

DOI: <https://doi.org/10.17816/JOWD66711>

The role of vaginal lactobacilli in restoring vaginal microbiota in women in the early postpartum period, depending on the method of delivery

© Dzhamilya G. Dadayeva¹, Olga V. Budilovskaya^{1, 2}, Anna A. Krysanova^{1, 2},
Tatyana A. Khusnutdinova^{1, 2}, Alevtina M. Savicheva^{1, 2}, Igor Yu. Kogan^{1, 3}

¹ Research Institute of Obstetrics, Gynecology, and Reproductology named after D.O. Ott, Saint Petersburg, Russia;

² Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russia;

³ Saint Petersburg State University, Saint Petersburg, Russia

BACKGROUND: Despite numerous studies of the vaginal microbiota, there is still a lack of knowledge regarding its restoring dynamics in the early postpartum period. The condition of the vaginal microflora during pregnancy plays a key role in maintaining the physiological microbiocenosis of the birth canal and creating conditions for the normal course of pregnancy, the establishment of an infant's intestinal microbiota, and the further development of the child.

AIM: The aim of this study was to estimate the role of certain types of lactobacilli in restoring the vaginal microbiota in women in the early postpartum period, depending on the method of delivery.

MATERIALS AND METHODS: We examined 150 women at 38–41 weeks of gestation. The clinical material for the study was vaginal discharge before and after delivery. To determine the species of lactobacilli and other microorganisms in the clinical material, we used quantitative real-time PCR.

RESULTS: Before delivery, lactobacilli were found in vaginal discharge in 144 out of 150 women (96.0%), their number in the majority being more than 10^6 GE. In the postpartum period, lactobacilli were found in 66/128 (51.5%) cases, while prevailing in women after vaginal delivery in 50/65 (76.9%) cases (4.6 ± 1.6 , $p = 0.000000$). Among the dominant species of lactobacilli was *L. crispatus*, found in vaginal discharge before delivery, which most often affects the recovery of the vaginal microbiota in the postpartum period (29 out of 61 women, 47.5%). *L. iners* detected in the lochia predisposes to the violation of uterine involution in the early postpartum period ($p = 0.03$).

CONCLUSIONS: Normal vaginal microbiota in the postpartum period is restored more quickly in women after vaginal delivery. Our study confirms that *L. crispatus* and *L. iners* play a major role in restoring the vaginal microbiota in the postpartum period.

Keywords: vaginal microbiota; lactobacilli; *Lactobacillus iners*; *Lactobacillus crispatus*; postpartum period.

To cite this article:

Dadayeva DG, Budilovskaya OV, Krysanova AA, Khusnutdinova TA, Savicheva AM, Kogan IYu. The role of vaginal lactobacilli in restoring vaginal microbiota in women in the early postpartum period, depending on the method of delivery. *Journal of Obstetrics and Women's Diseases*. 2021;70(4):15–23. DOI: <https://doi.org/10.17816/JOWD66711>

Received: 29.04.2021

Accepted: 30.06.2021

Published: 31.08.2021

УДК 618.2+618.6]-07:579.864

DOI: <https://doi.org/10.17816/JOWD66711>

Значение вагинальных лактобацилл в восстановлении микробиоценоза влагалища у родильниц в раннем послеродовом периоде в зависимости от способа родоразрешения

© Д.Г. Дадаева¹, О.В. Будиловская^{1, 2}, А.А. Крысанова^{1, 2}, Т.А. Хуснутдинова^{1, 2}, А.М. Савичева^{1, 2}, И.Ю. Коган^{1, 3}

¹ Научно-исследовательский институт акушерства, гинекологии и репродуктологии им. Д.О. Отта, Санкт-Петербург, Россия;

² Санкт-Петербургский государственный педиатрический медицинский университет, Санкт-Петербург, Россия;

³ Санкт-Петербургский государственный университет, Санкт-Петербург, Россия

Обоснование. Несмотря на многочисленные исследования состава микробиоты органов репродуктивной системы, знания о динамике восстановления вагинального микробиоценоза в раннем послеродовом периоде еще недостаточны. Состояние микрофлоры влагалища во время беременности играет ключевую роль в поддержании физиологического микробиоценоза родовых путей, в создании условий для нормального течения беременности, формирования микрофлоры кишечника новорожденного, а также для дальнейшего развития ребенка.

Цель — оценка значимости отдельных видов лактобацилл в восстановлении вагинального микробиоценоза у родильниц в раннем послеродовом периоде в зависимости от способа родоразрешения.

Материалы и методы. Обследовано 150 женщин в сроке гестации 38–41 нед. Клиническим материалом для исследования служило отделяемое влагалища до и после родов. Для определения видов лактобацилл и других микроорганизмов в клиническом материале использовали метод количественной полимеразной цепной реакции с детекцией результатов в режиме реального времени.

Результаты. До родов лактобациллы присутствовали в отделяемом влагалища практически у всех женщин (144/150; 96,0 %), и их количество у большинства было более чем 10^6 ГЭ. В послеродовом периоде лактобациллы были обнаружены у 66/128 (51,5 %), при этом преобладали они у женщин, родоразрешенных через естественные родовые пути в 50/65 (76,9 %) случаях (среднее значение — $4,6 \pm 1,6$; $p = 0,000000$). Среди доминирующих видов лактобацилл был вид *L. crispatus*, обнаруженный в отделяемом влагалища до родов, который чаще всего влияет на восстановление микробиоты влагалища в послеродовом периоде (у 29/61 женщин; 47,5 %). Выявленные в лохиях *L. iners* предрасполагают к нарушению инволюции матки в раннем послеродовом периоде ($p = 0,03$).

Заключение. Восстановление физиологического микробиоценоза влагалища в послеродовом периоде происходит быстрее у женщин, родоразрешенных через естественные родовые пути. Наше исследование подтверждает, что *L. crispatus* и *L. iners* играют основную роль в восстановлении микробиоценоза влагалища в послеродовом периоде.

Ключевые слова: микробиоценоз влагалища; лактобациллы; *Lactobacillus iners*; *Lactobacillus crispatus*; послеродовой период.

Как цитировать:

Дадаева Д.Г., Будиловская О.В., Крысанова А.А., Хуснутдинова Т.А., Савичева А.М., Коган И.Ю. Значение вагинальных лактобацилл в восстановлении микробиоценоза влагалища у родильниц в раннем послеродовом периоде в зависимости от способа родоразрешения // Журнал акушерства и женских болезней. 2021. Т. 70. № 4. С. 15–23. DOI: <https://doi.org/10.17816/JOWD66711>

BACKGROUND

Despite the large number of studies of vaginal microbiocenosis, data on its qualitative and quantitative composition in pregnant women and the role of microorganisms in the development of postpartum complications are rather scarce and contradictory.

The main microflora of the vagina includes lactobacilli and bifidobacteria, which make up 87%–98% of the vaginal biotope. The frequency of their detection ranges from 46.5% to 100%, and their number is normally 10^5 – 10^9 CFU/ml [1]. Lactobacilli are of particular importance in maintaining the physiological vaginal microbiocenosis.

Among the whole variety of vaginal lactobacilli, four species of the *Lactobacillus acidophilus* group prevail, namely *L. crispatus*, *L. jensenii*, *L. gasseri*, and *L. iners* [2].

The presence of lactobacilli actively producing hydrogen peroxide is associated with a low incidence of bacterial vaginosis, preterm delivery, and postpartum infectious complications [3]. The study of the genotypic and biochemical properties of vaginal lactobacilli revealed that *L. crispatus*, *L. jensenii*, and *L. vaginalis* are the most common species of peroxide-producing lactobacilli [4].

In one of the studies by J. Ravel et al. (2011), five types of vaginal microflora (community state types [CST]) were identified in the North American women of reproductive age. Type 1 (CST I) is characterized by the dominance of *L. crispatus*, type 2 (CST II) by *L. gasseri*, type 3 by *L. iners* (CST III), and type 5 by *L. genseii* (CST V). Type 4 (CST IV) is characterized by low *Lactobacillus* level and increased diversity of anaerobic bacteria, including *Prevotella*, *Dialister*, *Atopobium vaginae*, *Gardnerella vaginalis*, *Megasphaera*, *Peptoniphilus*, *Sneathia*, *Fingoldia*, and *Mobiluncus* [5].

L. iners is special among the species diversity of vaginal lactobacilli and its role in maintaining the vaginal health of women is still unclear. Thus, *L. iners* is quite often revealed both in normocenosis and dysbiosis. *L. iners* does not produce hydrogen peroxide and can adapt to high pH values of the vaginal environment [6].

Due to the unique structure of its genome, *L. iners* can quickly adapt to changing environmental conditions, altering its metabolism and using other substances instead of glycogen as food resources. Thus, under conditions of dysbiosis, *L. iners* produces cholesterol-dependent cytolysin, the inerolysin, which destroys cell walls and uses glycerol of destroyed cell membranes as a new food substrate [7]. Concurrently, other types of lactobacilli die, the concentration of lactic acid decreases, and the vaginal environment pH increases, leading to the propagation of anaerobic bacteria associated with bacterial vaginosis, which are rapidly occupying the vacant niche. Thus, *L. iners* is unable to effectively protect the female body from pathogenic microorganisms, like other lactobacilli, but, contrarily, predispose

to the dominance of opportunistic microorganisms in the vagina. *L. iners* is common in bacterial vaginosis and is found in women in preterm labor [8]. However, the incidence of *L. iners* as the predominant species in normocenosis is also common [5].

In the postpartum period, vaginal microbiocenosis depends on many factors. Childbirth leads to significant changes in the qualitative and quantitative composition of the vaginal microflora. This is due to the washing out of microorganisms from the vagina with amniotic fluid and blood, birth canal trauma, and vaginal contamination with intestinal microflora [9]. However, these changes are temporary. In the postpartum period, the vagina is gradually re-colonized with the bacterial characteristic of the ecological niche [10].

During 1 week postpartum period, the level of estrogen decreases by 100–1000 times. The rapidly decreased estrogen levels lead to a decreased amount of glycogen and, therefore, the glycogen breakdown products used by lactate-producing bacteria, which subsequently reduces the stability and resilience of the vaginal microbiome. Consequently, the dominant position of *Lactobacillus spp.*, caused by estrogens in the vaginal microbiocenosis before delivery, should dynamically change in the postpartum period [11].

From the first days of the physiological postpartum period, the vagina is intensively colonized with corynebacteria from the skin of the inguinal folds and the anogenital region. In the process of vital activity, corynebacteria lower the vaginal environment pH, decompose glucose and maltose, and play an important role in triggering the mechanisms for restoring vaginal microbiocenosis in the postpartum period. Research results by Z.M. Martikainen (1996) and J.Yu. Kolesaeva (2012) confirm the hypothesis about the leading role of corynebacteria in triggering the mechanisms to restore the physiological microbiocenosis of the vagina in the postpartum period. The insignificant frequency of lactobacilli detection in vaginal discharge is most probably associated with an increased pH of the lochia, which prevents lactobacilli reproduction. The pH of vaginal discharge decreases later on, mainly due to the activity of corynebacteria [10, 12].

Restoration of the impaired vaginal microbiocenosis indicates the successful course of the postpartum period.

The influence of the delivery method, use of antibiotic therapy in childbirth and the postpartum period, childbirth complications, and postpartum period recovery time of the vaginal microbiocenosis is poorly studied. Almost nothing is known about the influence of certain types of lactobacilli that prevail in the composition of the vaginal microbiota before childbirth, on the dynamics of its recovery in the postpartum period.

Comparative analysis of the vaginal microbiocenosis of pregnant women before childbirth and after delivery using

real-time polymerase chain reaction (RT-PCR) develops measures to predict and prevent postpartum infectious and inflammatory complications.

This study aimed to assess the significance of certain types of lactobacilli in the restoration of vaginal microbiocenosis of women in the early postpartum period, depending on the method of delivery.

MATERIALS AND METHODS

A total of 150 pregnant women, admitted to D.O. Ott Scientific Research Institute of Obstetrics, Gynecology, and Reproductology for delivery, were examined. The study was performed in two stages. Stage 1 is the analysis of vaginal microflora composition in women at 38–41 weeks of gestation. Stage 2 included the analysis of vaginal microflora of these women in the early postpartum period, on days 4–5. At this stage, 128 women out of 150 were examined.

The study inclusion criteria include age from 18 to 40 years inclusive, full-term singleton pregnancy, normal placental location and amount of amniotic fluid, and delivery at no later than 41 weeks of gestational age. The exclusion criteria include any type of diabetes mellitus, fever, multi-fetal pregnancy, cervical incompetence, and use of local or systemic antibacterial agents <3 months before study participation.

Two groups were formed; group 1 included women after vaginal delivery ($n = 81$) and group 2 consisted of female patients after cesarean section, who received a prophylactic course of antibacterial drugs in the perioperative period ($n = 69$).

The obstetric-gynecological anamnesis study assessed the generally accepted aspects, such as the number of pregnancies and their outcome; frequency of urogenital and urinary tract infections; and characteristics of the course of pregnancy, childbirth, postpartum period, and method of delivery.

For microbiological examination, vaginal discharge was obtained from the posterolateral vaginal fornix using a sterile swab. Swab contents were placed in an isotonic sodium chloride solution for subsequent molecular biological analysis by quantitative RT-PCR (Femoflor-16 test and a test system for research purposes, which determined the seven most common types of vaginal lactobacilli (*L. crispatus*, *L. iners*, *L. jensenii*, *L. gasseri*, *L. johnsonii*, *L. vaginalis*, and *L. acidophilus*) (DNA-Technology, Moscow). DNA of microorganisms was isolated from 100 μ l of a sample using the Proba-GS reagent kit (DNA-Technology, Moscow) according to the manufacturer's instructions. The total bacterial DNA concentration was determined as the total bacterial mass and the concentration (absolute and relative) of the species/genera of microorganisms *Lactobacillus*, *Enterobacteriaceae*, *Streptococcus*, *Staphylococcus*, *Gardnerella vaginalis*/

Prevotella bivia/*Porphyromonas*, *Eubacterium*, *Sneathia/Leptotrichia/Fusobacterium*, *Megasphaera/Veillonella/Dialister*, *Lachnobacterium* spp./*Clostridium*, *Mobiluncus* spp./*Corynebacterium*, *Peptostreptococcus*, and *Atopobium vaginae*. In addition, the absolute concentration of *Mycoplasma hominis*, *Mycoplasma genitalium*, *Ureaplasma*, and *Candida* was assessed.

DNA of *Lactobacillus crispatus*, *Lactobacillus acidophilus*, *Lactobacillus iners*, *Lactobacillus jensenii*, *Lactobacillus gasseri*, *Lactobacillus johnsonii*, *Lactobacillus vaginalis*, and *Lactobacillus* spp. in the vaginal discharge was detected by RT-PCR (qualitative analysis) (DNA-Technology, Moscow).

Uterine ultrasound examination (US) was performed on the LOGIC-200 apparatus (department of ultrasound diagnostics, headed by V.S. Prokhorova, Ph.D. in Medicine). US was performed for all puerperas on day 3 of the postpartum period. In this case, a) uterine biometrics (length, anteroposterior, and transverse size) and b) the anteroposterior size of the uterine cavity was measured and c) the presence, echogenicity, and homogeneity of the uterine cavity contents was determined. The uterine involution was considered normal, if a) the uterine cavity was closed or expanded to 1.0 cm and b) the uterine cavity contents were homogeneous and hyperechoic (decidual tissue). The uterine involution impairment ("subinvolution") was registered if a) the uterine cavity was 1.0–2.0 cm inclusive and b) areas of various sizes and echogenicity in the uterine cavity.

Statistical processing of the obtained data was performed using the STATISTICA 10.0 program. The nonparametric Mann-Whitney *U*-test and Pearson's chi-squared test (χ^2) was used to compare the quantitative and qualitative composition of the microbiota before delivery and the chi-square was calculated with Yates's correction or the exact two-tailed Fisher test for small samples. The data were tested for normality of distribution using the Shapiro-Wilk test, and the homogeneity of variances was assessed using the Levene test. Continuous variables with normal distribution were presented as arithmetic mean (M) \pm standard deviation. The *p*-value of < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The average age of patients was 31.3 ± 4.8 (18–42) years. Urinary tract infection (chronic cystitis, chronic pyelonephritis, and asymptomatic bacteriuria) and urogenital infection (chlamydial infection, trichomoniasis, and vulvovaginal candidiasis) were revealed in 17 out of 81 (21%) patients in group 1 and 34 out of 69 (49.3%) in the group 2. During pregnancy, these infections were detected in 21 pregnant women (26%) in group 1 and 19 (27.5%) in group 2. In group 1, 41 (50.6%) patients were primiparous and 40 (49.4%) were

multiparous; and 43 (62.3%) and 26 (37.7%), respectively in group 2.

Antibacterial drugs during pregnancy in the first trimester were taken by 2 women (2.5%) in group 1 and 4 (5.8%) in group 2 and by 10 (12.3%) and 2 (2.9%) women, respectively, in the second trimester. In the third trimester, antibacterial drugs were not taken in any group.

Premature rupture of membranes occurred in 20 women: 10 (12.3%) in group 1 and 10 (14.5%) in group 2. The duration of the rupture to the delivery interval of >6 h was registered in 10 (12.3%) women in group 1 and 6 (8.7%) in group 2. The average duration of labor in group 1 was 6.9 ± 2.3 h. In group 2, the duration of labor was 7.3 ± 8.7 h in 26 (37.7%) women with advanced labor and with emergency delivery, and 43 (62.3%) were operated on a scheduled basis.

The method of quantitative RT-PCR established the presence of lactobacilli before delivery in the vaginal discharge in 96% of women (144/150), and their level in most pregnant women was more than 10^6 genomic equivalent (mean value 6.2 ± 1.5 lg).

Figure 1 shows the proportion of different types of lactobacilli in the lactobacillus microflora in the vagina of women of the study groups. The specific gravity of each type of lactobacillus was determined. Most often, among lactobacilli, the species *L. vaginalis* (48.1%) was detected in the vaginal discharge before delivery, *L. crispatus* in 46.6%, *L. iners* in 39.1%, *L. gasseri* in 33.8%, *L. jensenii* in 33.1%, *L. johnsonii* in 13.5%, and *L. acidophilus* in 1.5%.

Taking into account the presence of several lactobacilli species simultaneously in the majority of vaginal samples, the dominant species in each sample was determined. The species was considered dominant if its concentration was 50% or more relative to the total lactobacillus microflora concentration. Based on the dominant species of lactobacilli, five main groups that reflect the types of vaginal microbial CST were identified, as previously identified for non-pregnant women of reproductive age in North America [5].

Among the women examined before childbirth, the most common type of vaginal microbiocenosis was CST I (*L. crispatus*, 41.2%). Other types of microbiocenosis, such as CST III (*L. iners*, 25%), CST II (*L. gasseri*, 17.6%), and CST V (*L. jensenii*, 11%), were less common. CST IV was characterized by a reduced content of *Lactobacillus* spp. and the prevalence of anaerobic bacteria, including *Prevotella* spp., *Clostridium* spp., *Atopobium* spp., and *Megasphaera* spp., which was noted in 5.1% of cases.

Among obligate anaerobic bacteria, various associations of microorganisms were found in pregnant women. In >40% of pregnant women in the vaginal biotope, *Gardnerella vaginalis* was found in combination with *Prevotella bivia* and *Porphyromonas* spp., as well as *Eubacterium* spp. Yeast-like fungi of the genus *Candida* were found in 10.7% of women, *Mycoplasma hominis* in 2%, and *Ureaplasma* spp. in 38.7%

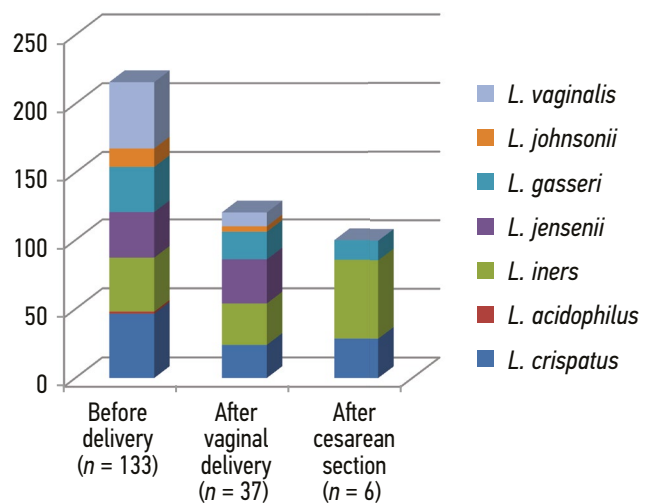


Fig. 1. The specific gravity of various types of lactobacilli in the composition of the vaginal lactobacillary microflora in female patients of the study groups

at a concentration of 3.7 ± 1.2 lg. This concentration of ureaplasmas in the vaginal biotope of pregnant women is considered insignificant [13].

The vaginal microbiocenosis in the early postpartum period is completely different. The analysis of the content of microorganisms in the lochia of 128 women examined by quantitative RT-PCR revealed a high frequency of *Enterobacteriaceae* (38.5 and 17.5%, $p = 0.007$), streptococci (41.5 and 3.2%, $p = 0.000000$), *Gardnerella vaginalis* (78.5 and 25.4%, $p = 0.000000$), and *Eubacterium* spp. (66.2 and 15.9%, $p = 0.000000$) after vaginal delivery, and *Ureaplasma* spp. (26.9 and 43.1%, $p = 0.05$) after cesarean section. No significant differences were established between the groups for other microorganisms, such as *Staphylococcus* spp. (16.9 and 11.1%, $p = 0.35$), *Candida* spp. (4.6 and 3.2%, $p = 0.68$), and *Mycoplasma hominis* (1.5 and 7.9%, $p = 0.09$).

Lactobacilli were found in 66 (51.5%) women in the early postpartum period, mainly in group 1. The detection rate of lactobacilli was 76.9%, with an average concentration of 4.6 ± 1.6 lg. In group 2, lactobacilli were found in 25.4% of women, with an average concentration of 4.1 ± 1 lg ($p = 0.000000$) (Fig. 2). Concurrently, not a single microorganism was detected in 33.3% of women in group 2. This was probably due to the use of a long course of antibacterial drugs in the perioperative period.

The proportion of different species of lactobacilli found in the lochia of group 1 revealed that the most common species was *L. jensenii*, which amounted to 32% of cases; *L. iners* in 30%, *L. crispatus* in 24%, *L. gasseri* in 20%, *L. vaginalis* in 10%, and *L. johnsonii* in 4%.

Both in women after the vaginal and cesarean delivery, the frequency of lactobacilli detection decreased, whereas the non-lactobacillary type of microbiocenosis prevailed, namely CST IV. In group 1, this type of microbiocenosis was detected with a frequency of 39.7% and 86.8% in group 2.

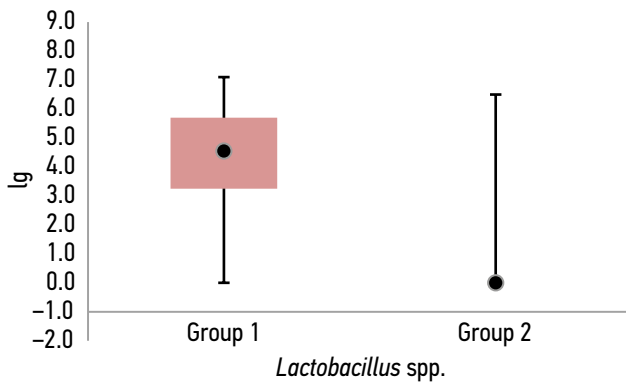


Fig. 2. The concentration of lactobacilli in the lochia in the postpartum women of groups 1 and 2 ($p = 0.000000$)

This is probably also associated with a long course of antibacterial drugs in the perioperative period. Concurrently, a statistically significant relationship was revealed between the duration of labor and the presence of CST IV in the postpartum period ($p = 0.03$).

In addition, *L. iners* dominated in the early postpartum period in 18.1% of cases (CST III). It is this type of lactobacillus that tolerates well the increased pH values of vaginal secretions, which are registered in the vaginal biotope after childbirth. Moreover, these lactobacilli were found in 23.8% of cases in group 1 and 10.5% in group 2.

CST I, with the dominance of *L. crispatus* in the postpartum period, was noted in 7.9% of cases in group 1 and 2.6% in group 2, and CST II (*L. gasseri*) in 9.5% of cases of group 1.

According to the data of numerous researchers, the peculiarities of the course of the postpartum period are presented by the dynamics of uterine involution [14]. With a complicated course of the puerperal period in the form of purulent-septic diseases, the rate of uterine involution slows down. The impairment of uterine involution was detected in 7 patients (8.6%) in group 1 and 2 (2.9%) in group 2. No symptoms of endometritis in the postpartum period or infiltrates in the sutures of the perineum were noted in any puerperas.

Among the variety of different types of microorganisms present in lochia of women with impaired uterine involution and physiological uterine involution, significant differences were revealed between the frequency of *Mycoplasma hominis* detection, as a common causative agent of chorioamnionitis [15] and obligate anaerobes (*Lachnobacterium* spp./*Clostridium* spp.).

The frequency of detection of various types of lactobacilli and types of microflora in the lochia of puerperas with impaired uterine involution are presented in Tables 1 and 2.

As for the lactobacilli, significant differences were revealed in the detection of *L. iners* and *L. jensenii* in the lochia of women with and without uterine involution disorders ($p = 0.03$ and $p = 0.009$, respectively). Moreover, in four cases, which amounted to 57.1%, uterine involution in disorder in the lochia, CST III was noted, whereas the dominant species of lactobacilli was precisely the species *L. iners* ($p = 0.006$). According to the international and Russian literature, *L. iners* can be a predictor of preterm birth and miscarriage [16, 17]. Perhaps this particular type of

Table 1. Frequency of detection of various types of lactobacilli in the lochia of puerperas with impaired uterine involution

Lactobacillus species	Impairment of uterine involution ("subinvolution") $n = 6$	Normal postpartum uterine involution $n = 60$	p -value
<i>L. crispatus</i>	33.3%	20%	>0.05
<i>L. acidophilus</i>	0	0	-
<i>L. iners</i>	66.7%	25%	0.03
<i>L. jensenii</i>	66.7%	20%	0.009
<i>L. gasseri</i>	0	18.3%	>0.05
<i>L. johnsonii</i>	0	3.3%	>0.05
<i>L. vaginalis</i>	16.7%	6.7%	>0.05

Table 2. Types of conditions of the vaginal microbial community in puerperas with impaired uterine involution

Types of vaginal microflora	Impairment of uterine involution ("subinvolution") $n = 7$	Normal postpartum uterine involution $n = 94$	p -value
CST I (<i>L. crispatus</i>)	0	6.4%	>0.05
CST II (<i>L. gasseri</i>)	0	6.4%	>0.05
CST III (<i>L. iners</i>)	57.1%	16%	0.006
CST IV (non-lactobacillary type)	42.8%	58.5%	>0.05
CST V (<i>L. genseii</i>)	14.3%	11.7%	>0.05

Note: CST—community state types.

lactobacilli can also be a factor of uterine involution disorder in the early postpartum period.

L. iners should discuss in detail, which was detected with a frequency of 39.1% before delivery (52/133) and after vaginal delivery, the frequency of detection of this type of lactobacillus was 29.4% (15/51) and 25% after cesarean section, (4/16). Like corynebacteria, *L. iners* is possibly more adaptive to survive in an environment with other concomitant microorganisms, can adapt to high pH values of the vaginal environment, and is a trigger of the reparation processes after childbirth [10]. Other types of lactobacilli do not play a significant role in the restoration of vaginal microflora in the postpartum period.

CONCLUSION

The process of vaginal microbiocenosis restoration in women occurs faster after vaginal delivery than after

a cesarean section, by days 4–5 of the postpartum period, since antibiotic therapy during a cesarean section affects the characteristics of vaginal microbiocenosis in the postpartum period, thus causing a longer recovery.

Among the dominant species, *L. crispatus*, found in the vaginal discharge before delivery, most often has a protective effect on vaginal microbiocenosis and its recovery in the postpartum period.

In turn, the presence of *L. iners* can be regarded as a triggering mechanism in the reparation processes after childbirth. However, the participation of *L. iners* in the development of postpartum infectious and inflammatory complications is not excluded.

Nevertheless, the influence of certain types of lactobacilli, prevailing in the composition of vaginal microbiota before childbirth and the dynamics of its recovery in the early postpartum period remains open and needs further investigation.

REFERENCES

1. Marco J, Coolen MJL, Post E, et al. Characterization of microbial communities found in the human vagina by analysis of terminal restriction fragment length polymorphisms of 16S rRNA genes. *Appl Environ Microbiol.* 2005;71(12):8729–8737. DOI: 10.1128/AEM.71.12.8729-8737.2005
2. Pavlova SI, Kilic AO, Kilic SS, et al. Genetic diversity of vaginal lactobacilli from women in different countries based on 16S rRNA gene sequences. *J Appl Microbiol.* 2002;92(3):451–459. DOI: 10.1046/j.13652672.2002.01547.x
3. Giakoumelou S, Wheelhouse N, Cuschieri K, et al. The role of infection in miscarriage. *Hum Reprod Update.* 2016;22(1):116–133. DOI: 10.1093/humupd/dmv041
4. Song Y, Kato N, Matsumiya Y, et al. Identification of and hydrogen peroxide production by fecal and vaginal lactobacilli isolated from Japanese women and newborn infants. *J Clin Microbiol.* 1999;37:3062–3064. DOI: 10.1128/JCM.37.9.3062-3064.1999
5. Ravel J, Gajer P, Abdo Z, et al. Vaginal microbiome of reproductive-age women. *Proc Natl Acad Sci USA.* 2011;108(Suppl 1):4680–4687. DOI: 10.1073/pnas.1002611107
6. Antonio MAD, Hawes SE, Hillier SL. The identification of vaginal *Lactobacillus* species and the demographic and microbiologic characteristics of women colonized by these species. *J Infect Dis.* 1999;180:1950–1956. DOI: 10.1086/315109
7. Rampersaud R, Planet PJ, Randis TM, et al. Inerolysin, a cholesterol-dependent cytolysin produced by *Lactobacillus iners*. *J Bacteriol.* 2011;193:1034–1041. DOI: 10.1128/JB.00694-10
8. Macklaim JM, Fernandes AD, Di Bella JM, et al. Comparative meta-RNA-seq of the vaginal microbiota and differential expression by *Lactobacillus iners* in health and dysbiosis. *Microbiome.* 2013;1:12. DOI: 10.1186/2049-2618-1-12
9. Dobrokhotova YE, Zatikyan NG. Sovremennye predstavleniya o mekhanizmaxh razvitiya disbioza vlagalishcha. *Akusherstvo, ginekologiya i reproduksiya.* 2008;(3):3–6. (In Russ.)
10. Martikaynen ZM. Korinebakterii zhenskikh genitaliy. [dissertation abstract]. Saint Petersburg; 1996. (In Russ.). [cited 2021 May 24]. Available from: <http://earthpapers.net/preview/486600/a#?page=9>
11. MacIntyre DA, Chandiramani M, Lee YS, et al. The vaginal microbiome during pregnancy and the postpartum period in a European population. *SciRep.* 2015;5:89–88. DOI: 10.1038/srep08988
12. Kolesaeva ZhJu. Mikrobiocenoz vlagalishha u rodil'nic poste estestvennyh rodov i operacii kesarevo sechenija. [dissertation abstract]. Saint Petersburg; 2012. (In Russ.). [cited 2021 May 24]. Available from: https://viewer.rusneb.ru/ru/000199_000009_005009137?page=1&rotate=0&theme=white
13. Mel'nikova TA. Osobennosti techenija beremennosti i rodov u zhenshin s razlichnoj stepen'ju kolonizacii nizhnego otdela reproduktivnogo trakta Ureaplasma urealiticum. [dissertation abstract]. Permian; 2020. (In Russ.). [cited 2021 May 24]. Available from: <https://www.dissercat.com/content/osobennosti-techeniya-beremennosti-i-rodov-u-zhenshchin-s-razlichnoi-stepenyu-kolonizatsii>
14. Morozova NA, Holodnjak TI, Ovsjanik MA. Sovremennij vzgljad na problem subinvoljucii matki. *Novosti mediciny i farmacii.* 2009;21(301):36–42. (In Russ.)
15. Kim MJ, Romero R, Gervasi MT, et al. Widespread microbial invasion of the chorioamniotic membranes is a consequence and not a cause of intra-amniotic infection. *Lab Invest.* 2009;89(8):924–936. DOI: 10.1038/labinvest.2009.49
16. Sinyakova AA, Shipitsyna EV, Budilovskaya OV, et al. Anamnestic and microbiological predictors of miscarriage. *Journal of Obstetrics and Women's Diseases.* 2019;68(2):59–70. DOI: 10.17816/JOWD68259-70
17. Petricevic L, Domig KJ, Nierscher FJ, et al. Characterisation of the vaginal *Lactobacillus* microbiota associated with preterm delivery. *Sci Rep.* 2014;4:5136. DOI: 10.1038/srep05136

СПИСОК ЛИТЕРАТУРЫ

1. Marco J., Coolen M.J.L., Post E. et al. Characterization of microbial communities found in the human vagina by analysis of terminal restriction fragment length polymorphisms of 16S rRNA genes // *Appl. Environ. Microbiol.* 2005. Vol. 71. No. 12. P. 8729–8737. DOI: 10.1128/AEM.71.12.8729-8737.2005
2. Pavlova S.I., Kilic A.O., Kilic S.S. et al. Genetic diversity of vaginal lactobacilli from women in different countries based on 16S rRNA gene sequences // *J. Appl. Microbiol.* 2002. Vol. 92. No. 3. P. 451–459. DOI: 10.1046/j.13652672.2002.01547.x
3. Giakoumelou S., Wheelhouse N., Cuschieri K. et al. The role of infection in miscarriage // *Hum. Reprod. Update.* 2016. Vol. 22. No. 1. P. 116–133. DOI: 10.1093/humupd/dmv041
4. Song Y., Kato N., Matsumiya Y. et al. Identification of and hydrogen peroxide production by fecal and vaginal lactobacilli isolated from Japanese women and newborn infants // *J. Clin. Microbiol.* 1999. Vol. 37. P. 3062–3064. DOI: 10.1128/JCM.37.9.3062-3064.1999
5. Ravel J., Gajer P., Abdo Z. et al. Vaginal microbiome of reproductive-age women // *Proc. Natl. Acad. Sci. USA.* 2011. Vol. 108. Suppl. 1. P. 4680–4687. DOI: 10.1073/pnas.1002611107
6. Antonio M.A.D., Hawes S.E., Hillier S.L. The identification of vaginal *Lactobacillus* species and the demographic and microbiologic characteristics of women colonized by these species // *J. Infect. Dis.* 1999. Vol. 180. P. 1950–1956. DOI: 10.1086/315109
7. Rampersaud R., Planet P.J., Randis T.M. et al. Inerolysin, a cholesterol-dependent cytolysin produced by *Lactobacillus iners* // *J. Bacteriol.* 2011. Vol. 193. P. 1034–1041. DOI: 10.1128/JB.00694-10
8. Macklaim J.M., Fernandes A.D., Di Bella J.M. et al. Comparative meta-RNA-seq of the vaginal microbiota and differential expression by *Lactobacillus iners* in health and dysbiosis // *Microbiome.* 2013. Vol. 1. P. 12. DOI: 10.1186/2049-2618-1-12
9. Доброхотова Ю.Э., Затицкая Н.Г. Современные представления о механизмах развития дисбиоза влагалища // *Акушерство, гинекология и репродукция.* 2008. № 1. С. 3–6.
10. Мартикайнен З.М. Коринибактерии женских гениталий: автореф. дис. ... канд. биол. наук. Санкт-Петербург, 1996. [дата обращения 24.05.2021]. Доступ по ссылке: <http://earthpapers.net/preview/486600/a#?page=9>
11. MacIntyre D.A., Chandiramani M., Lee Y.S. et al. The vaginal microbiome during pregnancy and the postpartum period in a European population // *SciRep.* 2015. Vol. 5. P. 89–88. DOI: 10.1038/srep08988
12. Колесаева Ж.Ю. Микробиоценоз влагалища у рожениц после естественных родов и операции кесарева сечения: автореф. дис. ... канд. мед. наук. Санкт-Петербург, 2012. [дата обращения 24.05.2021]. Доступ по ссылке: https://viewer.rusneb.ru/ru/000199_000009_005009137?page=1&rotate=0&theme=white
13. Мельникова Т.А. Особенности течения беременности и родов у женщин с различной степенью колонизации нижнего отдела репродуктивного тракта *Ureaplasma urealyticum*: автореф. дис. ... канд. мед. наук. Пермь, 2020. [дата обращения 24.05.2021]. Доступ по ссылке: <https://www.dissercat.com/content/osobennosti-beremennosti-i-rodov-u-zhenshchin-s-razlichnoi-stepenyu-kolonizatsii>
14. Морозова Н.А., Холодняк Т.И., Овсяник М.А. Современный взгляд на проблему субинволюции матки // *Новости медицины и фармации.* 2009. Т. 21. № 301. С. 36–42.
15. Kim M.J., Romero R., Gervasi M.T. et al. Widespread microbial invasion of the chorioamniotic membranes is a consequence and not a cause of intra-amniotic infection // *Lab. Invest.* 2009. Vol. 89. No. 8. P. 924–936. DOI: 10.1038/labinvest.2009.49
16. Синякова А.А., Шипицына Е.В., Будиловская О.В. и др. Клинико-анамнестические и микробиологические предикторы невынашивания беременности // *Журнал акушерства и женских болезней.* 2019. Т. 68. № 2. С. 59–70. DOI: 10.17816/JOWD68259-70
17. Petricevic L., Domig K.J., Nierscher F.J. et al. Characterisation of the vaginal *Lactobacillus* microbiota associated with preterm delivery // *Sci. Rep.* 2014. Vol. 4. P. 5136. DOI: 10.1038/srep05136

AUTHORS INFO

***Dzhamilya G. Dadayeva**, MD;
address: 3 Mendeleevskaya Line,
Saint Petersburg, 199034, Russia;
ORCID: <https://orcid.org/0000-0002-1190-0149>;
eLibrary SPIN: 2577-2236;
e-mail: djamilya2010@mail.ru

Olga V. Budilovskaya, MD;
ORCID: <https://orcid.org/0000-0001-7673-6274>;
eLibrary SPIN: 7603-6982; e-mail: o.budilovskaya@gmail.com

Anna A. Krysanova, MD;
ORCID: <https://orcid.org/0000-0003-4798-1881>;
eLibrary SPIN: 2438-0230; e-mail: annakr@inbox.ru

Tatyana A. Khusnutdinova, MD;
ORCID: <https://orcid.org/0000-0002-2742-2655>;
eLibrary SPIN: 9533-9754; e-mail: husnutdinovat@yandex.ru

ОБ АВТОРАХ

***Джамиля Гамбулатовна Дадаева**;
адрес: Россия, 199034, Санкт-Петербург,
Менделеевская линия, д. 3;
ORCID: <https://orcid.org/0000-0002-1190-0149>;
eLibrary SPIN: 2577-2236;
e-mail: djamilya2010@mail.ru

Ольга Викторовна Будиловская;
ORCID: <https://orcid.org/0000-0001-7673-6274>;
eLibrary SPIN: 7603-6982; e-mail: o.budilovskaya@gmail.com

Анна Александровна Крысанова;
ORCID: <https://orcid.org/0000-0003-4798-1881>;
eLibrary SPIN: 2438-0230; e-mail: annakr@inbox.ru

Татьяна Алексеевна Хуснутдинова;
ORCID: <https://orcid.org/0000-0002-2742-2655>;
eLibrary SPIN: 9533-9754; e-mail: husnutdinovat@yandex.ru

Alevtina M. Savicheva, MD, Dr. Sci. (Med.),
Professor, Honored Scientist of the Russian Federation;
ORCID: <https://orcid.org/0000-0003-3870-5930>;
Scopus Author ID: 6602838765;
eLibrary SPIN: 8007-2630;
e-mail: savicheva@mail.ru

Igor Yu. Kogan, MD, Dr. Sci. (Med.), Professor,
Corresponding Member of the Russian Academy of Sciences;
ORCID: <https://orcid.org/0000-0002-7351-6900>;
Scopus Author ID: 56895765600;
eLibrary SPIN: 6572-6450;
e-mail: iagmail@ott.ru

Алевтина Михайловна Савичева, д-р мед. наук,
профессор, засл. деят. науки РФ;
ORCID: <https://orcid.org/0000-0003-3870-5930>;
Scopus Author ID: 6602838765;
eLibrary SPIN: 8007-2630;
e-mail: savicheva@mail.ru

Игорь Юрьевич Коган, д-р мед. наук,
профессор, чл.-корр. РАН;
ORCID: <https://orcid.org/0000-0002-7351-6900>;
Scopus Author ID: 56895765600;
eLibrary SPIN: 6572-6450;
e-mail: iagmail@ott.ru