since there is an increased risk of sepsis as well as preterm birth. In about 30% of all preterm births there is evidence to link BV to PPRM (Gravett et al, 1986; Lamont et al, 1987; Martius et al, 1988). The proposed biochemical mechanism suggests that proteolytic enzymes such as elastases and proteases produced by anaerobic bacteria weaken the fetal membranes and this results in PPRM.

#### **Preterm labour and preterm birth**

Preterm birth is the major cause of death and handicap in neonates in the developed world. There is a well-established link between infection and an increased incidence of preterm birth. Several studies have demonstrated the association of BV with increased rates of preterm labour and delivery (Kurki et al, 1992; Hay et al, 1994). *G. vaginalis* has been found to be twice as common in women who delivered before 34 weeks gestation compared to those who delivered after 34 weeks.

Proinflammatory cytokines are found in higher concentration in the amniotic fluid of women in preterm labour with intra-amniotic infection (Romero et al, 1990; Hillier et al, 1993) and the measurement of these cytokines can be used to predict infection. By measuring levels of interleukins such as IL-1 $\beta$  and IL-6 in amniotic fluid samples, it could be possible to formulate a more sensitive method to detect women at risk of preterm birth.

#### **Postpartum endometritis**

Postpartum endometritis can occur following vaginal delivery or caesarean section and risk factors include prolonged labour, prolonged rupture of membranes and an increased number of vaginal examinations. Watts et al (1989) showed the presence of BV-related organisms in endometrial aspirates of 60% of women who developed postpartum endometritis. They also showed that in women who developed postpartum endometritis following caesarean section, BV diagnosed by Gram stain was six times more likely to be present compared to those with a normal Gram stain (Watts et al, 1990).

### **TREATMENT OF BV IN PREGNANCY**

It may be necessary to treat BV in pregnancy either because women are symptomatic or because they are at increased risk of adverse sequelae. The polymicrobial nature of the condition makes treatment difficult and high cure rates of greater than 80% are difficult to achieve. A number of studies have examined the use of antibiotics in women with abnormal genital tract colonization in early pregnancy. Unfortunately, a range of antibiotics administered by different routes and doses, and given to women with variable degrees of risk, have failed to show any consistent benefit, but research continues in this area. If antibiotic treatment is likely to work, then it is more likely to do so if given earlier in pregnancy to women with the full manifestation of abnormal flora associated with BV (Lamont, 2000).

## CONCLUSION

BV is an important cause of adverse sequelae in obstetrics and gynaecology. The diagnosis of the condition is cheap and simple to perform and early detection and treatment may be important. In pregnancy, symptomatic women should be treated and those who are at increased risk of adverse sequelae may benefit from early screening and treatment. **HM**

*Conflict of interest: none.*

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## KEY POINTS

- Bacterial vaginosis (BV) is a polymicrobial condition that can easily be diagnosed by a Gram stain of vaginal secretions.
- There is a strong association between BV and its related organisms and adverse obstetric sequelae such as late miscarriage, chorioamnionitis, spontaneous preterm labour and delivery and postpartum endometritis.
- Symptomatic pregnant or non-pregnant women with BV should be treated with antibiotics and women at risk of adverse sequelae should be screened in early pregnancy for BV.
- Inflammatory cytokine levels rise in both preterm and term labour and are associated with genital tract infection. This may identify a group of women with BV who are at a particularly increased risk of preterm birth.