

THE STATUS OF VAGINAL MICROBIOCENOSIS IN CHRONIC SALPINGOOPHORITE AND ITS ASSESSMENT

Ziyayeva E`tiborhon Rasuljonovna
Assistant Professor of the Department of
Obstetrics and Gynecology №1, PhD,

Abdullaeva Malika Azimovna
Senior Lecturer of the Department of
Obstetrics and Gynecology №1

Abstract

The long course of chronic salpingo-oophoritis, the use of various antibiotics for treatment lead to complex changes in the microbiocenosis of the body of sick women. These changes lead to a more severe course of SSO. A deep study of this condition allows you to restore the microbiocenosis of the vagina and cervix and improve the results of treatment.

Keywords: Chronic salpingoophoritis, bichenosis, mikrobichenoz.

Introduction

At the end of the last century, according to WHO, 40-50% of all pelvic inflammatory diseases develop due to infection with Neisseria gonorrhoeae. Thus, the development of acute purulent salpingitis is associated with the presence of a transmissible infection, usually gonorrhea. However, according to statistics from different countries, the incidence of pelvic inflammatory diseases in women is several times higher than that of gonorrhea [16, 18, 20, 21]. Thus, in 1999, the incidence of gonorrhea in Russia was 119.8 cases per 100,000 population, and pelvic inflammatory diseases - about 11 times higher - 1360.6 cases per 100,000 population [1, 2, 5, 17, 21].

In the 40-60s of the 20th century, streptococci (31.4%) took the leading place in the development of inflammatory diseases of the pelvic organs, in the 60-70s - staphylococci (54.5%). In the 80-90s, the main causative agents of inflammatory diseases of the uterine appendages were staphylococci, E. coli, gonococci and



chlamydia, and from the 80s to the present day, associations of pathogens have become more important than monocultures of microorganisms in the development of inflammatory diseases of the pelvic organs in women. Thus, in 41.7% of patients, both aerobic and anaerobic microorganisms were detected simultaneously. The leading initiators of SSO are gram-positive anaerobic bacteria that do not cause spirochetal pain, microorganisms belonging to the Enterobacteriaceae family - anaerobic spore-forming clostridia of the genus *Clostridium*, gonococci and gram-positive anaerobic bacteria that cause pelvic pain. The associations also include aerobic coccal microflora (strepto-, entero-, staphylococci), influenza viruses, chlamydia. At the same time, according to different researchers, the degree of occurrence of associations of aerobes and anaerobes varies significantly” [6, 11, 19].

In recent years, anaerobic infections have prevailed over aerobic ones - the frequency of detection of anaerobic microorganisms in SSO is 76.9%. A study of the composition of the cervical canal showed that the frequency of detection of microbial associations in patients with SSO using the bacteriological method reached 29.94% of cases. *U. urealiticum* was detected in 8.38% of patients, *E. coli* in 7.19%, *S. albicans* in 6.39%, and *S. haemolyticus* in 3.39%. Mycoplasmas, ureaplasmas, and corynebacteria are the causes of inflammatory diseases of the genital organs in the group of young women under 20 years of age. In patients over 30 years of age, anaerobic microorganisms play a leading role in the development of SSO. Up to 20% of cases of SSO are associated with the presence of *Tr.vaginalis* and mycoureaplasma infection, and the involvement of viruses in the development of the inflammatory process in the uterine appendages is confirmed in 67.3% of observations [3,6, 8, 10, 14, 16]. One of the main causative agents of SSO is *Ch. trachomatis*, which occurs in 44% of women diagnosed with adnexitis. However, the role of chlamydia in the formation of abscesses in SSO has not been sufficiently studied [4, 12, 19].

A characteristic feature of gynecological diseases in recent decades worldwide is a significant increase in the incidence of SSO caused by strains resistant to clinically used penicillin antibiotics [6, 11,]. In this regard, inflammatory diseases of the female genital organs are often characterized by the development of purulent-septic complications, which are often severe, requiring prolonged inpatient conservative and surgical treatment. It should be noted that the lack of effectiveness of



antibacterial therapy with selected drugs significantly increases the medical and economic costs of treating patients with adnexitis [5, 8, 9].

Purulent-inflammatory diseases of the uterine appendages can also be caused by opportunistic microflora, among which conditionally anaerobic microorganisms predominate. Thus, due to the wide range of potential pathogens of the infectious inflammatory process, it is very difficult to determine the etiology of SSO and the difficulty of collecting material for microbiological research from the source of inflammation located in the internal genital organs of a woman [13, 17, 18]. However, in the emergence and development of the inflammatory process, not only the virulence of the microbe, the specific effect of its toxic and enzymatic pathogenic factors, the mass of infection, but also the state of reactivity of the inflammatory process play a decisive role. The factor determining the individual characteristics of the course and outcome of the disease is the state of the female organism. As is known, local mechanisms of nonspecific protection of the female genital organs are implemented, first of all, due to the specific features of their structure and functions [3, 9, 17, 22]. Natural barrier mechanisms prevent the penetration of infectious agents into the female genital organs. Thus, the penetration and development of pathogenic microflora is prevented by the closed state of the genital slit, the contact of the labia majora and minora, which is ensured by the tension of the perineal muscles. The protective properties of the vagina are determined by the presence of keratin in the mucous epithelium and the constant desquamation of its cells [3, 4, 5, 11, 22].

In the etiopathogenesis of SSO, along with infectious factors, the state of the associated organs, and primarily the large intestine, is of great importance, which contributes to the chronicity and recurrence of the pathological process, mainly in the appendages of the uterus. As the disease progresses, and in some cases, the pathological process becomes more subtle [13, 17, 18], intestinal changes in IBS are facilitated by microcirculatory disorders, immunological homeostasis, hormonal regulation of gastrointestinal motility, and intestinal dysbiosis [8, 10, 18, 21].

Colorectal disorders, in turn, enhance and maintain inflammatory changes in the uterine appendages. Few studies have been devoted to the analysis of intestinal functions in inflammatory diseases of the reproductive system, and structural



disorders of the intestine remain unstudied by analyzing the state of its diffuse endocrine system (DET) in various forms of SSO [15, 16, 23].

It is known that 95-98% of the vaginal microflora of a healthy woman of reproductive age is represented by lactobacilli (*Lactobacillus*), the majority of which are H₂O₂-producing strains [19, 21, 22]. Typically, the microflora of the genital tract is represented by corynebacteria, diphtheria, anaerobes, and aerobic cocci, including hemolytic and non-hemolytic streptococci, *Klebsiella*, *Enterobacteriaceae*, *Proteus*, *Escherichia coli*, and *Candida* fungi [16, 19, 22, 23]. Vaginal normocenosis is characterized by a predominance of lactobacteria, the absence of gram-negative flora, spores, mycelium, pseudohyphae, the presence of single leukocytes and "pure" epithelial cells, depending on the phase of the menstrual cycle [16, 19, 22, 23].

Exogenous factors that negatively affect the vaginal microflora are chemical and thermal effects during the treatment of the vaginal walls for contraceptive purposes. Colonization of the lower parts of the urinary system and female genital organs by pathogenic microorganisms is prevented by an acidic environment (pH = 4.0-4.5), as well as a high level of secretory immunoglobulins, complement components, lysozyme, lysine, defensins, lactoferrin, interferons in the vaginal secretion, micro-, macrophages and other bactericidal factors. Local protective factors in the cervical canal also prevent ascending infection of the uterine appendages. The mucous membrane of the cervical canal has significant viscosity and provides a mechanical barrier to pathogenic factors, separating the lower and upper parts of the reproductive system. When using barrier methods of contraception, pelvic inflammatory diseases in women are reduced by 23%. An important protective role is played by the formation of a leukocyte cell barrier due to the denudation of the functional layer of the epithelium and the infiltration of the basal layer of the endometrium by micro-, macrophages and lymphocytes. Rich blood supply provides intensive delivery of specific and nonspecific humoral protective factors to the uterine tissues. Thus, in the body of a healthy woman, the uterus, fallopian tubes and ovaries have a multi-stage defense that limits the possibility of infection [16, 19,22,23]. Regular and not always justified use of antibiotics leads not only to the formation of resistant flora, but also to dysbiosis, polyvalent allergies, drug overload of the liver and urinary system. Periodic exacerbations of the disease lead



to a deterioration in the patient's quality of life and negatively affect the emotional and mental state [15].

In order to assess the microbiocenosis of the vagina and cervical canal of patients with SSO, we performed the task of determining the microbiocenosis of the vagina and cervical canal in the scientific diagnostic laboratory of the Andijan Medical Diagnostic Center using the enzyme-linked immunosorbent assay (ELISA) method with the detection of GVI, CMV, EBV, chlamydia, mycoplasma, ureaplasma and other microorganisms (laboratory head N.V. Startseva). In this case, real-time PCR research with the Femoflor-screen complex (DAK-technology, IIB, Russian Federation) was used: "an expanded molecular biological study of the qualitative and quantitative composition of the microflora of the genitourinary system in women. , allows you to control the collection of material and the total mass of bacteria" [12, 14]. The presence of 23 groups of microorganisms was studied: "Lactobacillus spp., Enterobacteriaceae family, Streptococcus spp., Staphylococcus spp., Gardnerella vaginalis, Prevotella bivia, Porphyromonas spp., Eubacterium spp., Sneathtrium spp., Fupacttrium spp. , Veilonella spp., Megasphaera spp., Dialister spp., Lachnobacterium spp., Clostridium spp., Mobiluncus spp., Corynebacterium spp., Peptostreptococcus spp., Atopobium vaginae, Mycoplasma hominum spp., , Mycoplasma genitalium" [12, 14, 22].

One of the tubes used a prototype for PCR amplification and control. Biomaterials were collected from the back of the vagina, cervical canal and urethra using a special brush. The tip of the brush with the biomaterial was cut off and placed in a special tube [12, 14, 22]. For interpretation, they were marked with color: "control indicators: white - compliance with the criteria, red - non-compliance; opportunistic microorganisms and yeast-like fungi: white - compliance with the criteria of the norm, yellow - average deviation, red - significant deviation from the norm; normal flora (lactobacteria): green - normocenosis (compliance with normal criteria), yellow - moderate dysbiosis (average deviation from the norm), red - severe dysbiosis; pathogenic microorganisms: white - not detected, red - detected" [12, 14].



Assessment of the microbiocenosis of the vagina and cervical canal of patients with SSO

Assessment of the microbiocenosis of the vagina and cervical canal of patients with SSO.

The microbiocenosis of the vagina and cervical canal of the studied patients was studied in real time using the Femoflor-screen complex (DAK-technology, IIB, Russian Federation) (Table 3.5).

Parasitocenoses of the reproductive system in patients with AG and SG with intensive (IQ) SSO were characterized by a significantly higher frequency of detection of almost all microorganisms compared to patients with IQ SSO, i.e. Due to the increase in the spectrum of microorganisms in the vagina, the exacerbation of SSO is more clinically pronounced.

With a normal bacterial mass, the normal flora represented by *Lactobacillus* spp. was shown in a low percentage in the studied groups - 57.41-76.92%, while we consider 80-100% to be the norm. Facultative anaerobic microorganisms were distinguished by a very rapid growth - Sem. In AG, enterobacteria were found in 66.67% of patients, in SG in 28.85%, and in NG in only 13.33%, so their growth exceeded the norm by 4.5-5 times, which is statistically significant ($p \leq 0.05$).). A similar trend was shown by *Streptococcus* spp. and *Staphylococcus* spp., so in AG these microorganisms were found in 51.85% of patients, and in SG in 42.31% and 46,15 respectively.

In NG *Streptococcus* spp. was detected in 13.33% (i.e. 3-4 times less, $p \leq 0.05$), and in *Staphylococcus* spp. was absent at all, which is undoubtedly statistically significant ($p \leq 0.05$). It is worth noting that in patients with SSO, the presence of *Candida* spp. was detected. in NG compared to 61.54-66.67% in the study groups, i.e. the frequency of fungal vaginosis increased statistically significantly by 6.2-6.7 times ($p \leq 0.05$).

Table 1. Microbiocenosis of the vagina and cervical canal of patients studied using the Femoflor-screen complex.

Instigators	BG(n=54)		CG (n=52)		CG (n=30)	
	Aбс	%	Aбс	%	Aбс	%
Total bacterial mass	10 ^{5,2}		10 ^{7,4}		10 ^{7,8}	
Lactobacillus spp.	31	57,41	40	76,92	30	100
Enterobacteriaceae family	36	66,67	15	28,85	4	13,33
Streptococcus spp.	28	51,85	22	42,31	4	13,33
Staphylococcus spp.	28	51,85	24	46,15	0	0,00
Eubacterium spp.	36	66,67	31	59,62	5	16,67
Sneathia spp. + Leptotrihia spp. + Fusobacterium spp.	21	38,89	18	34,62	4	13,33
Megasphaera spp + Veilonella spp. + Dialister spp.	17	31,48	16	30,77	1	3,33
Peptostreptococcus spp.	40	74,07	33	63,46	4	13,33
Atopobium vaginae	26	48,15	24	46,15	5	16,67
Candida spp.	36	66,67	32	61,54	3	10
Mycoplasma hominis	21	38,89	15	28,85	1	3,33
Ureaplasma (urealyticum + parvum)	16	29,63	15	28,85	2	6,67
Mycoplasma genitalium	21	38,89	15	28,85	1	3,33

Note: * - difference with NG at the $p \leq 0.05$ level.

Microorganisms such as Mycoplasma hominis and Mycoplasma genitalium were also found in SSO in the studied patients 9-12 times more often ($p \leq 0.05$), and Ureaplasma four times more often ($p \leq 0.05$).

In 44.34% of patients with SSO, microbial associations with various staphylococci were found in the flora.

Summarizing the results of the bacterial study, it was found that in the studied patients with SSO, there was a significant imbalance of the vaginal microflora, in particular, the growth of non-pathogenic microorganisms (lactobacteria, bifidobacteria) and opportunistic microflora (peptococcus, golden staphylococcus, hemolytic and viridans Streptococcus, Gardnerella, Corynebacteria, etc.). It should be noted that we found greater vaginal dysbiosis in representatives of AG with long-term SSO and STOS, which is quite expected and requires complex antimicrobial therapy of the body and vagina locally.

Among the methods of laboratory diagnostics of changes in the vaginal microflora, the most common is the Nugent method, which is based on the identification of three bacterial morphotypes: large gram-positive rods (lactobacteria), small gram-negative cocci and coccobacteria (*Gardnerella* and *Bacteroides*), and gram-negative rods (*Mobiluncus*) [8,19,22].

A score in the range of 0-3 corresponds to normal microflora, 4-6 points - intermediate, and 7-10 points - dysbiosis. The Nugent method has high sensitivity, specificity, standardization and reproducibility [8].

Thus, analyzing the results of the study of patients, we identified the types of microbiocenosis, which are reflected in Table 3.6.

Table 2. Types of vaginal microbiocenosis in patients of the study groups

Type of microbiocenosis	BG(n=54)		CG (n=52)		CG (n=30)	
	Abs	%	Abs	%	Abs	%
Normocenosis	9	16,67	32	61,54	26	86,67
Intermediate type	23	42,59	16	30,77	4	13,33
Dysbiosis	22	40,74	4	7,69	0	0,00

We also determined the average score using the Nugent method, so the average score in AG was 5.34 ± 0.46 points, in SG – 3.87 ± 0.52 points, in NG – 1.93 ± 0.24 points, therefore, according to the average score, AG and SG showed an intermediate type of microbiocenosis, and in NG - normocenosis.

When diagnosing bacterial vaginosis, the following treatment regimen was used: “combined antimicrobial vaginal suppositories (*Gynex*) intravaginally daily for 7 days or metronidazole gel 0.75% 5 g 1-2 times a day for 5 days; for nonspecific colpitis - clindamycin, vaginal cream 2% 5 g at night for 7 days, after the end of the etiotropic course of treatment, *Lactobacterin* is prescribed intravaginally 1 time per day for 7 days in 5 doses [15,19, 22].

Also, patients in both groups were prescribed “intestinal motility regulators” along with diet therapy: in diarrhea - *bioterol* 1-2 tablets 1 hour before meals 2 times a day until stool stabilization (5-7 days); *duspatalin* 1 capsule 2-3 times a day for up to 7 days” [15, 22].

REFERENCES

1. Abdullaeva M.A., Ziyaeva E.R., Sobirova M.R. The effect of soil therapy on immune changes in the blood in patients with chronic salpingo-oophoritis// *Medicine: New opportunities. Collection: 13th thematic scientific and practical conference mol.u chon TGMU with international participation.- Dushanbe.- 2018. - Vol.1.- P.126-127*
2. Brünahl C.A. Klotz S.G.R., Dybowski C.et al. Combined Cognitive-Behavioural and Physiotherapeutic Therapy for Patients with Chronic Pelvic Pain Syndrome (COMBI-STOS): study protocol for a controlled feasibility trial // *Trials. 2018 Jan 9 - #19(1) - p.20-27.* Bronovets I.N. Intestin disbioz: diagnos, profilaktika va davolash // *Tibbiy yangiliklar. – 2016. – №11. – s. 56–58.;*
3. Duc Ninh Nguyen, Thomas Thymann, Sandra K. Goericke-Pesch, Shuqiang Ren. Prenatal Intra-Amniotic Endotoxin Induces Fetal Gut and Lung Immune Responses and Postnatal Systemic Inflammation in Preterm Pigs // *Am J Pathol. - 2018 Nov; №188 (11). - P. 2629–2643.;*
4. Jackson L.W., Schisterman E.F., Dey-Rao R. et al. Oxidative stress and endometriosis // *Hum. Reprod. – 2018. – №20 (7). – P. 2014–2020*
5. Horner P., Blee K., Adams E. Time to manage *Mycoplasma genitalium* as an STI: but not with azithromycin 1g // *Curr. Opin. Infect. Dis. – 2014. – 27 (1). – P. 68–74. <https://psyttests.org/anxiety/stai-run.html>*
6. Karcioğlu O., Topacoglu H., Dikme O., Dikme O. A systematic review of the pain scales in adults: Which to use? // *Am.J. Emerg. Med. -2018. -Vol. 36. - №4. - P. 707-714*
7. Shigan E.N. *Methods of prediction and modeling in socio-hygienic research. — M., 1986. — 207 p.*
8. Kira E.F., Rogovskaya S.I., Artymuk N.V., Savicheva A.M. Results of a study on the effectiveness and safety of vaginal administration of ornidazole in the treatment of bacterial vaginosis // *Journal of Obstetrics and Gynecology. – 2015. - No. 8. – pp. 89-95*
9. Konoval A.A. Features of the immune status of women with chronic salpingo-oophoritis // *Scientific articles. Medical and pharmaceutical series. 2013. No. 25 (168). Issue 24 - pp. 84-89.* Mika Mizoguchi, Yuko Ishida, Mizuho Nosaka, Akihiko Kimura. Prevention of lipopolysaccharide-induced preterm labor by the

- lack of CX3CL1-CX3CR1 interaction in mice // Prog Clin Biol Res. - 2018. - V.92. - P. 263-272.
10. Men'shikov V.V. Clinical laboratory research methodology: Manual. Volume 3. Clinical microbiology.: M.: Labora, 2009. - 880 p.;
 11. Prilepskaya V.N., Bebneva T.N. The effectiveness of the immunomodulator Galavit in the treatment of colds of the pelvic organs // Russian Medical Journal. – 2013. – No. 1. – P. 10–14.;
 12. Prilepskaya V.N. Sexually transmitted infections. – M.: GEOTAR-Media, 2014. – 160 p.
 13. Shperling N.V., Shperling I.A., Vengerovsky A.I. The principle of therapy of pain syndrome in salpingoophoritis // Problems of gynecology, obstetrics and perinatology. – 2014. – No. 1. – P. 35–40
 14. Savicheva A.M., Shipitsyna E.V., Vorobyeva N.E. Vaginal infections and modern approaches to their diagnosis and treatment // Obstetrics and gynecology. – 2016. – No. 2. – P. 120–126.Schooley R.T. The human microbiome: implications for health and disease, including HIV infection // Top. Antivir. - Med. – 2018. – 26 (3). – p. 75-78
 15. Rishchuk S.V., Punchenko O.E., Malyisheva A.A. Vulvani endogen mikrobiotasi va uning regulatsiyasi // Orenburg ilmiy markazi bukleti, Ural OA RAH. - 2013. - № 4. - B. 9-15
 16. Ruzieva N. H., Pakhomova J. E. Endotoxin aggression in the pathogenesis of preterm birth // Journal of research in health science. Health Science.– Israel, Yashresh, 2019. - №1. - p. 50-54
 17. Volchegorskiy I.A., Pravdin E.V., Uzlova T.V./ Anti-infective properties of chronic endometritis and salpingo-oophoritis // Bulletin of Russian Obstetrics and Gynecology. – 2014. – No. 6. – P. 75–79Ziyaeva E.R. Microbiocenosis Of Open Cavities of The Body//The American Journal of Medical Sciences and Pharmaceutical Research,- 2021.- Vol.3. – №7, - P.1–45.
 18. Ziyaeva E.R. / Optimization of therapeutic measures in women with chronic salpingoophoritis complicated by pain syndrome. // Diss. PhD. 2025y. 136 p.
 19. Zakharova T.V. Volkov V.G. Experience in the treatment of bacterial vaginosis - candidal vulvovaginitis // Obstetrics and gynecology. – 2016. – №11. – P. 131–135.