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**Vaginal microbes confounders and implications on women's health**

Nori W *et al*. Genital microbes' role in women's health

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**Abstract**

The vagina has diverse vaginal microbes (Vm). A disturbance in the delicate balance maintained in Vm is linked to women's obstetrical and reproductive tract problems. Vaginal microbes play an essential role in protecting the health of the female reproductive tract by alleviating gynecological infection. However, Vm profiling has many confounders that need to be addressed during sampling, including age, race, pregnancy, medical illness, and smoking. Vm profiling improves reproduction odds, may serve as a marker for genital malignancies and have a therapeutic application in menopausal women and women with cervical cancers.

**Key Words:** Vaginal microbes; Lactobacillus; Infertility; Probiotics; Cancer; Menapuse

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**Core Tip:** The vaginal ecosystem has a key role in women's health. Vaginal microbes (Vm) affect the obstetrical performance of pregnant women and, in turn, can be affected by age, gestational age, race, and time of sampling. For infertile women, Vm composition can affect fertilization odds, the success of assisted reproduction technique, and even may predict the chances of live birth. The therapeutic aspect of Vm was introduced to enhance vaginal protection against infection, alleviate menopausal symptoms, and, finally, in genital malignancies. Vm was used as a signature marker in predicting and preventing ovarian and cervical malignancies, respectively.

**TO THE EDITOR**

We read with interest Liao *et al*'s study[1] published in *World J Clin Cases* that discusses the influence of vaginal microbes (Vm) on pregnant women's health and how the integrity of the vaginal ecosystem is maintained by a delicate balance of vaginal sanitation and group B streptococcus status[1].

Studying the Vm has many implications for obstetrical and gynecological diseases in women. Earlier work has examined confounders that can affect Vm, which was not discussed in Liao *et al’s* study[1], including; women's age, race, pregnancy and gestational age at sampling, smoking, and sexual activity[2-4].

A recent meta-analysis described the effect of race and age on the unique ecosystem of Vm. The study confirmed that Chinese females hosted a distinct Vm from other ethnicities. In good agreement, Dunlop *et al* discussed different Vm in a group of African American women *vs* non-African American study population they examined[5,6].

Certain behaviors and customs can influence human races. Male circumcision, which is performed in some societies, is believed to minimize Human papillomavirus (HPV) transmission, a significant factor in the development of cervical cancer. Furthermore, in other communities, females may have several male partners, which may enhance the transmission of sexually transmitted diseases, including HPV[7,8].

Other studies addressed the difference between Vm in the pregnant *vs* non-pregnant population due to different hormonal influences[5].

Even for pregnant women, the sampling timing affects the observed Vm seen, as Laghi *et al’s* study[9] suggested. Moreover, they discussed the effect of females' age, diet, smoking, and sex on modifying the Vm composition[9,10].

Diseases caused by vaginal infections inversely impact obstetrical performance, like preterm labor and abortion. Furthermore, the implication of Vm on fertility outcomes and women's health in menopause was explored, given the increasing number of women entering menopause. An emphasis was made on Vm's benefit in the management of menopausal symptoms, reducing the risk of osteoporosis, regulating the nervous system, and lipid profiling for menopausal women[11-13].

Polycystic ovarian syndrome is a common cause of female infertility; research showed reduced Lactobacillus in the vagina and cervix of affected women. Consequently, fertilization rates were reduced due to oocyte damage by colonizing microbes in the oocyte's follicular fluid[14,15]. For infertile couples seeking assisted reproductive technique(ART), an alteration in Vm and male seminal fluid microbes were linked to unsuccessful ART outcome; in fact, Lactobacillus presence in the women's lower and upper genital tract favors positive outcomes[16-18].

Additionally, Vm profiling was used to predict successful *in-vitro* fertilization with or without intracytoplasmic sperm injection cycle and showed a predictive accuracy of 94%. Lactobacillus dominance was key in predicting pregnancy success and odds of live birth (odds ratio 0.66, 95% confidence interval 0.50–0.88)[19,20].

It is well known that genital infection causes a change of Vm predominant; interestingly, a correlation was found between the alteration of Vm and the development of epithelial ovarian cancer, a malignancy that is usually present in late or advanced stages. It was proposed that Vm could serve as a useful biomarker for earlier diagnosis and prevention of ovarian and cervical cancers[21-23].

Detection and clustering of Vm were based on culture-dependent methods[9,21]. However, due to their limitations, detection of Vm was shifted to culture-independent methods in the last few years, for example, Sanger sequencing of the 16S rRNA of bacterial colonies and Illumina-based amplicon sequencing of the V6 region of the 16S rRNA gene[10,21].

A therapeutic avenue of Vm was also suggested; a probiotic is a preparation containing viable microbial agents to improve health. Treatment with probiotics to relieve genitourinary sequelae in postmenopausal women (PMW) is a promising option *via* restoring Lactobacillus abundance in the vagina. Recent evidence shows that oral and direct administration of probiotics in the vagina is an adjuvant therapy to estrogen withdrawal in PMW[13,24].

Probiotics were also used for their anticancer activities in cervical cancer *via* activating the maturation of natural killer cells and promoting cellular and humoral immunity. Additionally, probiotics were added to reduce the side effects of radiation therapy for cervical malignancies[25].

The Corona Virus Infectious Disease(COVID)-19 pandemic has had a detrimental effect on fetal-maternal outcomes[26]. Celik *et al*[27] discovered a considerable change in Vm in affected cases. In fact, the more severe the maternal illness, the more Vm is altered. As a result, the researchers hypothesized that COVID-19 fosters an undesirable vaginal microenvironment. These findings point to the potential use of microbiome-associated indicators as a risk assessment tool for preterm birth in COVID-19 pregnant women. In addition, a therapeutic avenue can be created *via* the modification of Vm in affected cases[27].

In conclusion, Vm have confounders that need to be adjusted before sampling; moreover, Vm has implication for women's obstetrical and fertility potential. Vm can protect against infection development, be a signature biomarker for predicting ovarian cancer, and have promising therapeutic applications for PMW and patients with cervical cancer.

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**REFERENCES**

1 **Liao Q**, Zhang XF, Mi X, Jin F, Sun HM, Wang QX. Influence of group B streptococcus and vaginal cleanliness on the vaginal microbiome of pregnant women. *World J Clin Cases* 2022; **10**: 12578-12586 [PMID: 36579104 DOI: 10.12998/wjcc.v10.i34.12578]

2 **Elovitz MA**, Gajer P, Riis V, Brown AG, Humphrys MS, Holm JB, Ravel J. Cervicovaginal microbiota and local immune response modulate the risk of spontaneous preterm delivery. *Nat Commun* 2019; **10**: 1305 [PMID: 30899005 DOI: 10.1038/s41467-019-09285-9]

3 **Romero R**, Hassan SS, Gajer P, Tarca AL, Fadrosh DW, Nikita L, Galuppi M, Lamont RF, Chaemsaithong P, Miranda J, Chaiworapongsa T, Ravel J. Correction: The composition and stability of the vaginal microbiota of normal pregnant women is different from that of non-pregnant women. *Microbiome* 2014; **2**: 10 [PMID: 24735933 DOI: 10.1186/2049-2618-2-10]

4 **Romero R**, Hassan SS, Gajer P, Tarca AL, Fadrosh DW, Bieda J, Chaemsaithong P, Miranda J, Chaiworapongsa T, Ravel J. The vaginal microbiota of pregnant women who subsequently have spontaneous preterm labor and delivery and those with a normal delivery at term. *Microbiome* 2014; **2**: 18 [PMID: 24987521 DOI: 10.1186/2049-2618-2-18]

5 **Hotkani ZG**, Ghaedmohammadi S, Mozdoori N. Meta-analysis of race and age influence on the vaginal microbiome in pregnant and nonpregnant healthy women. *Future Microbiol* 2022; **17**: 1147-1159 [PMID: 35950983 DOI: 10.2217/fmb-2021-0209]

6 **Dunlop AL**, Satten GA, Hu YJ, Knight AK, Hill CC, Wright ML, Smith AK, Read TD, Pearce BD, Corwin EJ. Vaginal Microbiome Composition in Early Pregnancy and Risk of Spontaneous Preterm and Early Term Birth Among African American Women. *Front Cell Infect Microbiol* 2021; **11**: 641005 [PMID: 33996627 DOI: 10.3389/fcimb.2021.641005]

7 **Hegazy AA**, Al-Rukban MO. Male circumcision: review and authors perspective. *The Health* 2012; **3**: 24–30

8 Hegazy DAA. Mode of Hepatitis C Transmission through Sexual Intercourse: Author Perspective. *AANAT* 2016;**2** [DOI: 10.21276/aanat.2016.2.2.1]

9 **Laghi L**, Zagonari S, Patuelli G, Zhu C, Foschi C, Morselli S, Pedna MF, Sambri V, Marangoni A. Vaginal metabolic profiles during pregnancy: Changes between first and second trimester. *PLoS One* 2021; **16**: e0249925 [PMID: 33831087 DOI: 10.1371/journal.pone.0249925]

10 **Song SD**, Acharya KD, Zhu JE, Deveney CM, Walther-Antonio MRS, Tetel MJ, Chia N. Daily Vaginal Microbiota Fluctuations Associated with Natural Hormonal Cycle, Contraceptives, Diet, and Exercise. *mSphere* 2020; **5** [PMID: 32641429 DOI: 10.1128/mSphere.00593-20]

11 **Kroon SJ**, Ravel J, Huston WM. Cervicovaginal microbiota, women's health, and reproductive outcomes. *Fertil Steril* 2018; **110**: 327-336 [PMID: 30098679 DOI: 10.1016/j.fertnstert.2018.06.036]

12 **Nori W**, Shallal F, Zghair MAG. Aspirin effect on Mid luteal Phase Doppler Indices in Patients with Recurrent Pregnancy Loss. *Int J Pharm Res* 2020; **12**:2929-2934 [DOI: 10.31838/ijpr/2020.12.03.413]

13 **Chen Q**, Wang H, Wang G, Zhao J, Chen H, Lu X, Chen W. Lactic Acid Bacteria: A Promising Tool for Menopausal Health Management in Women. *Nutrients* 2022; **14** [PMID: 36364729 DOI: 10.3390/nu14214466]

14 **Tu Y**, Zheng G, Ding G, Wu Y, Xi J, Ge Y, Gu H, Wang Y, Sheng J, Liu X, Jin L, Huang H. Comparative Analysis of Lower Genital Tract Microbiome Between PCOS and Healthy Women. *Front Physiol* 2020; **11**: 1108 [PMID: 33013474 DOI: 10.3389/fphys.2020.01108]

15 **Ali AI**, Nori W. Correlation of Serum Visfatin Level in Non-obese Women with Polycystic Ovary Syndrome and Matched Control. *Reprod Sci* 2022; **29**: 3285-3293 [PMID: 35687303 DOI: 10.1007/s43032-022-00986-z]

16 **Bracewell-Milnes T**, Saso S, Nikolaou D, Norman-Taylor J, Johnson M, Thum MY. Investigating the effect of an abnormal cervico-vaginal and endometrial microbiome on assisted reproductive technologies: A systematic review. *Am J Reprod Immunol* 2018; **80**: e13037 [PMID: 30133062 DOI: 10.1111/aji.13037]

17 **Chen S**, Xue X, Zhang Y, Zhang H, Huang X, Chen X, Deng G, Luo S, Gao J. Vaginal Atopobium is Associated with Spontaneous Abortion in the First Trimester: a Prospective Cohort Study in China. *Microbiol Spectr* 2022; **10**: e0203921 [PMID: 35311570 DOI: 10.1128/spectrum.02039-21]

18 **Tsonis O**, Gkrozou F, Paschopoulos M. Microbiome affecting reproductive outcome in ARTs. *J Gynecol Obstet Hum Reprod* 2021; **50**: 102036 [PMID: 33307241 DOI: 10.1016/j.jogoh.2020.102036]

19 **Koedooder R**, Singer M, Schoenmakers S, Savelkoul PHM, Morré SA, de Jonge JD, Poort L, Cuypers WJSS, Beckers NGM, Broekmans FJM, Cohlen BJ, den Hartog JE, Fleischer K, Lambalk CB, Smeenk JMJS, Budding AE, Laven JSE. The vaginal microbiome as a predictor for outcome of in vitro fertilization with or without intracytoplasmic sperm injection: a prospective study. *Hum Reprod* 2019; **34**: 1042-1054 [PMID: 31119299 DOI: 10.1093/humrep/dez065]

20 **Zeng H**, He D, Hu L, Abdullah RK, Zhang L, Jiang B, Xie H, Liu N. Non-Lactobacillus dominance of the vagina is associated with reduced live birth rate following IVF/ICSI: a propensity score-matched cohort study. *Arch Gynecol Obstet* 2022; **305**: 519-528 [PMID: 34370072 DOI: 10.1007/s00404-021-06171-y]

21 **Punzón-Jiménez P**, Labarta E. The impact of the female genital tract microbiome in women health and reproduction: a review. *J Assist Reprod Genet* 2021; **38**: 2519-2541 [PMID: 34110573 DOI: 10.1007/s10815-021-02247-5]

22 **Banerjee S**, Tian T, Wei Z, Shih N, Feldman MD, Alwine JC, Coukos G, Robertson ES. The ovarian cancer oncobiome. *Oncotarget* 2017; **8**: 36225-36245 [PMID: 28410234 DOI: 10.18632/oncotarget.16717]

23 **Nejman D**, Livyatan I, Fuks G, Gavert N, Zwang Y, Geller LT, Rotter-Maskowitz A, Weiser R, Mallel G, Gigi E, Meltser A, Douglas GM, Kamer I, Gopalakrishnan V, Dadosh T, Levin-Zaidman S, Avnet S, Atlan T, Cooper ZA, Arora R, Cogdill AP, Khan MAW, Ologun G, Bussi Y, Weinberger A, Lotan-Pompan M, Golani O, Perry G, Rokah M, Bahar-Shany K, Rozeman EA, Blank CU, Ronai A, Shaoul R, Amit A, Dorfman T, Kremer R, Cohen ZR, Harnof S, Siegal T, Yehuda-Shnaidman E, Gal-Yam EN, Shapira H, Baldini N, Langille MGI, Ben-Nun A, Kaufman B, Nissan A, Golan T, Dadiani M, Levanon K, Bar J, Yust-Katz S, Barshack I, Peeper DS, Raz DJ, Segal E, Wargo JA, Sandbank J, Shental N, Straussman R. The human tumor microbiome is composed of tumor type-specific intracellular bacteria. *Science* 2020; **368**: 973-980 [PMID: 32467386 DOI: 10.1126/science.aay9189]

24 **Petrova MI**, Lievens E, Malik S, Imholz N, Lebeer S. Lactobacillus species as biomarkers and agents that can promote various aspects of vaginal health. *Front Physiol* 2015; **6**: 81 [PMID: 25859220 DOI: 10.3389/fphys.2015.00081]

25 **Negi D**, Singh A, Joshi N, Mishra N. Cisplatin and Probiotic Biomass Loaded Pessaries for the Management of Cervical Cancer. *Anticancer Agents Med Chem* 2020; **20**: 589-598 [PMID: 31823703 DOI: 10.2174/1871520619666191211110640]

26 **Farhan FS**, Nori W, Al Kadir ITA, Hameed BH. Can Fetal Heart Lie? Intrapartum CTG Changes in COVID-19 Mothers. *J Obstet Gynaecol India* 2022; **72**: 479-484 [PMID: 35634476 DOI: 10.1007/s13224-022-01663-6]

27 **Celik E**, Ozcan G, Vatansever C, Paerhati E, Kuşkucu MA, Dogan O, Cekic SG, Ergonul O, Gürsoy A, Keskin Ö, Can F. Alterations in vaginal microbiota among pregnant women with COVID-19. *J Med Virol* 2023; **95**: e28132 [PMID: 36068653 DOI: 10.1002/jmv.28132]

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