



New Day in Medicine
Новый День в Медицине

NDM



TIBBIYOTDA YANGI KUN

Ilmiy referativ, marifiy-ma'naviy jurnal



AVICENNA-MED.UZ



ISSN 2181-712X.
EISSN 2181-2187

2 (88) 2026

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ТИББИЁТДА ЯНГИ КУН НОВЫЙ ДЕНЬ В МЕДИЦИНЕ NEW DAY IN MEDICINE

*Илмий-рефератив, маънавий-маърифий журнал
Научно-реферативный,
духовно-просветительский журнал*

УЧРЕДИТЕЛИ:

**БУХАРСКИЙ ГОСУДАРСТВЕННЫЙ
МЕДИЦИНСКИЙ ИНСТИТУТ
ООО «ТИББИЁТДА ЯНГИ КУН»**

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исследовательский центр хирургии имени
А.В. Вишневского является генеральным
научно-практическим
консультантом редакции

Журнал был включен в список журнальных
изданий, рецензируемых Высшей
Аттестационной Комиссией
Республики Узбекистан
(Протокол № 201/03 от 30.12.2013 г.)

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2 (88)

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2026
февраль

Received: 20.01.2026, Accepted: 06.02.2026, Published: 10.02.2026

УДК 618.618.1 – 089.618.14 – 008.6

THE ROLE OF CONDITIONALLY PATHOGENIC MICROFLORA IN THE UTERINE CAVITY IN FETAL DESCENT

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✓ Resume

The medical history of 233 women with a diagnosis of miscarriage was analyzed. Fetal miscarriage was observed in term from 5 to 22 weeks. Patients underwent retrospective, cross-sectional cohort research, clinical and anamnestic, laboratory, instrumental examinations. The obtained results show that the presence of opportunistic microflora forms hidden factors that contribute to the development of chronic endometritis and fetal miscarriage.

Key words: miscarriage, chronic endometritis, microflora.

BACHADON BO'SHLIG'IDAGI SHARTLI PATOGEN MIKROFLORANING HOMILA TUSHISHIDA O'RNI

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✓ Rezyume

Homila tushishi tashhisi bilan 233 ta ayollarning kasallik tarixi tahlil qilindi. Homila tushishi muddati 5 haftalikdan 22 haftaligacha tashkil qildi. Bemorlar retrospektiv ravishda kema kogort tadqiqoti, klinik, anamnestic, laborator va instrumental tekshiruvlar o'tkazilgan. Olingan natijalar shuni ko'rsatdiki, opportunistik mikrofloraning bachadon ichida mavjudligi surunkali endometritning rivojlanishiga va homila tushishiga olib keladigan yashirin omillarni shakllantirgan.

Kalit so'zlar: homila tushishi, surunkali endometrit, mikroflora.

РОЛЬ УСЛОВНО-ПАТОГЕННОЙ МИКРОФЛОРЫ ПОЛОСТИ МАТКИ ПРИ ВЫКИДЫШАХ

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✓ Резюме

Были проанализированы истории болезни 233 женщин с диагнозом выкидыш. Выкидыши наблюдались при сроках от 5 недель до 22 недель. Было проведено ретроспективное, поперечное когортное исследование, клинко-анамнестическое, лабораторное и инструментальное обследование больных женщин. Полученные результаты показали, что наличие условно-патогенной микрофлоры в матке формирует скрытые факторы, способствующие развитию хронического эндометрита и в последующем к выкидышу.

Ключевые слова: выкидыш, хронический эндометрит, микрофлора.

Relevance

High rates of miscarriage (MC) are associated not only with impaired reproductive function but also with a general deterioration in women's somatic health. Each year, the number of women capable of giving birth to a healthy child decrease by approximately 20% [1].

Women with a complicated obstetric and gynecological history demonstrate higher rates of miscarriage. One of the main causes is the structural and functional insufficiency of the endometrium at the site of implantation of the fertilized ovum in the uterine mucosa, which subsequently promotes the development of inflammatory processes [[2, 3, 4, 5, 6, 7].

According to statistical data, chronic endometritis (CE) is common among women of reproductive age and is therefore recognized as an independent nosological entity. According to various authors, the prevalence of chronic endometritis varies widely, ranging from 0.2% to 66.3% [2, 6, 8, 9]. V.M. Sidelnikova et al. reported that morphologically confirmed asymptomatic chronic endometritis was detected in 64% of women with a history of recurrent abortions [3].

Chronic endometritis, which contributes to infertility, failed attempts of in vitro fertilization (IVF), miscarriages, and complicated pregnancies and deliveries, has not only medical but also social significance [7, 10].

Most early miscarriages are believed to be associated with infectious factors. Long-term persistence of infection in the uterine cavity leads to damage of the endometrial receptor apparatus, resulting in abnormal invasion and trophoblast damage in early pregnancy [4, 11].

On the other hand, some foreign authors question the infectious theory of recurrent miscarriage, emphasizing that inflammatory infiltration of chorionic villi is often aseptic in nature [12, 13]. In this regard, analysis of the relationship between uterine microbiocenosis and miscarriage remains a relevant issue.

Aim of the Study: to assess the direct relationship between intrauterine infectious factors and miscarriage.

Materials and methods

Medical records of 233 women hospitalized in a gynecological department with a diagnosis of miscarriage were analyzed. Gestational age at miscarriage ranged from 5 to 22 weeks. A retrospective cross-sectional cohort study was conducted, including clinical and anamnestic evaluation, laboratory and instrumental examinations. The age of all pregnant women ranged from 18 to 45 years. Women with severe or moderate somatic diseases in the decompensation stage, acute infectious diseases of any localization, diagnosed alcoholism, smoking or drug addiction, mental retardation or psychiatric disorders, as well as those with language barriers that hindered cooperation during the examination, were excluded from the study.

Statistical Analysis. Statistical analysis was performed using the software package Statistica for Windows 6.0. Descriptive statistics and several nonparametric tests were applied to assess the significance of differences. Quantitative variables were presented as mean $\pm$ standard deviation ($M \pm SD$). Distribution of variables was assessed using the Kolmogorov–Smirnov test. Qualitative variables were expressed as absolute numbers and percentages (%) [14].

Results of the study

The mean age of the women was 32 ± 5.7 years.

The majority of patients did not have higher education (57.9%, 135/233), while most were employed (76.0%, 177/233).

According to medical history, 44.6% (104/233) of women had extragenital diseases, most commonly chronic diseases of the gastrointestinal tract.

Analysis of obstetric and gynecological history showed that 76.4% (178/233) of the examined women had various gynecological diseases. Inflammatory diseases of the uterine appendages were observed in 6.9% (16/233) of women, while chronic endometritis was detected and morphologically confirmed in 9.4% (22/233), significantly increasing the risk of miscarriage. Multiple gynecological diseases were present in 40.3% (94/233) of patients. The average number of nosological forms per patient was 1.4.

Analysis of obstetric history revealed that almost every fifth woman (19.3%, 45/233) had one or more previous miscarriages, and 6.0% (14/233) had a history of three or more miscarriages. In 3.4% (8/233) of women, pregnancy occurred as a result of assisted reproductive technologies.

Microbial associations in vaginal smears were detected in every third woman. Low titers of pathogenic microflora were identified in 6.9% (16/233) of patients, while samples without pathogenic microflora were found in 43.4% (101/233).

A high prevalence of microbial associations, including *Mycoplasma genitalium* and facultative anaerobes (*Gardnerella vaginalis*), was detected in every third woman.

Bacteriological examination of cervical canal discharge revealed pathogenic microflora at concentrations of $\geq 10^6$ CFU/ml in 44.2% (103/233) of women. In 14.6% (34/233) of cases, two or more pathogens were detected. The cervical flora was predominantly polymicrobial.

Table 1. Obstetric and gynecological history of women with miscarriage (n, %)

Indicators	n=233	%
Reproductive history		
Full-term births	178	76.4
History of 1 HT	45	19.3
History of 2 or more HT	14	6.0
Spontaneous miscarriage	66	28.9
Medical termination of pregnancy	23	9.2
Surgical termination of pregnancy	42	18.0
Ectopic pregnancy	8	3.4
History of gynecological diseases		
Not sick	55	23.6
Uterine fibroids	15	6.4
Endometriosis	8	3.4
Acute inflammation of the uterus	26	11.1
Chronic endometritis	32	13.6
Endometrial hyperplastic process	54	23.2
Ovarian retention cysts	29	13.0
Safe cervical diseases	137	59.8

Table 2. Laboratory examination of cervical canal discharge in women with miscarriage (n, %)

Nosologies	n=233	%
PCR-analysis		
Infection not detected	102	44.3
Sexually transmitted infections:		
Cytomegalovirus	10	4.4
<i>Mycoplasma genitalium</i>	30	12.8
Herpes virus types I and II	17	6.9
<i>Neisseria gonorrhoeae</i>	0	0
<i>Trichomonas vaginalis</i>	0	0
<i>Chlamydia trachomatis</i>	11	4.3
Infections caused by conditionally pathogenic microflora:		
<i>Ureaplasma urealyticum/parvum</i> 10^6	74	31.7
<i>Gardnerella vaginalis</i>	40	17.3
<i>Candida albicans</i>	18	7.8
Joint infections	70	31.0
Bacteriological examination:		
Pathogenic microflora not detected	100	42.8
<i>Escherichia coli</i>	62	26.3
<i>Staphylococcus aureus</i>	23	9.9
<i>Staphylococcus hemolyticus</i>	8	3.4
<i>Streptococcus agalactiae</i>	18	7.7
<i>Enterococcus faecalis</i>	30	13.4
Others	12	5.2

The results of histological examination of tissues taken from the uterine cavity in 87.1% (203/233) of women who underwent surgical curettage (curettage, vacuum aspiration) of the uterine cavity are presented in Table 3.

The results of histological examination of uterine curettage showed a normal morphological picture in 15.3% (31/203) of patients. Most often, leukocyte infiltration was detected in the histological analysis of patients (40.9%, 83/203), less often - lymphocyte infiltration (5.9%, 12/203).

Table 3. Histological examination of uterine cavity scrapings , n/%

Histological examination results	All (n=203)	
	abs	%
No changes detected.	31	15.3
Leukocyte infiltration	83	40.9
Lymphocytic infiltration	12	5.9
Necrotic tissue	18	8.4
Unspecified vascular changes	13	6.5
Focal thrombosis of veins	6	3.0
Periodic blood transfusions	5	2.5
Hypovascularization of chorionic villi	4	2.0
Chorionic villus tumor	32	15.8
Chorionic villus necrosis	7	3.5
Fibrinoid necrosis at the implantation site	33	16.3
Chorionic villus fibrosis	7	3.5
Chorionic villi wrapped around a fibroid	13	6.4
Dystrophic changes of chorionic villi	18	8.9

Changes characteristic of the chronic inflammatory process (lymphocytic infiltration, fibrosis of chorionic villi, fibroid-encrusted villi, dystrophic changes of chorionic villi) were detected in 24.6% (50/203) of women.

Changes characteristic of the acute stage of inflammation (leukocyte infiltration, chorionic villi edema, chorionic villi necrosis, fibrinoid necrosis and the presence of necrotic tissue in the implantation zone) were detected in 84.7% (172/203) of women.

Vascular disorders (focal vascular thrombosis, hemorrhages of varying degrees, hypovascularization of chorionic villi and unspecified vascular diseases) were detected in 13.8% (28/203) of patients.

In discussing the results, factor analysis was performed to identify three latent factors associated with the presence of infections.

The first latent factor describes 20% of the data on the microbiota and miscarriage and demonstrates a high correlation with intracellular pathogens.

The most discussed issue at present is the role of infections in spontaneous abortion. In this regard, the presence of bacterial vaginosis (BV) in pregnant women is an important factor. The presence of BV in the last 6 months is statistically significantly associated with spontaneous abortion ($p < 0.05$), while there is no significant association between BV and recurrent pregnancy loss ($p > 0.05$) [15]. The presence of *Gardnerella vaginalis* was detected in only 17% of patients in this study, which does not allow to draw a clear conclusion about its influence on miscarriage.

The role of other infections remains a subject of debate [16]. Factor analysis revealed that HT is associated with increased intracellular pathogens (*Ureaplasma urealyticum/parvum* and *Mycoplasma genitalium*), *E. coli* and *E. Faecalis*, as well as *Streptococcus* spp.

Donders G.G.G et al. reported that *Mycoplasma genitalium* is associated with cervicitis, pelvic inflammatory disease in non-pregnant women, and with premature birth and miscarriage in pregnant women, regardless of the presence of other sexually transmitted diseases [17]. However, Larsen B. et al. refuted this connection, citing several results that also emphasize the importance of *Ureaplasma urealyticum* [13].

The second factor is associated with an increase in the number of *E. coli* and *E. faecalis* (described in 19% of the data). The third latent factor showed that HT is associated with an increase in the number of *Streptococcus* spp bacteria (17% of the data were described).

The role of *E. coli* and *E. Faecalis*, as well as *Streptococcus* spp. in causing miscarriage, has not been studied and studies related to them have not been found in the available databases. There are several data indicating a role in increasing the risk of premature birth [18, 19].

Conclusion

Thus, the results obtained indicate that the presence of opportunistic microflora in the uterus forms latent factors leading to chronic endometritis and miscarriage.

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Entered 20.01.2026