Bacterial vaginosis and preterm birth: a prospective community-based cohort study

Pippa Oakeshott, Sally Kerry, Sima Hay and Phillip Hay

SUMMARY

Background: Preterm birth before 37 weeks' gestation is associated with 70% of perinatal morbidity and nearly half of long-term neurological morbidity. Hospital-based studies have shown that bacterial vaginosis is associated with preterm birth.

Aim: To estimate the relative risk of preterm birth in women with and without bacterial vaginosis, detected by self-administered vaginal swab at <10 weeks' gestation.

Design: Prospective cohort study.

Setting: Thirty-two general practices and five family planning clinics in South London.

Participants: A total of 1216 women with bacterial vaginosis status established before 10 weeks' gestation, by analysis of Gram stained vaginal smears by two independent observers.

Method: All women who did not miscarry or have a termination of pregnancy before 16 weeks' gestation were sent a brief confidential questionnaire at 16 weeks and at term asking about pregnancy outcome. Data on non-responders were obtained by searches of hospital and general practice records and by telephone calls to patients.

Results: Ascertainment was 87% (937/1072). The mean age of the women was 31 years. Thirteen per cent (122/925) had bacterial vaginosis and 5% (44/897) had a spontaneous preterm birth. The relative risk (RR) of preterm birth in women with bacterial vaginosis was 0.9 (95% confidence interval [CI] = 0.4 to 2.2). However, bacterial vaginosis was associated with late miscarriage at 13–23 weeks (RR = 4.0, 95% CI = 1.3 to 12.1). Preterm birth was not associated with previous preterm birth, black ethnicity, age <20 years, low social class, single marital status, or chlamydial infection. However, it was more common in women who reported smoking in pregnancy (RR = 2.9, 95% CI = 1.5 to 5.5). Of 867 responders, 552 (64%) said that providing a vaginal swab was at least as easy as providing a urine specimen.

Conclusions: In this low-risk community-based cohort, bacterial vaginosis was not a strong risk factor for preterm birth.

Keywords: bacterial vaginosis; cohort study; community; pregnancy; premature birth; sexually transmitted disease.

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Introduction

PRETERM birth before 37 weeks' gestation is the greatest cause of perinatal mortality and morbidity in the developed world, with the worst outcomes seen in babies born before 30 weeks.[1,2] It is associated with 50% of childhood neurological disability, including cerebral palsy and blindness.[3] Hospital-based studies have shown that preterm birth is more common in women with bacterial vaginosis.[4-6] Bacterial vaginosis is an imbalance of the normal vaginal flora, with an overgrowth of anaerobic bacteria, including *Gardnerella vaginalis*, and a lack of the normal lactobacillary flora.[7] It has been suggested that the risk of preterm birth is greater the earlier in pregnancy that bacterial vaginosis is diagnosed.[1] However, until recently,[8] treatment of asymptomatic bacterial vaginosis during pregnancy had not been shown to reduce the rate of preterm birth in low-risk women with no history of preterm birth.[7,9,10] The aim of this study was to estimate the relative risk (RR) of preterm birth in a community-based cohort of pregnant women with and without bacterial vaginosis, detected by self-administered vaginal swab at <10 weeks' gestation.

Methods

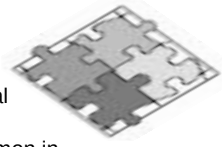
Thirty-two general practices and five family planning clinics in South London were asked to recruit consecutive pregnant women presenting at <10 weeks' gestation. Women who agreed to participate were asked to provide a self-administered vaginal swab, a vaginal smear, and a first-pass urine sample, and to complete a confidential postal questionnaire at 16 weeks' gestation[11] and at term. The questionnaires asked about known risk factors for preterm birth: previous preterm birth, Afro-Caribbean or black African ethnic origin, age <20 years, and low socioeconomic status.[2,12-14] Vaginal smears were Gram stained and examined for bacterial vaginosis by two independent observers using Nugent's scoring system.[9] Swabs and urine specimens were tested for *Chlamydia trachomatis* by ligase chain reaction assay.[15] At 16 weeks' gestation general practitioners were informed of all positive results for chlamydia or bacterial vaginosis. They were advised to refer women with chlamydial infection to the local genitourinary clinic. No recommendation was made on treatment of asymptomatic bacterial vaginosis.

Ethical approval was obtained from Wandsworth, Croydon and Riverside Research Ethics Committees.

Results

Between June 1998 and July 2000, 1216 women (mean age = 31 years, range = 16–48 years) were recruited. Data from the questionnaire at 16 weeks (published separately) showed that 121 women miscarried before 16 weeks, 22

HOW THIS FITS IN



What do we know?

Preterm birth is associated with perinatal morbidity and mortality. Hospital-based studies have shown that it is more common in women with bacterial vaginosis.

What does this paper add?

In a low-risk community-based cohort of 900 women, bacterial vaginosis before 10 weeks' gestation was not a strong risk factor for preterm birth, although it was associated with second trimester miscarriage. The study also showed that non-invasive screening for bacterial vaginosis in very early pregnancy is feasible in primary care. However, even if future trials confirm that treatment of bacterial vaginosis can reduce the risk of adverse pregnancy outcome, screening may not be worthwhile in a community-based population with a low prevalence of preterm birth.

had a termination of pregnancy, and one had an ectopic pregnancy.[11] These women were excluded from the questionnaire survey at term, which had a response rate of 57% (608/1072) (Figure 1). In a further 328 (31%) women, outcome data were obtained from hospital or general practice records, or from telephoning the patient. One hundred and thirty-five (13%) patients were lost to follow-up, of whom 125 had changed address. These 135 were similar in bacterial vaginosis status, social class, and ethnic group to those followed-up, but were more likely to be aged <25 years, to be single, or to have a chlamydial infection (21% [29/135] versus 11% [100/937]; 14% [14/99] versus 7% [66/889]; 7% [9/134] versus 2% [18/934], respectively).

Of 886 women who responded to the question, 79% described their ethnicity as white, 6% as Afro-Caribbean, 4% as black-African, 3% as Indian, 3% Pakistani, and 5% as other ethnic origin. Sixty-one per cent (514/841) were in social classes 1 and 2, and 92% (822/889) were married or living with a partner. Fifteen per cent (105/708) said they had smoked during pregnancy. Analysis of specimens taken at recruitment showed that 13% (122/925) of women had bacterial vaginosis and 2% (18/936) had chlamydial infection.

Pregnancy outcome

Table 1 shows the outcome of pregnancy after 13 weeks related to bacterial vaginosis status. We excluded four further

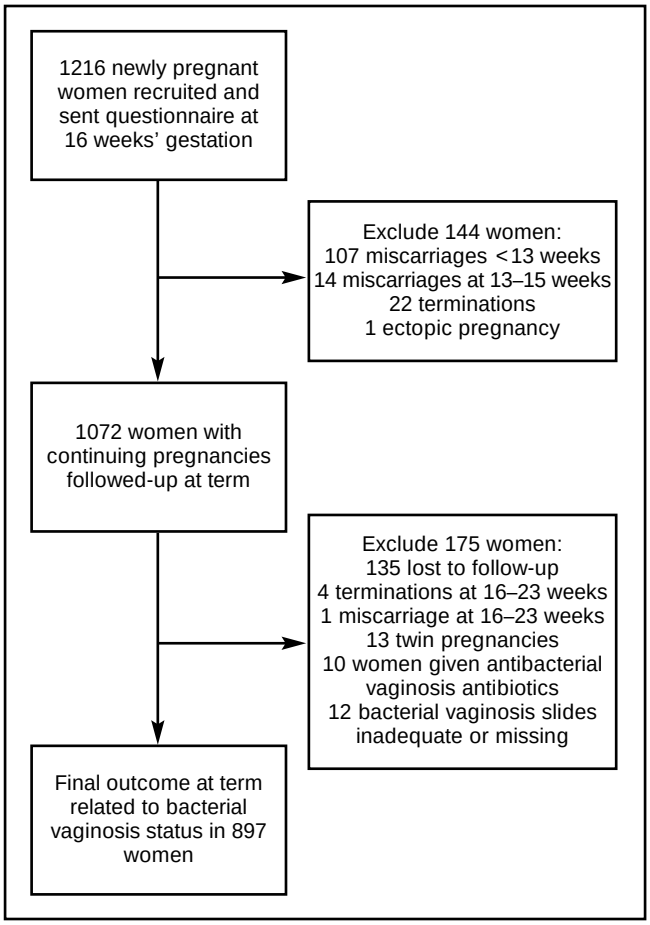


Figure 1. Flow chart of cohort study.

terminations between 16–23 weeks, 13 twin pregnancies, 12 women whose slides for bacterial vaginosis analysis were inadequate or missing, and 10 women who said that during pregnancy they had taken oral metronidazole (*n* = 9) or clindamycin (*n* = 1), which are antibiotics effective against bacterial vaginosis. The prevalence of spontaneous preterm birth was 5% (44/897) but it was not found to be more common in women with bacterial vaginosis (RR = 0.9, 95% confidence interval [CI] = 0.4 to 2.2). However, bacterial vaginosis was associated with late miscarriage at 13–23 weeks (RR = 4.0, 95% CI = 1.3 to 12.1). There were seven stillbirths (all in women without bacterial vaginosis) of which five were preterm deliveries.

Table 1. Outcome of pregnancy after 13 weeks' gestation related to bacterial vaginosis status.[a]

	Bacterial vaginosis positive[b] (*n* [%])	Bacterial vaginosis intermediate[c] (*n* [%])	Bacterial vaginosis negative[d] (*n* [%])
Spontaneous preterm birth at <37 weeks	5 (4.3)	1 (2.4)	38 (5.0)
Late miscarriage at 13–23 weeks[e]	5 (4.3)	2 (4.8)	8 (1.1)
Elective preterm delivery at <37 weeks	2 (1.7)	0 (0)	8 (1.1)
Term delivery	105 (90.0)	38 (92.7)	700 (92.8)
Admitted to special care baby unit	8 (6.8)	1 (2.4)	45 (6.0)

[a]This table excludes 107 miscarriages before 13 weeks, 26 terminations, 1 ectopic pregnancy, 10 women given antibiotics in pregnancy, 13 twins, 12 bacterial vaginosis slides, which were inadequate or missing, and 135 women who were lost to follow-up. [b]*n* = 117. [c]*n* = 41. [d]*n* = 754. [e]Bacterial vaginosis-positive women more likely than bacterial vaginosis-negative women to have a late miscarriage. RR = 4.0, 95% CI = 1.3 to 12.1, *P* = 0.04.

Table 2 shows that there were no significant associations between preterm birth and chlamydial infection, previous preterm birth, black ethnicity, age <20 years, low social class or single marital status. However, women who smoked during pregnancy were more likely to have a preterm birth (RR = 2.9, 95% CI = 1.5 to 5.5). This RR did not change much when adjusted for age (RR = 2.6, 95% CI = 1.3 to 5.3) or social class (RR = 3.1, 95% CI = 1.5 to 6.2). Similarly, the RR of preterm birth in women with bacterial vaginosis did not change when adjusted for smoking (RR = 0.9, 95% CI = 0.3 to 2.6).

Women's views on providing the specimens

The 16-week questionnaire asked women for their opinions about providing a self-administered vaginal swab and urine specimen. When asked which specimen was easier to provide, 36% (315/867) of responders said that the urine specimen was easier, 7% (59/867) said the vaginal swab, and 57% (493/867) both the same. When asked to comment, 112 women said the urine specimen was easier as they had done it before, 69 said both specimens were easy, and 20 said the swab was easiest as it was less messy (Box 1). However, 59 women said they were unsure if they had done the swab properly. Quality assessment of Gram-stained slides for bacterial vaginosis analysis showed that only 0.7% (7/932) of vaginal swabs were inadequate.

Discussion

In this low-risk cohort of healthy women, bacterial vaginosis at <10 weeks' gestation was not a strong risk factor for preterm birth, although it was associated with second trimester miscarriage.

Strengths and weaknesses

Strengths of the current study include the community basis, women were screened much earlier in pregnancy than in previous studies[4-6,10] (mean gestation = 49 days), and new non-invasive tests were used. The main limitation was that the sample only included women who presented to community health services very early in pregnancy. These women were older, 61% were in social classes 1 and 2 compared with 35% in Wandsworth in the 1991 census, and the 5% prevalence of preterm birth was lower than expected. Other weaknesses of the study were the small sample size and the 13% loss to follow-up. In addition, bacterial vaginosis in early pregnancy may clear spontaneously in about a third of women,[10] and we do not know how many women had ascending infection invading the uterus.[1,2]

Comparison with other studies

The lack of an association between bacterial vaginosis and preterm birth is in contrast to previous studies, which have all been hospital based.[4-6] The treatment trial by Carey *et al* was of a high-risk population: 70% black, mean age = 23 years, and a high (12%) prevalence of preterm birth.[10] Similarly, a recent trial by one of the authors was hospital based with an identical 12% prevalence of preterm birth in primiparous women with untreated bacterial vaginosis.[8] By contrast, our population, although also from South London, were at lower risk of preterm birth. We included women with second and subsequent pregnancies who were cared for solely by community midwives and would not have attended any hospital until much later in pregnancy. In addition, the 13% of the cohort who were lost to follow-up were younger than the remainder and may have been at higher risk of preterm birth. This difference in population, may also explain why we found an association between smoking and preterm birth that was independent of age or social class. Previous

Table 2. Outcome of pregnancy after 13 weeks' gestation related to bacterial vaginosis status.[a]

Characteristic	Women with spontaneous preterm birth (% [*n*/total])	Relative risk (95% CI)
Age (years) (*n* = 899)		
<20	8.0 (2/25)	1.6 (0.4 to 6.3)
Ž20	4.9 (43/874)	
Bacterial vaginosis status (*n* = 848)		
Positive	4.5 (5/110)	0.9 (0.4 to 2.2)
Negative	5.1 (38/738)	
Chlamydia status (*n* = 897)		
Positive	5.6 (1/18)	1.1 (0.2 to 7.6)
Negative	5.0 (44/879)	
Ethnic group (*n* = 851)		
Black Caribbean or black African	2.2 (2/88)	0.5 (0.1 to 1.9)
Other ethnic group	4.8 (37/763)	
Previous preterm birth if previously pregnant (*n* = 545)		
Yes	7.4 (2/27)	2.3 (0.5 to 9.3)
No	3.3 (17/518)	
Marital status (*n* = 853)		
Single, widowed, divorced	4.8 (3/63)	1.0 (0.3 to 3.3)
Married or cohabiting	4.6 (36/790)	
Social class (*n* = 808)		
Social class 3–5	4.1 (13/316)	0.8 (0.4 to 1.6)
Social class 1–2	5.1 25/492)	
Smoked during pregnancy (*n* = 657)		
Yes	12.8 (12/94)	2.9 (1.5 to 5.5)[b]
No	4.4 (25/563)	

[a]This table excludes 122 miscarriages before 23 weeks, 26 terminations, 1 ectopic pregnancy, 13 twins, 10 induced preterm births, 10 women given antibiotics during pregnancy, and 135 women lost to follow-up. [b]*P* = 0.001.

- '*Vaginal swab was not difficult, I just was not sure I was doing it correctly. No such doubts with urine sample!*'
- '*Preferred urine — worry of miscarriage with swab.*'
- '*Vaginal swab easy, not messy. (Hate trying to get wee in a small jar!)*'
- '*Both were simple to carry out with easy to understand instructions.*'
- '*Trying to do a swab in a surgery toilet with a toddler isn't easy! Limited space, and privacy. Have done many urine samples before!*'

Box 1. Women's comments on providing specimens

studies of an association between smoking and preterm birth have shown conflicting results:[13,14] both are associated with lower socioeconomic status. Finally, the association between bacterial vaginosis and late miscarriage confirms earlier work.[4]

The importance of the trial published in 2003, which included 494 bacterial vaginosis positive women recruited at 12–22 weeks' gestation, is that it showed clear benefits of screening.[8] It found that women with asymptomatic bacterial vaginosis, who were treated with oral clindamycin before 22 weeks' gestation, had fewer second trimester miscarriages and preterm births, with a number needed to treat of 108. However, this study must be replicated in a larger trial before introducing widespread screening for bacterial vaginosis in pregnancy.[16]

Implications

If bacterial vaginosis at <10 weeks' gestation is not a strong risk factor for preterm birth in low-risk women in the community, screening may only be worthwhile in a higher risk hospital-based population. In addition, our study does not support the hypothesis that the risk of preterm birth is greater the earlier in pregnancy that bacterial vaginosis is diagnosed.[1] But it does show that non-invasive screening for bacterial vaginosis in early pregnancy is feasible in primary care. Most women who took part found providing a vaginal swab to be easy; and the Gram stain screening method and generic antibiotic treatment are simple and inexpensive.[16] However, even if future trials confirm that treatment of bacterial vaginosis can reduce the risk of adverse pregnancy outcome, screening may not be cost-effective in a low-risk community-based population.

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