Meta-analysis: Bacterial vaginosis multiplies risk for preterm delivery

Leitich H, Bodner-Adler B, Brunbauer M, Kaider A, Egarter C, Husslein P. Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis. *Am J Obstet Gynecol*. 2003;189:139–147.

OBJECTIVE To evaluate bacterial vaginosis (BV) as a risk factor for preterm delivery.

RESULTS In early pregnancy, BV more than doubled the risk for preterm delivery.

METHODS This meta-analysis included 18 English-language reports of prospective or controlled trials involving 20,232 women. Gestational ages were less than 37 weeks; all women had intact amniotic membranes and had been screened for BV.

The outcomes were preterm delivery, spontaneous abortion, maternal or neonatal infection, and perinatal death.

OUTCOME BV greatly increased risk of preterm delivery (odds ratio [OR] 2.19; 95% confidence interval [CI], 1.54-3.12). Higher risks were calculated for women at less than 16 weeks' gestation (OR 7.55; 95% CI, 1.8-31.65) or less than 20 weeks (OR 4.2; 95% CI, 2.11-8.39).

BV also significantly increased the risk of spontaneous abortion (OR 9.91; 95% CI, 1.99-49.34) and maternal infection (OR 2.53; 95% CI, 1.26-5.08). No significant results were found for neonatal infection or perinatal death.

EXPERT COMMENTARY Preterm birth remains one of the most important problems in obstetrics. It occurs in 7% to 10% of all pregnancies in the United States and accounts for the majority of neonatal deaths and morbidity. The economic burden also is impressive: approximately $6 billion annually in additional costs for low birth weight.

Spontaneous preterm birth occurs between 24 and 37 weeks' gestation after spontaneous labor or spontaneous rupture of membranes. It is likely multifactorial, with infection implicated as a major factor. Since the late 1970s, accumulating evidence has implicated intrauterine infection as a cause of preterm labor and preterm rupture of membranes.[1]

The link between BV and preterm birth. Numerous studies have demonstrated a strong and consistent association between BV and preterm birth. While some evidence indicates that BV treatment may reduce the preterm birth rate in women at high risk,[2,3] BV-specific antibiotic therapy has not reduced the preterm birth rate in women with BV in the general population (see "Does metronidazole eliminate BV in asymptomatic gravidas?" page 44).[4] This suggests that a subgroup of women with BV are at risk for adverse outcomes.

Critical research goals are to identify the optimal treatment strategy and the subgroup in which to apply that strategy. Whether optimal treatment will consist of antimicrobial agents, immunomodulatory agents, or both, remains to be seen.

Strengths of the study. This comprehensive survey of research published from 1966 to 2003 summarized clinical trial data from an impressive total of 20,232 women. The investigators used rigorous criteria for including published data in their analyses and appropriately assessed the heterogeneity of various study designs and populations.

This study not only identifies an association between BV and preterm birth overall, but also estimates the association based on the gestational age at which BV is diagnosed, and highlights the strong association between BV and adverse pregnancy outcomes at early

gestational ages—specifically, at less than 16 weeks and less than 20 weeks.

Another great strength is documentation of the relationship between BV and other adverse pregnancy outcomes, such as spontaneous abortion and maternal infection.

Weaknesses. The fact that unpublished data were not included may introduce publication bias into the design and slant findings in favor of an association with BV. The heterogeneity among included trials did not obscure the statistically significant association between BV and preterm birth, as the investigators noted; however, that heterogeneity makes any estimate of the magnitude of the association between BV and preterm birth quite crude.

BOTTOM LINE This important meta-analysis summarizes a 20-year accumulation of literature supporting an association between BV and preterm birth. These data—along with a plethora of evidence supporting infection as an important cause of preterm delivery—underscore the importance of future studies exploring whether identifying high-risk women with BV and treating them early in pregnancy with a long course of oral therapy will play a role in preventing prematurity. Most important, however, are future trials designed to explore the mechanism by which women with BV are at risk of upper genital tract infection. ■

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