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The state of the vaginal microbiota in internally displaced women with hyperproliferative uterine diseases in the context of military aggression in Ukraine after treatment and prevention measures

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Powerful stressful factors during armed conflict can lead to disruption of adaptive systems, causing significant negative changes in the state of immunity and the functioning of endocrine organs (1).

Stress changes the production of cytokines that regulate the function of the hypothalamic-pituitary system (2). Cytokines alter the secretion of corticosteroids, glucocorticoids, somatotrophic, follicle-stimulating, luteinizing hormones, and prolactin. Psycho-emotional stress contributes to the activation of persistent viral and bacterial infections and, in particular, may be accompanied by a violation of the microecology of the genital organs (3).

It has been established that under stress conditions, pathological changes in the vaginal microbiome are formed. Stress-related maladaptation can be a background against which dysbiotic processes are formed and the ratio of associates in the genital tract microbiocenosis changes (4).

Changes in the endocrine system, immunity, and genital dysbiosis may play a role in the pathogenesis of benign tumors

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in women exposed to military aggression in Ukraine (5).

In order to assess the species and quantitative composition of the vaginal microbiota in women with hyperproliferative uterine diseases in the context of military aggression in Ukraine, a bacteriological examination of 30 internally displaced women before and after treatment was performed. The data obtained from the examination of 30 healthy women before the outbreak of hostilities in Ukraine were used as a control.

Cultures were carried out by the method of sectoral sowing on dense nutrient differential diagnostic media, which allows to determine the degree of microbial contamination and the possible spectrum of facultative aerobic and anaerobic microflora.

Identification of the isolated strains was performed on an automatic bacteriological analyzer Vitek 2 Compact 15 (bioMérieux, France).

Statistical processing of the obtained research results was performed using Microsoft Excel computer packages "Data Analysis".

Evaluation of the vaginal contents by bacterioscopy in internally displaced women before treatment shows that in 26.7% of patients, microbiota disorders correspond to the state of bacterial vaginosis, as well as an increase in the content of *Candida* fungi. In women, who were internally displaced, the cultural method revealed a tendency to increase the frequency and quantitative indicators in the vaginal microflora of obligate anaerobes *Gardnerella vaginalis* (23.3%) and *Atopobium* spp. (26.7%), *Paraclostridium bifermentans* (36.7%), *Clostridium novyi* (33.3%), and *Fusobacterium* spp. (16.7%) in the amount of $>lg\ 4.0$ CFU/ml. The vaginal microbiota of patients in this group was characterized by an increase in the level of *S. agalactiae* (20.0%), *S. epidermidis* gem + (16.7%) and enterobacteria (10%–13%), in an amount exceeding the diagnostic level ($>lg\ 4.0$ CFU/ml).

In 86.7% of internally displaced women, the microflora isolated from the vagina was in 2- or 4-component associations, which included *Candida* fungi with a significant frequency ($lg\ 4.8$ CFU/ml). In the composition of the vaginal microflora, 73.3% of the examined women also had a deficiency of *Lactobacillus* spp. The quantitative indicators of the lactoflora were $lg\ 3.8$ CFU/ml.

We have studied vaginal discharge after treatment by

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bacterioscopic method in internally displaced women. The obtained results indicate a decrease in dysbiosis of the vaginal microbiota. The state of the vaginal microbiota after treatment was characterized by a low content of vaginosis-associated microflora in 13.3% of patients and a moderate content of other gram-positive and gram-negative microflora. The frequency of fungi detection tended to decrease. The presence of *Lactobacillus* has increased.

The results of the bacteriological examination of patients indicate that after the treatment, the frequency of vaginal discharge of Firmicutes (*S. aureus* – 6.7%, *S. epidermidis* gem+ – 6.7%) and *Candida* fungi (10%) significantly decreased in internally displaced women. The quantitative indicators of these types of microorganisms statistically significantly decreased and amounted to lg 2.8–lg 3.0 CFU/ml ($p < 0.05$). Quantitative indicators of vaginal contamination with *Candida* fungi were also normalized after treatment (lg 3.4 CFU/ml).

Quantitative analysis of the composition of the vaginal microflora in internally displaced women after treatment indicates positive changes in the registration of enterobacteria. Thus, the most positive dynamics were observed in the cultures of *E. coli* (lg 3.0 CFU/ml), *Enterobacter* spp. (lg 3.4 CFU/ml), and *Klebsiella* spp.

In women, who were internally displaced, after treatment, there was an increase in the qualitative (93.3%) and quantitative (lg 6.0 CFU/ml) indicators of *Lactobacillus* spp.

Against the background of the treatment, an improvement in the inoculation of potentially pathogenic species of obligate anaerobic microflora was recorded in internally displaced women. Thus, the frequency of sowing of *Paraclostridium bifermentans* decreased by 20%, *Clostridium novyi* by 16.7%, *Fusobacterium* spp. by 10%. The quantitative indicators of the inoculation of these anaerobic microorganisms were also normalized (lg 2.5 CFU/ml – lg 3.5 CFU/ml).

The results of the examination of internally displaced women after treatment indicate a decrease in the frequency of detection of vaginosis-associated microflora (*Gardnerella vaginalis* –13.3%, *Atopobium vaginae* –10%). Their quantitative level of sowing reached the normal range and amounted to lg 3.4 CFU/ml – lg 3.5 CFU/ml.

After treatment, the frequency of registration of associative forms of vaginal bacterial contamination

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decreased in the examined women: three-component associations - 26.4% , two-component - 16.7%.

Thus, the results of the examination of internally displaced women after treatment indicate positive changes in the genital tract microbiota, which consisted of a decrease in the qualitative and quantitative indicators of vaginal contamination with potentially pathogenic aerobic and anaerobic microflora, a decrease in the frequency of bacterial-fungal associations, and the restoration of quantitative indicators of normal microflora (*Lactobacillus* spp.).

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