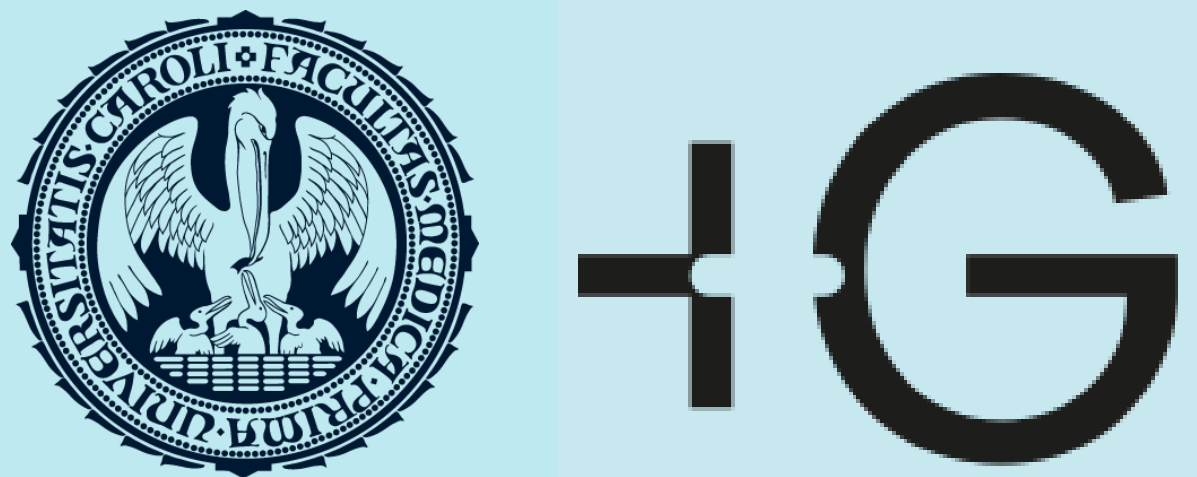


Vaginal microbial ecosystem and the risk of recurrent preterm labor: a prospective cohort study



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Objectives

To characterize the mid-pregnancy vaginal microbial ecosystem in asymptomatic pregnant women with a history of spontaneous preterm birth or second-trimester miscarriage, and to evaluate its association with subsequent spontaneous preterm birth while accounting for established clinical predictors of preterm birth.

Methods

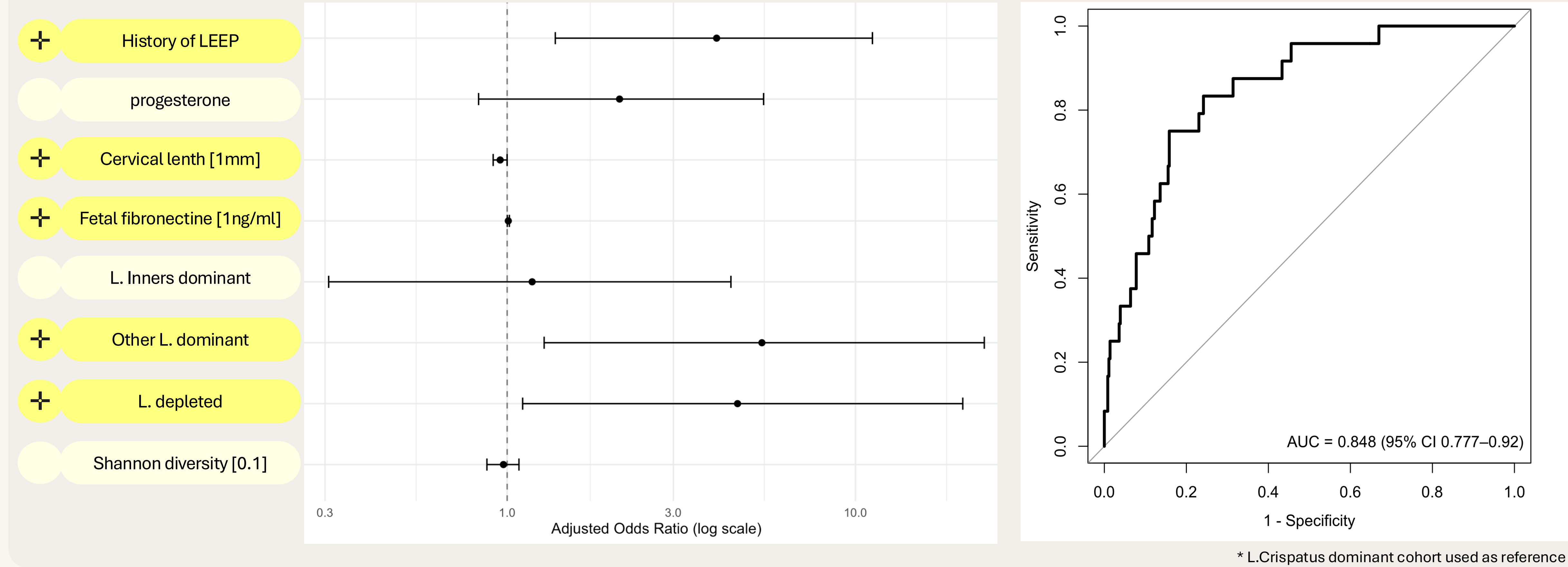
We conducted a prospective cohort study of asymptomatic women with singleton pregnancies and a prior spontaneous preterm birth or second-trimester miscarriage. Vaginal fluid samples were collected for quantitative fetal fibronectin testing and for DNA extraction, followed by 16S ribosomal RNA gene sequencing. Transvaginal ultrasound cervicometry was subsequently performed. The vaginal microbiota was classified based on the relative abundance of *Lactobacillus* species. Perinatal outcomes were compared across the classified microbial groups.

Results

A total of 384 women were included. Preterm birth before 37 weeks occurred in 25% (96/384) and did not differ between groups ($P = 0.590$). In contrast, preterm birth before 34 weeks varied significantly across microbial profiles, occurring in 3% (5/151) in CST I (*L. crispatus*) and 4% (5/113) in CST II (*L. iners*), compared with 11% (5/45) in other *Lactobacillus*-dominant CSTs and 12% (9/75) in *Lactobacillus*-depleted microbiota ($P = 0.030$).

In multivariable analysis preterm birth before 34 weeks was independently associated with prior cervical surgery (aOR, 3.994; 95% CI, 1.375–11.189), shorter cervical length (aOR, 0.955; 95% CI, 0.912–1.000), higher fetal fibronectin levels (aOR, 1.008; 95% CI, 1.001–1.015), and vaginal microbial ecosystems depleted in *Lactobacillus* (aOR, 4.587; 95% CI, 1.108–20.333) and dominated by *Lactobacillus* species other than *L. crispatus* or *L. iners* (aOR, 3.388; 95% CI, 1.277–23.441).

Forest plot and ROC for Firth model for Preterm birth < 34 weeks



Conclusions

Mid-pregnancy vaginal microbiome composition helps refine preterm birth risk stratification, with non-crispatus, non-iners *Lactobacillus*-dominant or *Lactobacillus*-depleted profiles indicating a biologically vulnerable environment for preterm birth before 34 weeks. No significant association was observed between the vaginal microbial ecosystem and recurrent preterm birth before 37 weeks' gestation.

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