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Impact of intrauterine devices on microbiota in women: Identification of bacterial colonization

Impact of iuds on microbiota in women

Tahsin Takcı¹, Şerife Özlem Genç², Meral Çetin²

¹ Clinic of Obstetrics and Gynecology, Sivas Numune Hospital, Türkiye.

² Department of Obstetrics and Gynecology, Faculty of Medicine, Cumhuriyet University, Sivas, Türkiye.

Abstract

Aim: The intrauterine device (IUD) is the second most widely used contraceptive method globally due to its effectiveness, affordability, and reliability. There are two primary types: copper and hormonal. However, IUDs are associated with potential complications, including ectopic pregnancy, uterine perforation, and pelvic inflammatory disease. This study aims to assess and compare the safety and complication rates of copper and hormonal IUDs, with a focus on their impact on vaginal microbiota.

Methods: The study included 233 women who had their IUDs removed at our clinic. The IUDs were analyzed using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) to identify the microbiota present on the devices.

Results: Participants' ages ranged from 20 to 70 years, with a mean age of 39.64 ± 8.37 . The majority (84.4%) used copper IUDs, while 15.6% used levonorgestrel-releasing IUDs. Among the patients, 41.2% reported vaginal discharge, 39.5% experienced dyspareunia, and 18.5% had a history of pelvic inflammatory disease or tubo-ovarian abscess.

Conclusion: IUD use significantly impacts vaginal microbiota, with *Escherichia coli* being a common pathogen in both copper and hormonal IUD users. Regular gynecological check-ups, sterile insertion practices, and patient education on infection symptoms are crucial for mitigating risks. Probiotics may help maintain microbiota balance during IUD use. Future studies should investigate long-term microbiota changes, compare different IUD types, and explore infection prevention strategies. This research is a vital contribution to understanding the effects of IUDs on vaginal microbiota.

Keywords

intrauterine devices, microbiota, women's health, *escherichia coli*

DOI: 10.4328/ACAM.22412 Ann Clin Anal Med 2025;16(1):52-56

Received: 2024-09-18 Accepted: 2024-11-04 Published Online: 2024-11-12 Printed: 2025-01-01

Corresponding Author: Tahsin Takcı, Clinic of Obstetrics and Gynecology, Sivas Numune Hospital, Türkiye.

E-mail: tahsintakci@gmail.com P: +90 542 288 47 92

Corresponding Author ORCID ID: <https://orcid.org/0000-0003-1709-1597>

Other Authors ORCID ID: Serife Ozlem Genc, <https://orcid.org/0000-0002-9811-2726> . Meral Cetin, <https://orcid.org/0009-0000-2949-8226>

Introduction

IUDs are a widely utilized and effective method of birth control globally.¹ However, there is a scarcity of studies in the literature regarding the impact of IUDs on the female microbiota. The influences of the microbiota on human health, ranging from the immune to the digestive system, and in the prevention of diseases, are known.² Understanding the effects of IUD usage on the patterns of bacterial colonization in women's microbiota is thus of critical importance.

IUDs have been one of the most commonly used methods of contraception worldwide for many years, due to their high efficacy and safety, long-term usage, cost-effectiveness, and the absence of side effects seen with hormonal contraceptives.¹ Consequently, the effects associated with IUDs have gained significance. To date, the microbiome of the reproductive tract has received less research attention compared to that of the gut. However, there is increasing evidence to suggest its potential influence on general and reproductive health, fertility, and pregnancy outcomes.³ The composition of the vaginal microbiota is affected by various factors, including hormonal changes, sexual activity, and personal hygiene practices.

Limited studies have been conducted in healthy women of reproductive age to determine what constitutes a 'normal' microbiota profile. Commensal bacteria, such as *Lactobacillus*, modulate the host immune system and may aid in preventing pathogen colonization. *Lactobacillus* consumes estrogen-dependent glycogen produced in the vaginal epithelium.⁴ The lactic acid produced by *Lactobacillus* decreases the local pH and possesses bactericidal properties.^{5,6} contributing to the maintenance of bacterial balance and the prevention of bacterial vaginosis and aerobic vaginitis.⁷ The vaginal microbiome may also play a role in protecting against adverse pregnancy outcomes, such as early miscarriage,⁸ and preterm birth,⁹ as well as gynecological cancers.¹⁰

The aim of this study is to examine the potential effects of IUDs on the vaginal microbiota through the identification of bacterial colonization in women using IUDs. The study focuses on understanding the microbial effects of IUD usage on female reproductive health. In this context, the study aims to investigate whether IUDs induce changes in the vaginal microflora, the potential health outcomes of these changes, and the long-term effects of IUD usage on women's health. Additionally, another goal is to contribute to the development of preventative strategies to reduce the risk of infection during IUD usage, based on the findings obtained.

Materials and Methods

This study included 233 women who had their IUDs removed at our clinic. Using a descriptive study design, we aimed to analyze the diversity of vaginal microbiota in women using IUDs. This design was selected for its ability to assess the microbiota's current state without intervention. Participants remained eligible for inclusion even if the device was removed due to bleeding, infection, or personal preference. To minimize potential confounders, we carefully set inclusion criteria, excluding women with more than one sexual partner, a body mass index (BMI) over 35, recent use of vaginal douches, or sexual activity within the previous 48 hours. These measures were taken to ensure a homogeneous study group, facilitating more precise and reliable microbiota analysis.

MALDI-TOF MS was employed for bacterial identification due to its high accuracy and speed in detecting a broad spectrum of microorganisms. This technique is particularly well-suited for microbiota studies as it enables the rapid identification and differentiation of bacterial species based on their distinct protein profiles. However, it is important to acknowledge that while MALDI-TOF MS is highly reliable, it may underrepresent certain slow-growing or low-abundance bacterial species.

The incubation times for bacterial cultures were tailored to optimize the growth of the most common vaginal bacteria. Cultures were incubated for up to 72 hours, depending on the expected growth rates of the target organisms. This step ensured that even slower-growing bacteria could be detected, providing a more comprehensive view of the microbiota.

The study was conducted under sterile conditions by directly culturing IUDs. This process was designed to allow for the direct and precise examination of microbial colonization on the surfaces of the IUDs. IUD samples were aseptically removed using sterilized ovum forceps and immediately transferred to culture dishes containing specialized media for the identification of bacterial species. These cultures were then evaluated using MALDI-TOF MS, which facilitates the rapid and accurate identification of bacterial species. MALDI-TOF MS identifies species by measuring the protein profiles of microorganisms isolated from cultures. The findings from the research were analyzed using IBM SPSS Statistics 25 (IBM Corp., Armonk, NY, USA).

After conducting descriptive statistical analyses (frequency, percentage distribution, mean $\pm$ standard deviation), it was found that the assumptions of the Chi-square test could not be met when applied to the multi-way arrays. Therefore, instead of computing the Chi-square value, the Fisher's Exact Test with Monte Carlo simulation was employed. A significance level of $p < 0.050$ was considered statistically significant.

Ethical Approval

This study was approved by Sivas Cumhuriyet University Faculty of Medicine Local Ethics Committee (Date: 06.02.2018, Decision No: 2018-02/05).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean $\pm$ standard deviation for continuous variables and frequency (percentage) for categorical variables. Due to the violation of chi-square test assumptions in multi-way tables, Fisher's exact test with Monte Carlo simulation was used for group comparisons. A p value < 0.05 was considered statistically significant.

Reporting Guidelines

The study was reported in accordance with STROBE guidelines.

Results

The study revealed significant alterations in the vaginal microbiota of women using IUDs, regardless of the type of device. A notable finding was the decrease in *Lactobacilli*, a crucial component of healthy vaginal microbiota, and an increase in *Escherichia coli*, indicating a shift towards a less protective microbiota composition. These changes were observed consistently across both copper IUDs (Cu-IUDs) and levonorgestrel-releasing IUDs (LNG-IUDs), suggesting that the IUD itself may influence microbiota

composition, rather than the specific material or hormone it releases.

The study focused exclusively on women using IUDs, aiming to analyze the diversity of their vaginal microbiota in detail. Most

Table 1. Types of IUDs in the study

Type of IUD	(n = 196)	(%)
Cu-IUD	195	83.7
LNG-IUD	38	16.3

Cu-IUD: Copper IUD, LNG-IUD: levonorgestrel-releasing IUD.

Table 2. Distribution of Microbiota in Women Using IUDs

Results	(n = 78)	(%)
No growth	77	32.6
Escherichia coli	27	11.6
Lactobacillus species	16	7.3
Streptococcus agalactiae	15	6.4
Staphylococcus epidermidis	14	6.0
Enterococcus faecalis	13	5.6
Candida albicans	12	5.2
Corynebacterium species	9	3.8
Candida glabrata	7	3.0
Staphylococcus aureus	7	3.0
Staphylococcus haemolyticus	5	2.1
Streptococcus anginosus	5	2.1
Corynebacterium aurimucosum	4	1.7
Gardnerella vaginalis	4	1.7
Corynebacterium striatum	3	1.3
MRSA	2	0.9
Haemophilus influenzae	2	0.9
Actinomyces	2	0.9
Staphylococcus cohnii	2	0.9
Eikenella corrodens	1	0.4
Streptomonas maltophilia	1	0.4
Saccaromyces cerevisiae	1	0.4
Staphylococcus hominis	1	0.4
Klebsiella pneumoniae	1	0.4
Citrobacter freundii	2	0.9

MRSA: Methicillin-resistant Staphylococcus aureus

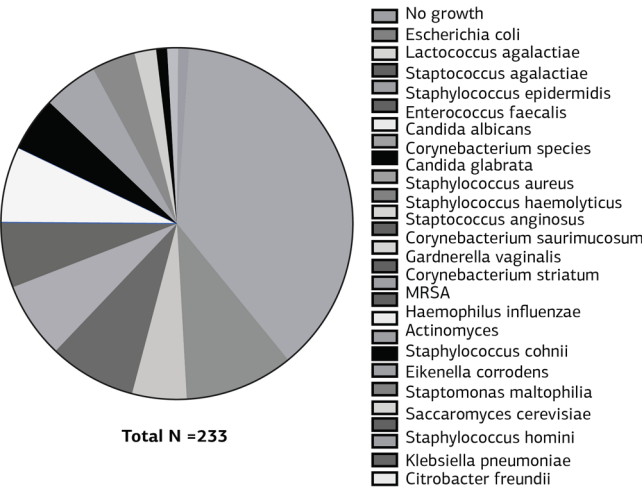


Figure 1. Distribution of IUD microbiota changes

participants were using Cu-IUDs, as reflected in Table 1, with ages ranging from 20 to 70 years and an average age of 39.64 ± 8.37 years.

The results highlighted a significant reduction in the proportion of Lactobacilli and an increase in Escherichia coli in the vaginal microbiota of IUD users (Table 2), which may suggest that IUDs play a role in altering bacterial colonization patterns. Furthermore, when comparing the microbiota of Cu-IUD and LNG-IUD users, it was found that the ranking of the most common microorganisms remained consistent across both groups (Figure 1), indicating that the type of IUD may have less impact on the specific bacteria present than initially expected.

Discussion

Our findings contribute to the growing body of evidence that IUDs can significantly alter the vaginal microbiota. The observed decrease in Lactobacilli and increase in Escherichia coli are particularly concerning, as they suggest a shift towards a microbiota composition that may be more susceptible to infections. This aligns with previous studies that have highlighted the potential risks of dysbiosis in the reproductive tract. However, the lack of correlation with clinical symptoms in this study limits the conclusions that can be drawn regarding the clinical significance of these microbiota changes.

The microbiota in the reproductive tract is predominantly comprised of bacteria from the Lactobacillus genus, indicative of a healthy microbiome state.¹¹ Research has demonstrated that dysbiosis in the reproductive tract microbiota correlates with a heightened risk of various health issues, such as pelvic inflammatory disease, endometriosis, and infertility.^{12,13}

The effects of IUD usage on the microbiota involve various mechanisms. These include local immune responses triggered by the presence of the device, hormonal changes induced by certain types of IUDs, disruption of the natural barrier function of the reproductive tract, direct interactions between the device materials and bacteria, alterations in the microenvironment within the uterus. These factors collectively contribute to shifts in microbiota composition and diversity. Further research is needed to fully understand the implications of these changes for reproductive health and disease. The employment of IUDs may disrupt this equilibrium, leading to dysbiosis - a microbial imbalance.¹⁴ While IUDs are generally safe and effective, it's essential for women to discuss potential risks and benefits with their healthcare providers before choosing this form of contraception.¹⁵

Our study diverges from previous research in that it directly investigates the effects of IUD usage by conducting cultures from the device's intrauterine environment. This approach allows for a more direct examination of the microbiota within the uterine cavity in relation to IUD presence, contrasting with prior studies that may have relied on indirect measures or sampled from different anatomical sites. By culturing directly from the IUD, our study aims to provide novel insights into the specific microbial dynamics influenced by IUD usage, potentially shedding light on mechanisms underlying any observed effects on women's health.

In our study, the cultures examined from IUD users showed a 30.8% non-proliferation rate in those with copper IUDs (Cu-IUD) and a 42.1% non-proliferation rate in those with levonorgestrel-releasing IUDs (LNG-IUD). However, among the cases where proliferation

occurred, *Escherichia coli* was the most frequently identified pathogen (11.6%). The increased presence of *Escherichia coli* in women with IUDs suggests a possible association between IUD insertion and alterations in the microbiota, creating a conducive environment for the proliferation of opportunistic pathogens. Conversely, the presence of *Lactobacilli*, which is known for its role in maintaining vaginal health by producing lactic acid and sustaining an acidic environment, was observed as the second most common microbiota element in our study. Specifically, an increase in certain bacterial species can elevate the risk of infections, while a decrease in others may weaken the protective functions of the microbiota.

In a study examining the impact of Cu-IUDs on the vaginal microbiota in baboons, it was found that Cu-IUDs did not significantly alter the microbiota.¹⁶ Conversely, our findings indicated that in women with Cu-IUDs, the microbiota composition was not compatible with the literature. In our study, *Escherichia coli* was more frequently observed in women with IUDs, with *Lactobacilli* being the second most common. Several factors may contribute to this discrepancy, including differences in study populations.

Contrary to our findings, a study conducted by Basis and colleagues, which investigated the effects of intrauterine contraceptive devices on the vaginal microbiota, concluded that neither LNG-IUDs nor Cu-IUDs significantly altered the vaginal microbiota.¹⁷

Pruthi and colleagues, in their investigation of pathogens on IUDs, identified the most common pathogens as *Staphylococcus aureus* (16%), *Staphylococcus epidermidis* (18%), and *Pseudomonas aeruginosa* (5%).¹⁸ Our study differed, with *Escherichia coli* (11.6%), *Lactobacillus* (7.3%), and *Streptococcus agalactiae* (6.4%) being the top three microbiota components.

Limitations

Single-center, descriptive design without a control group and lack of longitudinal follow-up limit causal interpretation; culture-based microbiota analysis may have missed some organisms.

Conclusion

This study provides valuable insights into the alterations of vaginal microbiota associated with copper and levonorgestrel-releasing IUDs. The findings reveal distinct microbiota profiles between the two types of IUDs. Notably, a higher proportion of LNG-IUD users (42.1%) showed no bacterial growth compared to Cu-IUD users (30.8%), while the presence of bacteria such as *Escherichia coli* and *Streptococcus agalactiae* was slightly more frequent in LNG-IUD users. In contrast, *Staphylococcus epidermidis* and *Candida albicans* were found at higher rates among Cu-IUD users. These differences may indicate that the type of IUD can influence vaginal microbiota composition, though the clinical implications of these variations remain unclear.

While this study provides important data on the short-term effects of IUD use on vaginal microbiota, further research is needed to establish a clearer link between these microbial changes and clinical outcomes, such as infection rates or other reproductive health issues. In particular, longitudinal studies tracking microbial shifts over the long term would provide deeper insights into how extended IUD use influences vaginal health. Larger patient cohorts and more precise sample selection would also strengthen future investigations, offering a more comprehensive understanding of IUDs' effects on microbiota.

Additionally, the potential for interventions, such as probiotic supplementation, should be explored as a means to mitigate any negative effects of IUD use on the vaginal microbiota, potentially improving reproductive health outcomes for women.

Declarations

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Written informed consent was obtained from all participants prior to inclusion in the study.

Data Availability

The datasets used and/or analyzed during the current study are not publicly available due to patient privacy reasons but are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare that there is no conflict of interest.

Funding

None.

Abbreviations

BMI: Body mass index
Cu-IUD: Copper intrauterine device
IUD: Intrauterine device
LNG-IUD: Levonorgestrel-releasing intrauterine device
MALDI-TOF MS: Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry
STROBE: Strengthening the reporting of observational studies in epidemiology

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How to Cite

Tahsin Takcı, Şerife Özlem Genç, Meral Çetin. Impact of intrauterine devices on microbiota in women: identification of bacterial colonization. *Ann Clin Anal Med* 2025;16(1):52-56. doi:10.4328/ACAM.22412