Vaginal microbiota are associated with in vitro fertilization during female infertility

Tao Wang¹, Penghao Li², Xue Bai³,⁴, Shilin Tian⁵, Maosen Yang⁴, Dong Leng⁴, Hua Kui⁴, Sujuan Zhang², Xiaomiao Yan², Qu Zheng², Pulin Luo², Changming He², Yan Jia², Zhoulin Wu⁵, Huimin Qiu⁷, Jing Li⁷, Feng Wan⁸, Muhammad Akhtar Ali⁹, Rurong Mao², Yongxin Liu³, Diyan Li¹

¹School of Pharmacy, Chengdu University; ²Chengdu Jinjiang Hospital for Maternal and Child Health Care; ³Agricultural Genomics Institute at Shenzhen, Chinese Academy of Agricultural Sciences; ⁴College of Animal Science and Technology, Sichuan Agricultural University; ⁵College of Life Sciences, Wuhan University; ⁶College of Food and Biological Engineering, Chengdu University; ⁷Kunming University; ⁸Chengdu University of Traditional Chinese Medicine; ⁹University of the Punjab

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**Research Background**

Infertility is a global health problem. It affects around 2 to 10.5% of women between the ages of 20 and 44, leading to primary and secondary infertility.

- **Reason:** ovulation problems, polycystic ovary syndrome, fallopian tube problems, uterus problems, and endometriosis.

- The prevalence of infertility is rising, and assisted reproductive technologies (ART) are increasingly in demand, as well as becoming safer and more successful.

**Vaginal microbiome refers to the community of microorganisms that live in a woman's vagina and plays an important role in maintaining vaginal health and reproductive health.**

- Subclinical changes in the microbiota leading to bacterial vaginosis (often caused by *Gardnerella vaginalis*) are also thought to be associated with an increased risk of miscarriage.

- Infertile patients possess distinct reproductive tract microbiota (lower and/or upper).

- The composition of the vaginal microbiome in infertility also appears to be linked to the likelihood of natural conception and ART cycle success.

The vaginal microbiome may predict the outcome of in vitro fertilization. It is important to consider whether IVF outcomes could be influenced by the microbial composition of the reproductive tract among women with different types of infertility.
Introduction

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- The analysis reveals correlations between clinical and biochemical parameters and infertility;
- identifying microbiome signatures associated with these clinical and biochemical measurements;
- Potential bacterial markers for good IVF outcomes were also identified.

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1. Phenotype and vaginal microbial composition

- Age and levels of luteinizing hormone, prolactin, and anti-mullerian hormones were negatively correlated, and it was positively correlated with follicle-stimulating hormone.

- At species level, we detected the following species belonging to the Lactobacillus genus: *L. iners* (41.54%), *L. crispatus* (31.12%), *L. jensenii* (2.63%), and *L. hominis* (1.41%).

- A significantly widespread presence of *Lactobacillus*, which was all negatively correlated with the abundance of other 14 genera, respectively. *Gardnerella* and *Prevotella* were significantly positively correlated with 13 and 11 genera respectively.
2. Community types of vaginal microbiota in infertility women

- This analysis revealed five major groups and nine sub-groups of microbial communities.

- The taxonomic composition at the species level of samples designated to each CST typically aligned with that of the related reference centroid.

- Variations in Shannon diversity were noted among the sub-CSTs.

- The co-occurring vaginal bacterial networks showed several differences between the five community types with samples of more than one hundred and eighty.
3. Association of the vaginal microbiota with biochemical and clinical measurements

- Estradiol (E2) was found to be significantly associated with the largest number of microorganisms.

- In women of reproductive age, the relative abundances of *Lactobacillus* were found to be positively correlated with age. ——Suggesting an increase in the colonization of these bacteria in the vagina as females age.

- *Lactobacillus* was a biomarker for age, *G. vaginalis* was a biomarker for weight.
Among the 1231 women with infertility, most of them (783, 63.61%) were diagnosed with an inflammation condition, namely chronic salpingitis, endometritis, and pelvic inflammatory disease.

Only 12 and 7 infertility-associated bacterial taxa were identified in females with low AMH and intrauterine adhesion, respectively.

Type III-A samples showed a high-level distribution of scarred uterus (n = 81). The highest proportion of type IV-B samples were from women who were diagnosed with salpingectomy.
5. Association of vaginal microbiota composition with IVF outcomes

- Only age, AMH, and LH had a significant effect on the pregnancy rate.
- Type I and type III contained the largest number of women.
- *L. jensenii* is a biomarker for this CST showed the highest pregnancy rate.
- In type IV-B, the *Lactobacillus* was a biomarker for the pregnant women.
At the genus level, the vaginal flora was also dominated by *Lactobacillus*, followed by *Gardnerella* and *Prevotella*.

At the species level, *L. jensenii* exhibited a relatively higher abundance in pregnant women --- That *L. jensenii* was a marker for CST III-B with the highest pregnant rate.

Compared to the pregnant women, the non-pregnant women contained more annotated genes and antimicrobial resistance genes (ARGs) than pregnant women.
Summary

- Pregnancy rates vary among women with different vaginal microbiome communities.

- Too high abundances of both *Lactobacillus crispatus* and *Lactobacillus iners* have negative effects on in vitro fertilization (IVF) outcomes.

- A moderate abundance (around 80%) of *Lactobacillus* is more beneficial for pregnancy.

- These findings may aid the development of strategies for predicting vaginal microbiota to control IVF outcomes.

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