© Baturin V. A., Boshyan R. O., 2018
UDC 615.45:618.13-08
DOI – <https://doi.org/10.14300/mnnc.2018.13087>
ISSN – 2073-8137

THE IMMUNE STATUS OF OUT-PATIENT WOMEN OF REPRODUCTIVE AGE WITH PELVIC INFLAMMATORY DISEASE

Baturin V. A.^{1,2}, Boshyan R. O.^{1,2}

¹ Stavropol State Medical University, Russian Federation

² Center for Clinical Pharmacology and Pharmacotherapy, Stavropol, Russian Federation

ИЗУЧЕНИЕ ИММУННОГО СТАТУСА У ЖЕНЩИН РЕПРОДУКТИВНОГО ВОЗРАСТА ПРИ ВОСПАЛИТЕЛЬНЫХ ЗАБОЛЕВАНИЯХ ОРГАНОВ МАЛОГО ТАЗА В ПОЛИКЛИНИЧЕСКИХ УСЛОВИЯХ

В. А. Батурин^{1,2}, Р. О. Бошнян^{1,2}

¹ Ставропольский государственный медицинский университет,
Российская Федерация

² Центр клинической фармакологии и фармакотерапии, Ставрополь,
Российская Федерация

The immune status of 123 out-patient women of a reproductive age with pelvic inflammatory disease (PID) was studied. Immunodeficiency was observed in 100 (81 %) patients: B-type in 46 (56 %), T-type – 27 (34 %), and admixed type – 10 (8 %) patients. Women with deficient humoral immunity did not have *Enterococcus faecalis*, which was present in women with deficient cellular immunity – 6 (18 %) or admixed type – 5 (15 %), and 100 % of those with PID. Some patients with B-type immunodeficiency had *Chlamydia trachomatis* – in 13 (23 %) or *Escherichia coli* – 5 (9 %).

Keywords: pelvic inflammatory disease, microflora, urogenital tract, microbial associations, immunodeficiency, cellular immunity, humoral immunity

Изучен иммунный статус 123 женщин репродуктивного возраста с воспалительными заболеваниями органов малого таза (ВЗОМТ) в поликлинических условиях города Ставрополя. Исследование показало, что состояние иммунодефицита наблюдалось у 100 пациенток (81 %): по В-типу – у 46 (56 %), по Т-типу – у 27 (34 %), по смешанному типу – у 10 (8 %). Было установлено, что у женщин с дефицитом гуморального звена иммунитета *Enterococcus faecalis* не выделялся, вместе с тем обнаруживался при дефиците клеточного звена – у 6 больных (18 %) и при смешанном типе – у 5 (15 %). При этом выделение возбудителя всегда сопровождалось выраженными клиническими проявлениями ВЗОМТ. У пациенток с иммунодепрессией по В-типу в большинстве случаев выявлялись *Chlamydia trachomatis* – у 13 женщин (23 %) и *Escherichia coli* – у 5 (9 %).

Ключевые слова: воспалительные заболевания органов малого таза, микрофлора урогенитального тракта, микробные ассоциации, иммунодефицит, клеточный иммунитет, гуморальный иммунитет

For citation: Baturin V. A., Boshyan R. O. The IMMUNE STATUS OF OUT-PATIENT WOMEN OF REPRODUCTIVE AGE WITH PELVIC INFLAMMATORY DISEASE. *Medical News of North Caucasus*. 2018;13(3):493-496.
DOI – <https://doi.org/10.14300/mnnc.2018.13087>

Для цитирования: Батурин В. А., Бошнян Р. О. ИЗУЧЕНИЕ ИММУННОГО СТАТУСА ЖЕНЩИН РЕПРОДУКТИВНОГО ВОЗРАСТА ПРИ ВОСПАЛИТЕЛЬНЫХ ЗАБОЛЕВАНИЯХ ОРГАНОВ МАЛОГО ТАЗА В ПОЛИКЛИНИЧЕСКИХ УСЛОВИЯХ. *Медицинский вестник Северного Кавказа*. 2018;13(3):493-496. DOI – <https://doi.org/10.14300/mnnc.2018.13087>

CICs – Circulating Immune Complexes
ID – Immunodeficiency

Ig – Immunoglobulin
PID – Pelvic Inflammatory Disease

Pelvic inflammatory disease (PID), a widespread gynecologic pathology, occurs in 60–65 % of gynecologic patients [1, 2, 3], and is the most frequent cause of poor reproductive health in women, with a high medical, social and economic burden [4, 5, 6]. According to the National Center of Control, the case rate of PID in the US is about 1 million cases

annually, that is 1 in 10 women of reproductive age has chronic inflammation of organs in the small pelvis, and 1 in 4 of these women have complications [7, 8, 9, 10].

Immunodeficiency (ID) has an important role in the pathogenesis of PID [11, 12], and a weakened immune system leads to chronic disease and recurrence

involving various organs and systems [13, 14]. Furthermore, immunodepression leads to disturbances of microbiocenosis in the urogenital tract [15, 16].

The aim of this study was to evaluate the immune status of out-patient women of reproductive age with PID and to assess their pathogenic microorganisms.

Material and Methods. Overall, 123 patients of reproductive age with pathological changes in the microbiota of the urogenital pathway were examined. Diagnoses were established on the basis of complaints, anamnesis, a clinical picture of disease, results of clinical laboratory inspection including dabs of vaginal and cervical flora, diagnosis of «latent» infections (*Chlamydia trachomatis*, *Mycoplasma genitalium* and *hominis*, *Ureaplasma spp.*, *Trichomonas vaginalis*) by polymerase chain reaction, bacterial crops of microflora from the cervical channel (with determination of sensitivity of the allocated microorganisms to antibacterial and antifungal medicines), and dabs of atypical cells or Pap smears. Blood and serum were used to assess the general immunoreactivity by the following methods: 1) immunocytochemistry using monoclonal antibodies to immunophenotype subpopulations of lymphocytes; and 2) radial diffusion using a method reported by Mancini to measure levels of immunoglobulin Ig G, Ig A, and Ig M.

Exclusion criteria were gonorrheal or herpetic cervicitis, or conditions of ID connected with the accompanying somatic pathology.

The obtained data underwent statistical analysis by Student's *t*-test and Fisher's exact test. Statistical significance was assumed when $p < 0.05$.

Results and Discussion. The immune response in patients with PID is formed under the influence of many different factors. In this regard, the anamnesis of patients was studied in detail. The patients had frequent respiratory viral diseases in 50 (41 %), recurring tonsillitis – 50 (41 %), chickenpox – 40 (33 %), measles – 11 (9 %) and other infectious diseases. One in 3 patients had chronic bilateral adnexitis in remission. Forty (32 %) women had anamnesis of sexually transmitted infections. In the gynecologic anamnesis the following nosological forms were noted: a small myoma in the uterus in 15 (12 %), premenstrual syndrome – 12 (10 %), diffuse fibrocystic mastopathy – 12 (10 %), diffuse form of adenomyosis – 10 (8 %), dysfunction of the ovaries in the reproductive period – 10 (8 %), chronic cystitis in remission – 8 (7 %), polycystic ovary syndrome – 6 (5 %), dysmenorrhea – 5 (4 %), retention cysts of the ovaries – 5 (4 %), insufficiency of the luteal phase – 4 (3 %), hyperprolactinemia controlled by pharmacological agents – 3 (2.4 %), insulin resistance – 3 (2.4 %), syndrome of increased androgens of mixed genesis – 2 (2 %), tubal peritoneal infertility – 2 (2 %), infertility of mixed genesis – 2 (2 %), endocrine infertility – 2 (2 %), papilloma virus – 2 (2 %), and recurring genital herpes in remission – 2 (2 %).

Patients with the following accompanying somatopathies were noted: chronic gastritis – 10 (8 %), myopia of moderate severity – 3 (2.4 %), varicose veins of the lower extremities – 3 (2.4 %), biliary dyskinesia – 2 (2 %), chronic pyelonephritis – 2 (2 %), and pollinosis – 2 (2 %).

Different forms of PID were noted: aerobic vaginitis in 55 (45 %), chronic cervicitis – 35 (28 %), cervicitis associated with *Enterococcus faecalis* – 23 (19 %), mycotic vulvovaginitis – 23 (19 %), bacterial vaginosis – 11 (9 %), ureaplasma cervicitis – 8 (7 %), chlamydial cervicitis – 6 (5 %), and cervicitis associated with *Escherichia coli* – 6 (5 %), *E. aerogenes* – 3 (2 %), or *Staphylococcus aureus* – 2 (2 %). The assessment of

microbial number indicated body height in individuals with cervicitis was associated with *E. aerogenes* in 3, *St. aureus* in 2, and *E. faecalis* in 23. Of all microbial associations in 50 (41 %), the most common were *E. faecalis*, *E. coli*, *Candida spp.*, and *C. trachomatis*.

Immunologic analysis of patient's ID indicated that 100 (81 %) patients (Table 1) had B-type in 56 (46 %), T-type – 34 (27 %), or admixed type – 10 (8 %). Normal immune conditions were observed in 23 patients.

Table 1
The characteristic of indicators of systemic immunity in women with PID (n=100) (M±m)

Indicators	Rate	Patients with an ID on B-type (n=56, 46 %)	Patients with an ID on T-type (n=34, 27 %)	Patients with an ID on the admixed type (n=10, 8 %)
Leucocytes, $\times 10^9/l$	4.3–7.5	5.1±0.18	5.14±0.18	3.8±0.17
Lymphocytes, %	23–45	20±2.01	30±2.13	25.1±2.15
T-Lymphocytes (CD3), %	41–70	55.1±8.24	39±5.12	43.1±6.18
T-suppressors (CD8), %	17–25	19.3±2.11	16.1±2.11	19.1±3.18
T-helpers (CD4), %	23–48	26.4±2.23	28.1±2.17	30.2±3.11
CD4/CD8	1.1–2.2	3.1±0.3	1.8±0.18	1.56±0.11
B-Lymphocytes (CD22), %	22.0±3.5	18.1±2.12	19.1±2.11	25.2±0.1
CD3/CD22	2.4±0.5	3.05±0.13	2.1±0.11	1.7±0.12
Ig A, g/ml	0.8–2.8	0.3±0.12	2.82±0.13	4.9±0.11
Ig M, g/ml	0.5–1.9	0.7±0.17	1.43±0.14	4.96±1.16
Ig G, g/ml	5.4–16.1	9.1±2.21	19.42±3.1	15.77±3.11
CICs (conventional units)	10.0–54.0	66.42±10.24	143.1±15.13	82.2±10.18

The main changes in indicators of deficient cellular immunity were reduced numbers of T-type of lymphocytes (39.0±5.12) and the CD3/CD22 (2.1±0.11) index. Patients with ID had reduced numbers of B lymphocytes (18.1±2.12). This indicated the reduced production of antibodies in ID patients compared with normal subjects.

A deficiency of immunity with the admixed type was noted in patients with leukopenia and lymphopenia and characterized by a shift in CD3/CD22 towards activation of humoral immunity and high levels of IgA (4.9±0.11), IgM (4.96±1.16), and IgG (82.2±10.18).

Normal immune system conditions were noted in 19 patients (83 %), of which 4 (17 %) had moderately increased levels of IgA, IgM, IgG and circulating immune complexes (CICs).

We found that aerobic vaginitis was present in women with T-type in 13 (38 %), B-type – 20 (36 %), or admixed type – 2 (20 %) ID, and in 17 (74 %) women with standard immunity. The existence of chronic cervicitis was observed in 12 patients with T cell deficiency (35 %), 15 with B cell deficiency (27 %), 5 with admixed deficiency (50 %), and 7 with normal immunity (30 %).

Patients with a deficiency in cellular immunity were positive for microflora in the vagina and the cervical channel (Table 2): *Candida spp.* in 6 (18 %), *E. faecalis* – 5 (15 %), *Gardnerella vaginalis* – 3 (9 %), *U. spp.* – 2 (6 %), *St. agalactiae* – 1 (3 %), and *E. aerogenes* – 1 (3 %).

Changes of the immune status of women with PID depending on the microbiota present in the urogenital tract (n=123)

Patients with an ID on B-type (n=56, 46 %)		Patients with an ID on T-type (n=34, 27 %)		Patients with an ID on the admixed type (n=10, 8 %)	
<i>Candida spp.</i>	n=15 27 %	Aerobic vaginitis	n=13 37 %	<i>Enterococcus faecalis</i>	n=3 30 %
<i>Enterococcus faecalis</i>	n=14 25 %	<i>Candida spp.</i>	n=6 18 %	<i>Gardnerella vaginalis</i>	n=2 20 %
<i>Chlamydia trachomatis</i>	n=13 23 %	<i>Enterococcus faecalis</i>	n=5 15 %	<i>Escherichia coli</i>	n=2 20 %
<i>Ureaplasma spp.</i>	n=5 9 %	Chronic cervicitis	n=4 12 %	<i>Enterobacter aerogenes+ Leptothrix</i>	n=1 10 %
<i>Escherichia coli</i>	n=5 9 %	<i>Gardnerella vaginalis</i>	n=3 9 %		
<i>Staphylococcus aureus</i>	n=2 4 %	<i>Ureaplasma spp.</i>	n=2 6 %	<i>Ureaplasma spp.</i>	n=1 10 %
<i>Mycoplasma genitalium</i>	n=1 1.5 %				
<i>Mycoplasma hominis+ Enterobacter aerogenes</i>	n=1 1.5 %	<i>Streptococcus agalactiae+ Enterobacter aerogenes</i>	n=1 3 %	<i>Candida spp.</i>	n=1 10 %

Analysis of microbiota in the urogenital tract of patients with a deficiency in humoral immunity indicated the following microorganisms were present: *Candida spp.* in 15 (27 %), *E. faecalis* – 14 (25 %), *C. trachomatis* –

13 (23 %), *E. coli* – 5 (9 %), *U. spp.* – 5 (9 %), *St. aureus* – 2 (4 %), *M. genitalium* – 1 (1.5 %), and *E. aerogenes* + *M. hominis* – 1 (1.5 %). Analysis of microbiota in the urogenital tract of patients with admixed type ID had the following microorganisms: *E. faecalis* – 3 (30 %), *G. vaginalis* – 2 (20 %), *E. coli* – 2 (20 %), *U. spp.* – 1 (10 %), *Candida spp.* – 1 (10 %), and *E. aerogenes* + *Leptothrix* – 1 (10 %).

In 23 patients (19 %) with normal levels of immunity with microflora in the urogenital tract developed aerobic vaginitis – 17 (74 %), chronic cervicitis – 7 (30 %), or candidosis vulvovaginitis – 4 (17 %).

Ureaplasma spp. was found in all ID groups and its quantitative assessment was not higher than 10^4 , and indicated moderate signs of PID. Patients with humoral ID did not have *E. faecalis*, but it was found in those with cellular ID in 6 (18 %) or admixed type – 5 (15 %), and was found in all cases of PID. Patients with B-type ID had *C. trachomatis* in 13 (23 %), *E. coli* – 5 (9 %), *M. genitalium* – 1 (2 %), *M. hominis* – 1 (2 %), and *St. aureus* – 1 (2 %). *C. trachomatis* was not noted in patients cellular or admixed type ID.

Conclusions. Of 100 (81 %) out-patient women with PID 46 % had B-type, 27 % had T-type, and 8 % had admixed type. Patients with T-type ID had moderate clinical symptoms, whereas patients with humoral or admixed type ID developed PID symptoms. Depending on the ID type, the type of microorganisms in the microbiota of the urogenital tract differed significantly, especially in those with B-type or admixed type. Patients with humoral ID did not have *E. faecalis*. Patients with B-type ID commonly had *C. trachomatis* and *E. coli*.

Disclosures:

The authors declare no conflict of interest.

Acknowledgment. We thank Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

References

- Khryanin A. A., Reshetnikov O. V. Rational therapy of combined urogenital infections: analysis of free trends. *Pharmateka*. 2016;12:29-36.
- Kolesnichenko A. A. Inflammatory diseases of the uterine appendages: what's new? *The young scientist*. 2016;22 (1):4-17. <https://moluch.ru/archive/126/35084/>
- Petrov Y. A. Aspects of microbiological and immune diagnosis of chronic endometritis. *Modern problems of science and education*. 2016;4:9-10. <https://doi.org/10.1177/1933719113508817>
- Dikke G. B. Polimikrobnnye associations in the etiology of inflammatory diseases of the genital organs in women. *Obstetrics and Gynecology*. 2017;6:151-158. <https://doi.org/10.1856/aig.2017.6.151-8>
- Obstetrics and gynecology. Clinical recommendations. Edited by Serov V. N., Sukhikh G. T. 4th edition. Moscow: GEOTAR-Media. 2014;1011.
- Shirokova D. V., Kalinina E. A., Polina M. L., Petrov Yu. A. Morphofunctional variability of the endometrium as a basis for differentiated infertility treatment. *Modern problems of science and education*. 2015;6:270.
- Schindlbeck C., Schindlbeck D., Dziura, Mylonas I. Diagnosis of pelvic inflammatory disease (PID): intraoperative findings and comparison of vaginal and intra-abdominal cultures. *Arch. Gynecol. Obstet.* 2014;289(6):1263-1269. <https://doi.org/10.1007/s00404-014-3150-7>
- Sharma H., Tal R., Clark N. A. [et al.] Microbiota and pelvic inflammatory disease. *Semin. Reprod. Med.* 2014;32(1):43-49. <https://doi.org/10.1055/s-0033-1361822>
- Kutsenko I. I., Kravtsova E. I., Musolyants R. A., Nazarenko E. I. Peculiarities of the development of chronic pelvic pain related components in peritoneal endometriosis. *Medical News of North Caucasus*. 2016;11(2):189-191. <https://doi.org/10.14300/mnnc.2016.11033>
- Workowski K. A., Berman S. Sexually transmitted diseases treatment guidelines. *Morbidity and Mortality Weekly Report*. 2010;59(12):63-67.
- Pitirimova L. N., Zagorodnaya E. A., Gumilevsky B. Yu. Features of allelic polymorphism of genes of interleukins and cytokine balance of women with miscarriages. *Obstetrics and gynecology*. 2014;3:33-38. (In Russ.).
- Tetelyutina F. K., Kopieva O. V. Possibilities of immune correction in chronic inflammatory diseases of pelvic organs. *Modern problems of science and education*. 2015;1(1):1370-1371. Available at: <https://www.science-education.ru/ru/article/view?id=18247>.
- Murashko A. V., Murashko A. A. Modern approaches to the therapy of PID. *Medical advice*. 2014;9:103-105. <https://doi.org/10.21518/2079-701X-2014-9-103-105>
- Sweet R. L. Pelvic Inflammatory Disease: Current Concepts of Diagnosis and Management. *Curr. Infect. Dis. Rep.* 2012;4:194-203. <https://doi.org/10.18203/2320-1770.ijrcog20150097>
- Prilepskaya V. N., Bebnova T. N. The effectiveness of Galovit immunomodulator in the treatment of inflammatory diseases of the pelvic organs. *Breast cancer*. 2013;1:31.
- Utkin E. V., Kulavsky V. A. Inflammatory diseases of the pelvic organs in women. Moscow: GEOTAR-Media, 2015; 112. [https://doi.org/10.1016/S0140-6736\(69\)90749-1](https://doi.org/10.1016/S0140-6736(69)90749-1)

About authors:

Baturin Vladimir Aleksandrovich, DMSc, Professor, Head of Department for Clinical Pharmacology with Course of Post-Graduate and Additional Training. Head Physician of the Center for Clinical Pharmacology and Pharmacotherapy;
tel.: +79054901856; e-mail: prof.baturin@gmail.com

Boshyan Roberta Ovikovna, Gynecologist of the Center for Clinical Pharmacology and Pharmacotherapy. Graduate student of the Department for Clinical Pharmacology with Course of Post-Graduate and Additional Training; tel.: +79624598090; e-mail: ms.roberta@inbox.ru

© Group of authors, 2018

UDC 614.38:616.9 (470)

DOI – <https://doi.org/10.14300/mnnc.2018.13088>

ISSN – 2073-8137

COMPREHENSIVE RISK ASSESSMENT OF EPIDEMIOLOGICAL SITUATION AGGRAVATION AS REGARDS NATURAL-FOCAL INFECTIOUS DISEASES DURING THE XXI FIFA WORLD CUP IN THE RUSSIAN FEDERATION IN 2018

Udovichenko S. K.¹, Ivanova A. V.¹, Toporkov V. P.¹, Kouklev E. V.¹, Kuznetsov A. A.¹, Tarasov M. A.², Sludsky A. A.¹, Boiko A. V.¹

¹ Russian Research Anti-Plague Institute «Microbe», Saratov, Russian Federation

² Center of Hygiene and Epidemiology in the Saratov Region, Russian Federation

КОМПЛЕКСНАЯ ОЦЕНКА РИСКОВ ОСЛОЖНЕНИЯ ЭПИДЕМИОЛОГИЧЕСКОЙ ОБСТАНОВКИ ПО ПРИРОДНО-ОЧАГОВЫМ ИНФЕКЦИОННЫМ БОЛЕЗНЯМ ПРИ ПРОВЕДЕНИИ XXI ЧЕМПИОНАТА МИРА ПО ФУТБОЛУ В РОССИЙСКОЙ ФЕДЕРАЦИИ В 2018 г.

С. К. Удовиченко¹, А. В. Иванова¹, В. П. Топорков¹, Е. В. Куклев¹, А. А. Кузнецов¹, М. А. Тарасов², А. А. Слудский¹, А. В. Бойко¹

¹ Российский научно-исследовательский противочумный институт «Микроб», Саратов, Российская Федерация

² Центр гигиены и эпидемиологии Саратовской области, Российская Федерация

The paper identifies major epidemiological threats associated with holding the XXI World Cup in 11 cities of the Russian Federation. Epidemiological conjuncture of enzootic natural focal infectious diseases of bacterial and viral etiology registered in FWC-2018 host-entities was analyzed from the standpoint of epidemiological risk. It is shown that hemorrhagic fever with renal syndrome was the most significant internal threat for the Republic of Tatarstan and Mordovia, Samara and Nizhny Novgorod Regions, Ixodidae tick-borne borreliosis – for Moscow, Saint Petersburg, and Sverdlovsk Region. The average risk of tick-borne viral encephalitis was determined for the Sverdlovsk Region. During the World Cup-2018, the probability of Crimean hemorrhagic fever occurrence existed in the Rostov Region (medium risk), West Nile fever – in Volgograd Region (medium risk). A clearer understanding of the epidemiological threats picture enabled us to formulate better strategies and possible to scientifically substantiate a set of preventive measures in areas of epidemiological risk.

Keywords: *natural-focal infectious diseases, epidemiological risk, comprehensive risk assessment, FIFA World Cup-2018*

Определены эпидемиологические угрозы, сопряженные с проведением в 11 городах Российской Федерации XXI Чемпионата мира по футболу (ЧМ-2018). Проведен анализ эпидемиологической конъюнктуры по эндемичным (энзоотичным) природно-очаговым инфекционным болезням бактериальной и вирусной этиологии в принимающих ЧМ-2018 субъектах. Показано, что геморрагическая лихорадка с почечным синдромом являлась наиболее значимой внутренней угрозой для республик Татарстан и Мордовия, Самарской и Нижегородской областей; иксодовые клещевые боррелиозы – для Москвы, Санкт-Петербурга и Свердловской области. Для клещевого вирусного энцефалита средний риск определен для Свердловской области. В период проведения ЧМ-2018 вероятность возникновения случаев заболевания крымской геморрагической лихорадкой существовала в Ростовской области (средний риск), лихорадкой Западного Нила – Волгоградской области (средний риск). Таким образом, дифференцирование и ранжирование внутренних эпидемиологических угроз по степени опасности позволило обосновать комплекс профилактических мероприятий в зонах эпидемиологического риска.

Ключевые слова: *природно-очаговые инфекционные болезни, эпидемиологический риск, комплексная оценка риска, ЧМ-2018*