

# The Association of Bacterial Vaginosis and Preterm Labor

Vida Modares Nejad, Shahla Shafaie

Department of Obstetrics and Gynaecology, Kerman University of Medical Sciences and Health Services, Kerman, Iran.

## Abstract

**Introduction:** To determine the relationship between bacterial vaginosis and preterm labour.

**Method:** In this study 160 labouring women admitted in Bahonar Hospital were studied for the presence of bacterial vaginosis based on the presence of clue cells. Control group consisted of 80 women with the gestational age of more than 38 weeks and the case group consisted of 80 women with the gestational age of 20- 37 weeks. The two groups were compared in regard to the presence of bacterial vaginosis.

**Results:** In the study group 25% of subjects with preterm labour had bacterial vaginosis, while in the control group only 11.3% had symptoms of bacterial vaginosis that shows a significant difference ( $P= 0.039$ ).

**Conclusion:** Bacterial vaginosis can induce preterm labor. Therefore the screening of high-risk women for bacterial vaginosis is highly recommended (JPMA 58:104;2008).

## Introduction

Preterm labour is the greatest cause of perinatal mortality and morbidity in industrial countries. In 80% of the cases, prenatal mortality has no relation with congenital abnormalities.<sup>1-3</sup> Previous studies have shown that vaginitis and cervicitis may have important roles in preterm labour, and this can be prevented.<sup>1</sup>

The prevalence of bacterial vaginosis (BV) ranges from 4 to 64%, depending on the racial, geographic and clinical characteristics of the study population. In asymptomatic women, the prevalence varies from 12 to 25%, and similar percentages are observed in pregnant women. Although BV is associated with several adverse outcomes, such as upper genital tract infections, pelvic inflammatory disease, endometritis, preterm birth and low birthweight, many basic questions regarding the pathogenesis of BV remain unanswered. Mucosal immune system activation may represent a critical determinant of adverse consequences associated with BV. An unequal risk for BV acquisition and/or recurrence could derive from different mucosal immune host abilities and/or capability of invading microbes to produce factors that inactivate the local immune response. BV is associated with a two-fold increased risk of preterm birth, with the greatest risk when BV is present before 16 weeks of gestation (odds ratio = 7.55). This may indicate a critical period during early gestation when BV-related organisms can gain access to the upper genital tract and set the stage for spontaneous preterm labour later in gestation. The results of treatment trials for pregnant women with BV have been heterogeneous, with anywhere from an 80% reduction to a two-fold increase in preterm birth among women who received treatment.<sup>4</sup>

Bacterial vaginosis is one of the most common

cause of vaginal discharge in reproductive age.<sup>5</sup> The exact mechanism of bacterial vaginosis in inducing preterm labor is unknown, but it seems that anaerobic vaginal flora such as bacteroides, gardnerella vaginalis, mycoplasma hominis and peptostreptococcus replace vaginal aerobic lactobacilli<sup>6,7</sup> and alter vaginal flora. The products of anaerobic bacteria stimulate deciduas and cause preterm labour through increase in cytokines phospholipase A2 and prostaglandin release.<sup>8,9</sup>

Several studies have shown that vaginal anaerobic flora and bacterial vaginosis have relation with intrauterine infection, intrauterine foetal growth, premature rupture of membranes, spontaneous abortion and preterm labor.<sup>1</sup>

Protection by peroxides producing lactobacilli may have an important role in preventing ascending infection, prostaglandin release and membrane deficiency.<sup>10</sup>

There are some evident mechanisms involved in intrauterine infection at the end of pregnancy which are different from those causing abortions. Inflammatory reactions following ascending infection due to bacterial vaginosis can lead to spontaneous abortion.<sup>10</sup> The rate of complications resulting from bacterial vaginosis is higher in ascending infection cases such as using IUD.<sup>11</sup>

The treatment of choice for bacterial vaginosis has been metronidazole in the United States. Trials have found a significant reduction in the rate of premature births among pregnant women who presented high risk of prematurity and whose bacterial vaginosis was treated with metronidazole.<sup>12,13</sup> On the other hand, there are similar trials that did not find a decrease in the prematurity rates among low-risk populations.<sup>14-16</sup> The lack of beneficial effect from metronidazole may, however, be related to the dosing regimens used.

However, until recently, 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.

Considering the probable relationship of bacterial vaginosis and the risk of preterm labour, this study was designed to investigate this relationship in Kerman City with the aim of decreasing preterm labour rate by screening and treatment of pregnant women.

### Patients and Methods

This case-control study was done in the Delivery Ward of Bahonar Hospital (Kerman University of Medical Sciences, Kerman / Iran) with the aim of investigating the relationship between bacterial vaginosis and preterm labor. Considering previous studies and the expected Odds ratio of 2.5, the prevalence rate of 10% for BV in our society,  $\alpha = 0.05$  and  $\beta = 20\%$ , number of subjects in each group was calculated 66, but in order to increase the accuracy, 80 subjects were studied in each group.

With the consequent sampling method, 160 patients were enrolled into the study. Preterm labour was the main inclusion criteria for selecting the patients. We define preterm labour as follow: A. at least four contractions in 20 minutes or 8 contractions in 40 minutes causing B. cervical dilatation ( $> 1$  cm) and C. effacement ( $>80\%$ ). Those with cervical deficiency, placenta previa, abruptio placenta, Premature rupture of membrane (PROM), uterus abnormality and multiple pregnancies were excluded from the study. Subjects of control group were selected from full term pregnant women referred to the Delivery Ward because of labour pain.

Vaginal discharge was taken with an ayre spatula from the posterior culdesac and spread on two lamellae. The first lamella was used for Whiff test. That is after adding KOH in the case of amine odor, the diagnosis of BV was confirmed. The second lamella was fixed in alcohol for Pap-Smear test and was studied by an expert for the presence of clue cells.

The diagnosis of BV was established when three of four Amsell's criteria were positive:

1. Vaginal fluid pH  $\geq 4.6$
2. Gray homogeneous vaginal discharge
3. Positive Whiff test
4. The presence of clue cells in Pap Smear or wet mounts

The collected data were analyzed by SPSS and adjusted OR was calculated for various factors.

### Results

In this study 160 pregnant women (80 with preterm labor and 80 with term labor as controls) referring to

**Table 1. Classic ORs for preterm labor based on different variables.**

Variable	N	%	OR	95%CI	P value
Positive BV	29	18.1	2.63	1.03-6.85	0.024
History of Preterm labor	21	13.1	3.75	1.19-12.6	0.010
Housewife	121	75.6	1.61	0.73-3.6	0.19
Being educated	124	77.5	1.15	0.51-2.61	0.7

**Table 2. Multivariate adjuster ORs for preterm labor based on different variables**

Variable	N	%	OR	95%CI	P value
Positive BV	29	18.1	1.5	1.1-2.0	0.008
History of Preterm labor	21	13.1	3.5	1.3-9.7	0.0123
Housewife	121	75.6	2.7	0.9-7.7	0.054
Being educated	124	77.5	0.7	0.3-1.5	0.482

Niknafs Delivery Ward of Bahonar Hospital (Kerman/ Iran) were studied for the presence of bacterial vaginosis. There was no significant difference between the two groups with regard to age, gravidity, parity and abortion .

The participants of both groups were similar regarding age, gravidity, parity and abortion. In the preterm group, 20 (25%) and in the full term group 9 (11.3%) had bacterial vaginosis (P=0.024) and the obtained OR by classic calculation was 2.63. OR for subjects with history of preterm labour was also positive (Table 1).

As it is thought that other variables such as job, history of abortion and educational level, are effective in the occurrence of preterm labour, Regression Model was used to determine the effect of these factors. The results are shown in Table 2. Based on these results, the obtained ORs are 1.5, P=0.008 for bacterial vaginosis and 3.5, P=0.012 for the history of preterm labor. For other variables the obtained ORs were not significant.

The obtained OR for positive history of preterm labour (95% CI: 1.19-12.6, P= 0.010) by classic calculation was 3.75 that after logistic regression calculation did not differ significantly 3.5 (95% CI: 1.3-9.7, P= 0.012).

The obtained OR for bacterial vaginosis (95% CI: 1.03-6.85, P= 0.024) was 2.63 after decrease in logistic regression calculation (Table 1).

The obtained ORs for job, history of abortion and educational level in none of classic or logistic regression calculations were significant (Tables 1 and 2).

### Discussion

Bacterial vaginosis is the most common cause of vaginal discharge in reproductive age with the prevalence rate of 10-15%.<sup>7</sup> Bacterial vaginosis is often asymptomatic and is found in upto 20% women during pregnancy

depending on how often the population is screened.<sup>15</sup>

In surveying the relationship between bacterial vaginosis and educational level, no significant difference was observed. Newton's study reported that bacterial vaginosis had direct relationship with low cultural level.<sup>17</sup>

Eschenbach and coworkers were among the first researchers who studied the relationship between bacterial vaginosis and preterm labour. In their study 49% in preterm group and 24% in full term group had bacterial vaginosis. Later they showed the correlation between bacterial vaginosis and chorioamnionitis and preterm labor.<sup>18</sup>

Prematurity Prediction Study carried out on 3000 women in the United States has shown the relationship between bacterial vaginosis and preterm labor.<sup>17</sup> In the present study, 20 women (25%) in the preterm group had bacterial vaginosis while in the full term group only 9 women (11.3%) had BV that shows a significant difference between the two groups and proves the association of BV with preterm labor.

The prevalence rate of BV during pregnancy has been reported to be 10-30% in various studies. In a study done in Isfahan, the prevalence rate of BV in preterm subjects was 27.7%.<sup>19</sup> The results of the present study are similar to other studies.

In our study, 20% of preterm subjects had previous history of preterm labour, while in the full term group only 6.3% had history of preterm labour which is a significant difference between the two groups.

In a study done in 1996 in England, 500 cases of repeated abortion were surveyed and a higher rate of BV was found in those with history of abortion in the second trimester comparing to those with early abortion.<sup>6</sup>

In our study, no significant difference in the prevalence rate of BV was found between preterm cases with different history of abortion.

In a study done on 2000 subjects in Indonesia, the sensitivity and specificity of Whiff Test for the detection of BV were respectively 6.58% and 73.2% and the sensitivity and specificity of clue cells were respectively 43.1% and 99.6%.<sup>6</sup>

A Brazilian study has found 20% prevalence of bacterial vaginosis among asymptomatic pregnant women.<sup>19</sup> In addition, a significantly increased risk of neonatal complications was found among this population.<sup>20</sup> This study was conducted to evaluate the impact of treatment for bacterial vaginosis among a population of Brazilian pregnant women. Our study compares well with the Brazilian study.

## Conclusion

This study proves the association of bacterial vaginosis and preterm labour. Since preterm labour is one of the important health problems in Iran and neonates' mortality and morbidity rates are among indices used for comparing Health care systems, BV as one of the causative factors of preterm labour deserves more attention.

## References

1. Gravett MG, Hitti J, Hess DL, Eschenbach DA. Intrauterine infection and preterm delivery: evidence for activation of the fetal hypothalamic-pituitary-adrenal axis. *Am J Obstet Gynecol* 2000;182:1404-13.
2. Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. *N Engl J Med* 2000;342:1500-7.
3. Kenyon SL, Taylor DJ, Tarnow-Mordi W. ORACLE Collaborative Group. Broad-spectrum antibiotics for spontaneous preterm labour: the ORACLE II randomised trial. *Lancet* 2001;357:989-94.
4. Guaschino S, De Seta F, Piccoli M, Maso G, Alberico S. Aetiology of preterm labour: bacterial vaginosis. *Bjog* 2006;113 Suppl 3:46-51.
5. Colli E, Bertulesi C, Landoni M, Parazzini F. Bacterial vaginosis in pregnancy and preterm birth: evidence from the literature. *J Int Med Res* 1996;24:317-24.
6. Hillier SL. Diagnostic microbiology of bacterial vaginosis. *Am J Obstet Gynecol* 1993;169:455-9.
7. Shanon H. Diagnostic microbiology of bacterial vaginosis. *Am J Obstet Gynecol* 1993; 165: 1240-4.
8. Lamont RF, Anthony F, Myatt L, Booth L, Furr PM, Taylor-Robinson D. Production of prostaglandin E2 by human amnion in vitro in response to addition of media conditioned by microorganisms associated with chorioamnionitis and preterm labor. *Am J Obstet Gynecol* 1990;162:819-25.
9. Lamont RF. Prostaglandin E2 by Human associated with preterm labour. *Am J Obstet Gynaecol* 1990; 162: 819-25.
10. Donders GG, Van Bulck B, Caudron J, Londers L, Vereecken A, Spitz B. Relationship of bacterial vaginosis and mycoplasmas to the risk of spontaneous abortion. *Am J Obstet Gynecol* 2000;183:431-7.
11. Roy S. Nonbarrier contraceptives and vaginitis and vaginosis. *Am J Obstet Gynecol* 1991;165:1240-4.
12. Morales WJ, Schorr S, Albritton J. Effect of metronidazole in patients with preterm birth in preceding pregnancy and bacterial vaginosis: a placebo-controlled, double-blind study. *Am J Obstet Gynecol* 1994;171:345-7.
13. Hauth JC, Goldenberg RL, Andrews WW, DuBard MB, Copper RL. Reduced incidence of preterm delivery with metronidazole and erythromycin in women with bacterial vaginosis. *N Engl J Med* 1995;333:1732-6.
14. Carey JC, Klebanoff MA, Hauth JC, Hillier SL, Thom EA, Ernest JM, et al. Metronidazole to prevent preterm delivery in pregnant women with asymptomatic bacterial vaginosis. National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. *N Engl J Med* 2000;342:534-40.
15. McDonald HM, O'Loughlin JA, Vigneswaran R, Jolley PT, Harvey JA, Bof A, et al. Impact of metronidazole therapy on preterm birth in women with bacterial vaginosis flora (*Gardnerella vaginalis*): a randomised, placebo controlled trial. *Br J Obstet Gynaecol* 1997;104:1391-7.
16. McClean H. Impact of metronidazole therapy on preterm birth in women with bacterial vaginosis flora. *Br J Obstet Gynaecol* 1998;105:1239-40.
17. Newton ER, Piper J, Peairs W. Bacterial vaginosis and intraamniotic infection. *Am J Obstet Gynecol* 1997;176:672-7.
18. Eschenbach DA, Gravett MG, Chen KC, Hayme UB, Holmes KK. Bacterial vaginosis during pregnancy: An association with prematurity and postpartum complications. In: Mardh PA, Taylor Robinson D, eds. *Bacterial vaginosis*. Stockholm: Almqvist and Wiksel. 1984; pp 214-18.
19. Simoes JA, Giraldo PC, Faundes A. Prevalence of cervicovaginal infections during gestation and accuracy of clinical diagnosis. *Infect Dis Obstet Gynecol* 1998;6:129-33.