

MICROBIOME

Gestational shaping of the maternal vaginal microbiome

The diversity of the vaginal microbiome is linked to ethnicity, preterm birth and transitions to a healthier profile upon pregnancy.

Maria Gloria Dominguez-Bello

The vagina houses one of the least diverse microbiomes in the human body. Often colonized by *Lactobacillus* species during reproductive years, the acidic metabolites of these species maintain low pH and low microbiota diversity in the vagina^{1,2}, impairing colonization by acid-sensitive bacteria, including both gut aerobes and anaerobes. As the vaginal pH increases, for example due to infection, the vaginal environment becomes more permissive to colonization by more diverse microbial communities, including species from the genera *Gardnerella*, *Atopobium*, *Dialister*, *Peptoniphilus*, the Lachnospiraceae BVAB1 and other anaerobes^{1,3}. High vaginal microbiome diversity is associated with symptoms of infection that define a condition that is known as bacterial vaginosis (BV). The presence of BV is associated with a reduction of the vaginal community's resistance to colonization by pathogens, including HIV⁴⁻⁶. BV is associated with pelvic inflammation, which in pregnancy can increase the risk for preterm birth (PTB)^{7,8}. In the United States, women of African descent also have higher vaginal bacterial diversity and high preterm birth rates. However, the low vaginal *Lactobacillus* and high bacterial diversity that typifies BV is necessary but not a sufficient condition for additional disease, and there also are individual and ethnic variations in the threshold of harmful diversity⁹. There is still much to be learned about the relationships between increased diversity, BV, the pathogenic mechanism behind symptomatic episodes and the risk of downstream disease and preterm birth. It is known, however, that the disparity of microbiome diversity among women is reduced during pregnancy. Changes that occur in the vagina during pregnancy^{7,10} lead to increased *Lactobacillus* dominance and decreased species diversity. In this issue of *Nature Medicine*, two articles contribute to the understanding of these

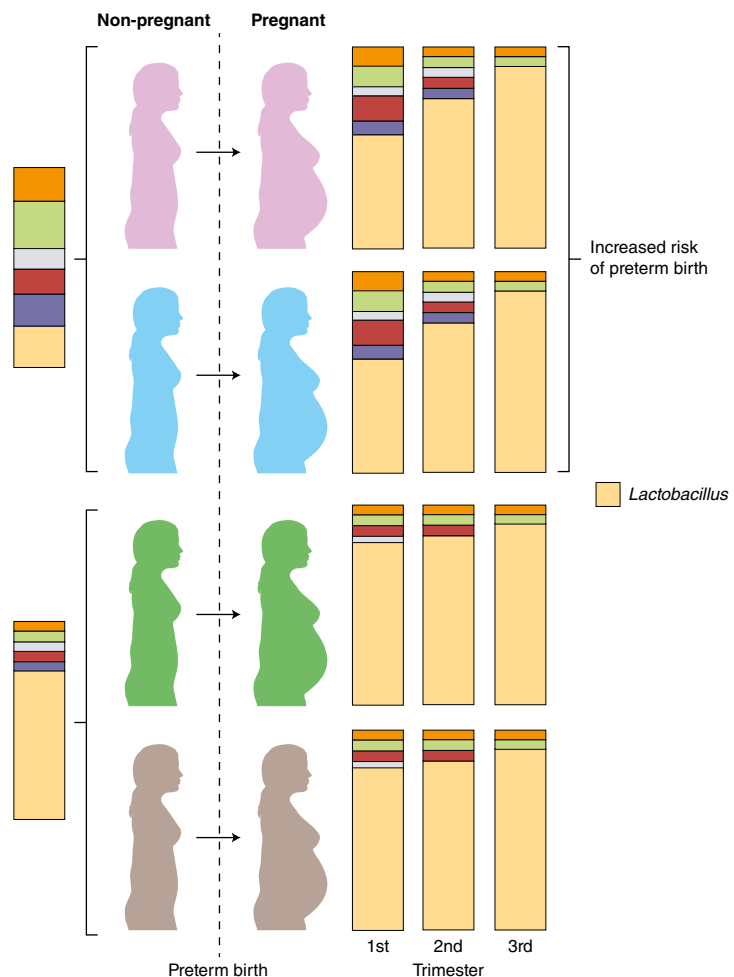


Fig. 1 | The link between the vaginal microbiome, preterm birth and ethnicity. There is variation in vaginal microbiome diversity in healthy women according to ethnic group, with women of African ancestry (shown in pink) showing higher diversity and women of European (shown in green) and Asian (shown in taupe) ancestry showing lower diversity. High vaginal diversity also is associated with BV and preterm birth. Pregnancy leads to the convergence of the maternal microbiome into a low-diversity, *Lactobacillus*-dominated microbiota, and the observed gestational changes are more pronounced in women of African and Hispanic ancestry (shown in blue) than in Asians or Caucasians, since they have higher baseline diversity. High vaginal diversity during pregnancy is associated with increased risk of pre-term birth. The colored bars represent different species of bacteria.

changes in the context of the interplay between vaginal microbiome diversity, ethnicity¹¹ and PTB¹².

Serrano et al.¹¹ studied single time points from 1,969 non-pregnant and 613 pregnant women and followed a cohort of 90 pregnant

women. They show that the early pregnancy differences in the vaginal microbiome that are linked to ethnicity are altered by the gestational dynamics that occur in early pregnancy, with the convergence of all pregnant women toward a *Lactobacillus*-dominated vaginal microbiome profile, low evenness (that is, unevenly distributed species with dominance of few taxa) and a simpler metabolic gene profile (Fig. 1). The study suggests that in the case of a high-diversity vaginal microbiome during pregnancy, the microbiome composition could be manipulated to reduce adverse risks of pregnancy.

Fettweiss et al.¹² mined data from the National Institutes of Health (NIH)-sponsored Human Microbiome Project (HMP), indicating the broad utility of such data. The authors analyze multi-omic data from 45 women who gave birth preterm and 90 women whose pregnancies went to full term, who were predominantly of African ancestry. They show that preterm birth was

linked to a low relative abundance of vaginal *Lactobacillus crispatus* and *Lactobacillus* metabolites, high vaginal microbial diversity and high expression of vaginal proinflammatory cytokines.

These two studies provide evidence that gestational changes transform the vaginal microbiota toward a community structure that promotes anti-inflammatory cytokines and that may be more resistant to infections, consistent with an increased evolutionary fitness of mother and baby. The evolutionary implications of racioethnic differences in the vaginal microbiome are not clear, but evolutionary processes have provided gestational mechanisms that decrease disease risks and maximize health. The structure of the vaginal microbiota during gestation may hold predictive value for preterm birth, particularly in women of African ancestry. □

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Competing interests

The author declares no competing interests.