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Impact of Antibiotic Use on Vaginal Microbiome and Biochemical Profiles in Women Undergoing Assisted Reproductive Technologies (ART)

Saika Khursheed[1], Showkat Ahmad Bhat[2], Omar Rashid[3*]

[1]Senior Resident, Department of Obs/ Gynae, SKIMS Soura

[2]Associate Professor, Biochemistry, GMC, Handwara

[3*]Assistant Professor, Microbiology GMC, Handwara

***Corresponding Author:** Omar Rashid
*Assistant Professor, Microbiology GMC, Handwara
Email- omareal07@yahoo.com

Abstract
The use of antibiotics is common among women undergoing Assisted Reproductive Technologies (ART) to prevent infections and improve reproductive outcomes. However, antibiotics may disrupt the vaginal microbiome, leading to potential alterations in biochemical profiles and negatively impacting ART success. This prospective study evaluates the effects of antibiotic use on the vaginal microbiome and biochemical markers, including reproductive hormones and inflammatory markers, in women undergoing ART at Department of Obs/ Gynae, SKIMS Soura and GMC Handwara from June 2023 to June 2024. The findings suggest that antibiotic-induced changes in the vaginal microbiome may adversely influence reproductive health and ART outcomes.

Keywords: Antibiotics, Vaginal Microbiome, Biochemical Profiles, Assisted Reproductive Technologies, ART Outcomes, Reproductive Health, Northern India

Introduction

Assisted Reproductive Technologies (ART), including in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI), have revolutionized the treatment of infertility. The success of ART is influenced by numerous factors, one of which is the vaginal microbiome. The vaginal microbiome plays a crucial role in maintaining reproductive health by protecting against infections and creating a conducive environment for embryo implantation (1, 2).

Antibiotic therapy is frequently administered to women undergoing ART to prevent infections that could compromise reproductive outcomes (3). However, broad-spectrum antibiotics may disrupt the normal vaginal flora, characterized primarily by *Lactobacillus* species, leading to dysbiosis. Dysbiosis can trigger inflammatory responses and hormonal imbalances, potentially affecting the likelihood of successful implantation and pregnancy (4, 5).

The objective of this study is to assess the impact of antibiotic use on the vaginal microbiome and biochemical profiles, including hormone levels and inflammatory markers, in women undergoing ART at SKIMS Soura (Trust) and GMC Handwara. Understanding these relationships is vital for optimizing ART protocols and improving clinical outcomes.

Materials and Methods

Study Design and Population

This prospective observational study was conducted at Department of Obs/ Gynae, SKIMS Soura and GMC Handwara from June 2023 to June 2024. A total of 100 women aged 25-40 years who were

undergoing ART procedures (IVF or ICSI) were enrolled in the study. Participants were divided into two groups:

- **Group A (n = 50):** Received broad-spectrum antibiotics as part of their ART protocol.
- **Group B (n = 50):** Did not receive antibiotics unless medically indicated.

Exclusion Criteria

Women with chronic infections, autoimmune disorders, recent antibiotic use (within the past three months), those undergoing repeated ART cycles, or with known allergies to antibiotics were excluded from the study.

Sample Collection

Vaginal swabs were collected from all participants at baseline (prior to antibiotic administration) and one week after the completion of antibiotic therapy. Blood samples were drawn to measure biochemical markers, including estradiol, progesterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and inflammatory markers (C-reactive protein [CRP], interleukin-6 [IL-6], and tumor necrosis factor-alpha [TNF-α]).

Vaginal Microbiome Analysis

The vaginal microbiome was analyzed using 16S rRNA gene sequencing of the vaginal swab samples to evaluate microbiome composition and diversity. Relative abundances of *Lactobacillus*, *Gardnerella*, and other bacterial species were assessed to determine the impact of antibiotic treatment.

Biochemical and Inflammatory Marker Assessment

Reproductive hormone levels were measured using enzyme-linked immunosorbent assay (ELISA) techniques. Inflammatory markers (CRP, IL-6, and TNF-α) were quantified using standard laboratory techniques.

Outcome Measures

Primary outcomes included changes in the vaginal microbiome composition and biochemical profiles. Secondary outcomes involved ART success rates, including embryo implantation and clinical pregnancy rates.

Results

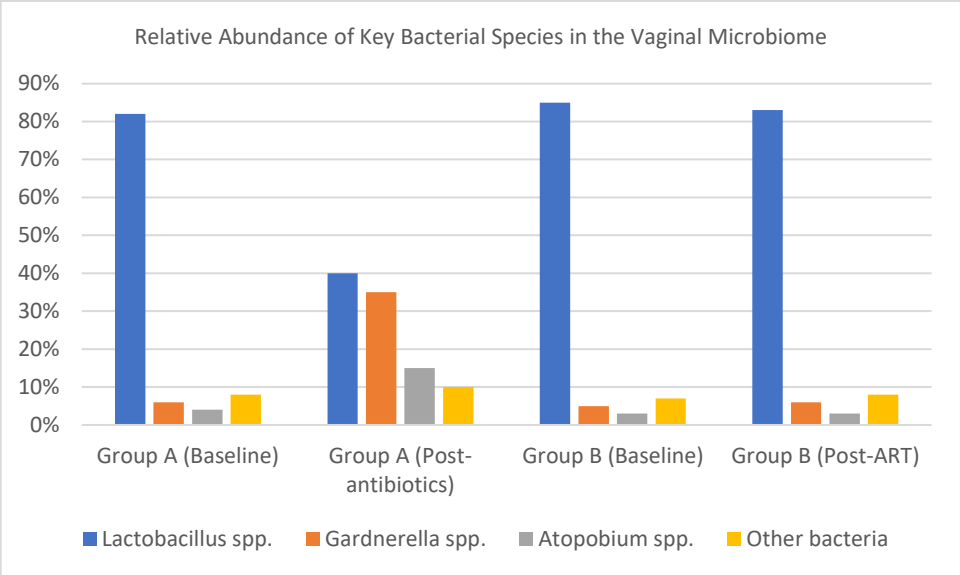
Vaginal Microbiome Changes

The vaginal microbiome in Group A (those who received antibiotics) showed a significant decrease in the relative abundance of *Lactobacillus* species, with an increase in the diversity of bacterial species, particularly *Gardnerella* and *Atopobium*. In contrast, Group B (non-antibiotic group) maintained a stable *Lactobacillus*-dominant microbiome.

Table 1 illustrates the changes in the relative abundance of key bacterial species before and after antibiotic treatment.

Table 1: Relative Abundance of Key Bacterial Species in the Vaginal Microbiome

Bacterial Species	Group A (Baseline)	Group A (Post-antibiotics)	Group B (Baseline)	Group B (Post-ART)
Lactobacillus spp.	82%	40%	85%	83%
Gardnerella spp.	6%	35%	5%	6%
Atopobium spp.	4%	15%	3%	3%
Other bacteria	8%	10%	7%	8%



Biochemical Profiles

Biochemical analysis revealed significant changes in hormone levels and inflammatory markers in Group A post-antibiotic administration. Estradiol and progesterone levels significantly decreased ($p<0.05$), while inflammatory markers CRP and IL-6 increased, indicating a heightened inflammatory response. Group B showed no significant changes in these parameters.

Table 2 summarizes the biochemical changes observed in both groups.

Table 2: Changes in Biochemical and Inflammatory Markers

Marker	Group A (Baseline)	Group A (Post-antibiotics)	Group B (Baseline)	Group B (Post-ART)
Estradiol (pg/mL)	140 ± 35	98 ± 30*	138 ± 32	140 ± 34
Progesterone (ng/mL)	20 ± 5	12 ± 4*	21 ± 6	22 ± 5
LH (mIU/mL)	15 ± 3	14 ± 3	16 ± 2	15 ± 3
FSH (mIU/mL)	8 ± 2	8 ± 2	7 ± 2	7 ± 2
CRP (mg/L)	5.6 ± 2.1	10.2 ± 3.5*	5.3 ± 1.8	5.4 ± 1.9
IL-6 (pg/mL)	2.8 ± 0.9	5.7 ± 1.2*	3.1 ± 0.8	3.0 ± 0.9

*Statistically significant changes ($p<0.05$)

ART Outcomes

The success rates of ART were significantly lower in Group A. Clinical pregnancy rates were 34% in Group A compared to 48% in Group B ($p<0.05$). Similarly, embryo implantation rates were lower in Group A at 28% compared to 42% in Group B.

Table 3 details the ART success rates for both groups.

Table 3: ART Success Rates

Outcome	Group A (Antibiotics)	Group B (No Antibiotics)
Clinical Pregnancy Rate	34%	48%
Embryo Implantation Rate	28%	42%

Discussion

The findings of this study conducted at SKIMS Soura (Trust) and GMC Handwara highlight the significant impact of antibiotic use on the vaginal microbiome and biochemical profiles of women

undergoing ART. The substantial reduction in *Lactobacillus* species in the antibiotic group corresponds with previous studies that emphasize the importance of a balanced vaginal microbiome for reproductive health (1, 2, 4, 6).

The alterations in biochemical profiles, including decreased levels of reproductive hormones and increased inflammatory markers, suggest a potential mechanism through which antibiotics could impair ART outcomes. Elevated inflammatory markers have been associated with decreased implantation rates and overall lower fertility (7, 8).

These findings underscore the necessity of a careful approach to antibiotic prescribing in the context of ART. While the primary aim is to prevent infections, the potential risks of disrupting the vaginal microbiome and inducing inflammatory responses should be taken into consideration (9, 10).

Further research could explore the use of probiotics or other strategies to maintain microbiome health during ART procedures. Recent literature indicates that probiotic supplementation may help restore a healthy vaginal microbiome, potentially improving ART outcomes (11, 12).

Conclusion

This prospective study demonstrates that antibiotic use during ART significantly alters the vaginal microbiome and biochemical profiles, potentially leading to lower ART success rates. Clinicians should exercise caution when prescribing antibiotics in ART settings and consider the implications for vaginal health. Further research is warranted to develop protective strategies for maintaining vaginal health during ART.

Conflict of Interest: None.

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