ASSOCIATION OF BACTERIAL VAGINOSIS, TRICHOMONAS VAGINALIS, AND VAGINAL ACIDITY WITH OUTCOME OF PREGNANCY

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Background: Bacterial vaginosis and Trichomons vaginalis are believed to be the risk factors for preterm labor birth and preterm prelabor rupture of membranes. The objective of this study was to investigate the association between bacterial vaginosis, T. vaginalis, and vaginal pH with preterm labor birth and preterm prelabor rupture of membranes after excluding other known risk factors.

Methods: In this cohort study, we enrolled 1223 pregnant women with gestational age of 16 – 36 weeks from Amir-Almomenin General Hospital in Semnan, Iran, who had no known medical risk factors for preterm labor birth. Bacterial vaginosis and T. vaginalis were determined on the basis of vaginal pH, saline wet mount, and Amsel tests. The principal outcome was delivery before 37 weeks of gestation and preterm prelabor rupture of membranes.

Results: Bacterial vaginosis and T. vaginalis were detected in 16.0% and 5.5% of these women, respectively. Bacterial vaginosis was positive in 65 (33.1%) patients at 16 – 20 weeks of gestation and in 134 (66.9%) patients at 36 weeks of gestation or during labor (developing preterm labor birth or preterm prelabor rupture of membranes). The frequencies for T. vaginalis were 20 (29.9%) and 47 (70.1%) patients, respectively. All patients with bacterial vaginosis and T. vaginalis had a vaginal pH ≥ 5. There was a significant correlation between bacterial vaginosis and vaginal pH ≥ 5, with preterm labor birth (OR: 5.99; CI: 3.79 – 9.49) and preterm prelabor rupture of membranes (OR: 2.34; CI: 1.07 – 4.99). Moreover, a significant correlation was found between vaginal pH ≥ 5 with preterm labor birth (OR: 5.82; CI: 2.96 – 11.39) and preterm prelabor rupture of membranes (OR: 4.11; CI: 1.62 – 10.12). There was no significant correlation between T. vaginalis with preterm labor birth (OR: 0.73; CI: 0.22 – 2.17) and preterm prelabor rupture of membranes (OR: 1.22; CI: 0.29 – 5.05).

Conclusion: The presence of bacterial vaginosis or vaginal pH ≥ 5 at 16 – 36 weeks of gestation is associated with an increased risk of preterm labor birth and preterm prelabor rupture of membranes.

Keywords: Bacterial vaginosis • preterm labor birth • preterm prelabor rupture of membrane • Trichomonas vaginalis • vaginal pH

Introduction

Preterm birth remains the most important cause of prenatal mortality and nearly half of the long-term neurologic morbidities. Causes of spontaneous preterm birth have not yet been well-understood, but bacterial vaginosis (BV) and Trichomons vaginalis (TV) have been proposed as important factors. BV is defined as an imbalance in the normal vaginal flora with diminution in the normally-predominant lactobacilli and the proliferation of other anaerobic bacteria.

A cause and effect relationship between BV and adverse pregnancy outcome can be better determined in cohort studies, in which BV is diagnosed before the onset of a number of pregnancy complications such as preterm labor birth (PLB) or premature preterm rupture of membranes.
Association of bacterial vaginosis, *T. vaginalis*, and vaginal pH with pregnancy outcome

Some other studies have shown a significant correlation between BV and PLB. However, others have not shown such a correlation. Different reports on the correlation between TV and PLB, have also been reported despite controversies.

It is worth mentioning that all previous reports are based on performing tests by different methods for diagnosing BV or TV and finding the related bacteria. So it would be difficult to compare previous studies. Therefore, we performed this cohort study on pregnant women with gestational age of 16 – 36 weeks, to evaluate the association of BV, TV, and vaginal pH with PLB and PPROM.

**Patients and Methods**

This cohort study, comprised 1223 pregnant women with gestational ages of 16 – 36 weeks who visited at Amir-Almomenin General Hospital in Semnan, Iran, from March 2002 through March 2003.

Women with systemic diseases (e.g., diabetes mellitus, hypertension, renal, or heart disease), placenta previa, abruption, uterine abnormalities, incompetent cervix, twin pregnancies, prior preterm labor pain, prior use of tocolytic and corticosteroid agents during the current pregnancy, or use of antibiotics in the preceding two weeks, were excluded from this study. No history of smoking or alcohol consumption was reported in our patients.

Gestational age was calculated according to the last menstrual period date and ultrasonography performed before the 20th week of pregnancy.

At first, a clean unlubricated speculum was introduced into the vagina and vaginal pH was measured with pH strips (Merck, Germany). Then, sterile cotton swabs were used to obtain material from the posterior vaginal fornix for vaginal smear.

Wet smear of vaginal secretions from the posterior vaginal fornix was diluted with normal saline and examined microscopically (<400 magnification) for identification of clue cells, bacterial morphology, and trichomonads with special flagellated motility. BV was diagnosed if at least three of four Amsel criteria were met:

- Diffuse gray vaginal discharge;
- Vaginal pH >4.5;
- Positive Whiff test (a fishy odor after the addition of a drop of 10% KOH onto a vaginal swab); and
- Presence of clue cells in the wet smear.

If tests were negative for BV and TV at the first time, specimens were again obtained at 34 – 36 weeks of gestation or at the time of admission for labor. Diagnosis of PPROM was performed using the positive nitrazin and fern tests or clinical signs such as gush of fluid from vagina, before the 37th week of gestation.

Women who delivered between the 20th and 37th weeks of gestation were categorized as having had a preterm delivery without any evidence of PPROM.

Correlation between BV, TV, and vaginal pH with PLB and PPROM was identified by using $\chi^2$ and Student’s *t*-tests. *P* values <0.05 were considered statistically significant. The study was approved by the Ethical Committee of Semnan University of Medical Sciences and all patients gave written informed consents before entering the study.

**Results**

BV and TV were detected in 196 (16.0%) and 67 (5.5%) of the patients, respectively. BV was positive in 65 (33.1%) patients with gestational age of 16 – 20 weeks and in 134 (66.9%) patients at the 36th week of gestation or during labor (if developed PLB or PPROM). The frequencies for TV were 20 (29.9%) and 47 (70.1%) patients, respectively. All patients with BV and TV had a vaginal pH ≥5.

The mean ± SD age of women with BV and TV were 25 ± 4.75 and 24.5 ± 4.69 years, respectively, as compared to 25 ± 4.56 in uninfected women. There was no statistical difference between the mean age of infected women with BV or TV, as compared to uninfected women (no BV no TV) ($P = 0.872$).

One hundred and thirty-eight (11.3%) patients had PLB and 41 (3.4%) had PPROM. From those women who had BV, 47 (24%) developed PLB and 11 (5.6%) had PPROM, as compared to 50 (4.9%) and 40 (2.9%) in uninfected women, respectively. Women infected with BV were more likely ($P < 0.05$) to deliver preterm (OR: 5.99; CI $95\%$: 3.79 – 9.49) and had PPROM (OR: 2.34; CI $95\%$: 1.07 – 4.99) (Table 1). From those women who had TV, 4 (6%) developed PLB and 2 (3%) had PPROM, as compared to 77 (8.4%), and 23 (3.4%) in uninfected women ($P = 0.55$ and $P = 0.26$), respectively (Table 2).

In patients with a pH ≥5, 17 (16.6%) developed PLB and 8 (7.9%) had PPROM, as compared to 33...
In patients with BV, all preterm deliveries were before the 32nd week of gestation; 68.1% during 28–30 weeks of gestation, and 31.9% during 31–32 weeks, as compared to 12.4% during 30–32 weeks, 30.2% during 33–34 weeks, and 57.4% during ≥35 weeks in uninfected women.

In women with BV, PPROM occurred in 58.2% of patients during 28–29 weeks of gestation, 29.8% during 30–32 weeks, 7% during 33–34 weeks, and 5% over ≥35 weeks, as compared to 13% during 28–29 weeks, 17% during 30–32 weeks, 60% during 33–34 weeks, and 10% over ≥35 weeks of gestation in uninfected women.

In women with BV, PLB (P < 0.001) and PPROM (P < 0.001) occurred earlier than women without BV.

Discussion

We detected BV in 16.0% and TV in 5.5% of patients. These rates are in agreement with those presented in other studies (12–32% for BV).3, 8–9 Hillier et al detected BV in 16% of 10397 women studied.5 Cotch et al reported TV in 12.6% of pregnant women.10

There was no significant difference between the mean age of infected women with BV and TV, as compared to uninfected women (P = 0.872). Gratacos et al also reported a mean ± SD age of 27.5 ± 5.6 years, which showed no significant difference between the studied groups.31 Other studies have shown a significant correlation between BV and PLB.2, 4, 5, 7, 8, 11, 13

According to our results, vaginal pH >5 was associated with PLB and PPROM (P < 0.05).

Subtil et al showed no significant association between BV and PLB.7 Jacobsson et al reported that the risk for spontaneous preterm birth among women with BV was doubled, but not significantly, even though the samples were obtained early in pregnancy.12 Oakeshott et al also reported that in low-risk patients, BV was not a strong risk factor for preterm birth.2

Leitich et al performed a metaanalysis and concluded that BV increased the risk of PLB more than two folds.15

Although the number of women with adverse pregnancy outcome in TV-positive women was too small, like other studies, we could not detect any positive association between TV with PLB (P = 0.55) and PPROM (P = 0.026).5, 7 However, Cotch et al showed a significant correlation between TV and PLB.10

Gjerdingen et al showed that the sensitivity of high vaginal pH in identifying women with BV or TV >5 was significantly higher than women with vaginal pH ≤5.

Table 1. Distribution of term deliveries, preterm labor, and preterm prelabor rupture of membranes in women with BV and non-BV.

<table>
<thead>
<tr>
<th>BV</th>
<th>Term</th>
<th>PLB</th>
<th>PPROM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>No</td>
<td>880</td>
<td>92.2</td>
<td>50</td>
<td>4.9</td>
</tr>
<tr>
<td>Yes</td>
<td>138</td>
<td>70.4</td>
<td>47</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>1018</td>
<td>88.1</td>
<td>97</td>
<td>8.4</td>
</tr>
</tbody>
</table>

BV = bacterial vaginosis; PLB = preterm labor birth; PPROM = premature preterm rupture of membranes.

≥35 weeks of gestation in uninfected women. In women with BV, PLB (P < 0.001) and PPROM (P < 0.001) occurred earlier than women without BV.

Table 2. Distribution of term deliveries, preterm labor, and preterm prelabor rupture of membranes in women with TV and non-TV.

<table>
<thead>
<tr>
<th>TV</th>
<th>Term</th>
<th>PLB</th>
<th>PPROM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>No</td>
<td>860</td>
<td>88.6</td>
<td>77</td>
<td>8.0</td>
</tr>
<tr>
<td>Yes</td>
<td>61</td>
<td>91</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>921</td>
<td>89.7</td>
<td>81</td>
<td>7.9</td>
</tr>
</tbody>
</table>

TV = Trichomonas vaginalis; PLB = preterm labor birth; PPROM = premature preterm rupture of membranes.

Table 3. Distribution of term deliveries, preterm labor, and preterm prelabor rupture of membranes in women with a vaginal pH of ≤5 or >5.

<table>
<thead>
<tr>
<th>Vaginal pH</th>
<th>Term</th>
<th>PLB</th>
<th>PPROM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>pH ≤ 5</td>
<td>870</td>
<td>94.0</td>
<td>33</td>
<td>3.6</td>
</tr>
<tr>
<td>pH &gt; 5</td>
<td>77</td>
<td>75.5</td>
<td>17</td>
<td>16.7</td>
</tr>
<tr>
<td>Total</td>
<td>947</td>
<td>92.2</td>
<td>50</td>
<td>4.9</td>
</tr>
</tbody>
</table>

PLB = preterm labor birth; PPROM = premature preterm rupture of membranes.
TV is 84.4% and pH >5 associates with an adverse pregnancy outcome. Hauth et al also obtained the same results.16

In this study, we did not treat any patient with BV, because a few references indicating the controversy. In a metaanalysis, no evidence was found to support the use of antibiotic to treat BV or TV in pregnancy to reduce the risk of preterm birth or its associated morbidities in low- or high-risk women.17 The search on Cochrane pregnancy and in the childbirth group trials showed that antibiotic treatment can eradicate BV in pregnancy. However, this review provides little evidence that screening and treating all pregnant women with asymptomatic BV will prevent preterm birth and its consequences. For women with a previous preterm birth, there is some suggestion that treatment of BV may reduce the risk of PPROM and low birth weight.18 The results of several large prospective studies have shown that racial differences persist for rates of BV, even when other known risk factors are controlled. Studies on the gene-environment interaction, examining the genetic aspects of immune response, may explain racial differences and why some, but not all, women with BV experience complications. Trials to prevent preterm birth by the treatment of BV in pregnancy were disappointing. Resistance to clindamycin by BV-associated anaerobic organisms has been also documented. The currently-recommended treatment options for BV are associated with high rates of recurrence. Further studies are still needed to determine whether prevention or control of BV, particularly approaches that rely not only on antibiotic treatment, but also on maintenance of a healthy vaginal ecosystem, can reduce adverse health outcomes.19

We therefore, recommend that:

• Further studies on the treatment of infected pregnant women with BV to evaluate this strategy on the prevention of PLB, PPROM, and the rate of persistent form of the disease should be conducted.

• We can identify pregnant women that are in risk of developing BV and PLB by measuring the vaginal pH—an easy and inexpensive test.

• Screening for BV in all pregnant women with a previous preterm birth. And,

• Treatment of asymptomatic BV in all pregnant women with a previous preterm birth.

Acknowledgment

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References


negative bacteria as an etiologic factor in preterm birth. 


