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CLINICAL ANALYSIS OF TREATMENT OUTCOMES IN WOMEN WITH INFERTILITY AGAINST THE BACKGROUND OF POLYCYSTIC OVARIES SYNDROME AND CHRONIC ENDOMETRITIS

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Abstract

Introduction. In women with polycystic ovary syndrome, infertility is a serious and urgent problem, which is caused not only by anovulatory menstrual cycles [1], but also by changes in the histological structure of the endometrium, which adversely affects embryo implantation and subsequent pregnancy. Thus, chronic endometritis and polycystic ovary syndrome are among the causative factors of repeated unsuccessful embryo implantation in assisted reproductive technology (ART) programs [2-3].

Aim of the study. To analyze the clinical outcomes of patients with infertility against the background of PCOS and chronic endometritis (CE) in ART protocols, depending on the treatment scheme.

Materials, methods and their discussion. The study included 140 patients with infertility against the background of PCOS and CE. Study group I comprised 43 patients with PCOS and CE, who were offered conventional treatment for chronic endometritis. Study group II comprised 63 patients with PCOS and CE, who were treated using a modified scheme that additionally included alpha-lipoic acid, endometrial plasma therapy and lipid

infusions (to reduce cytotoxicity) on the day of frozen embryo transfer (FET). In both groups, delayed embryo transfer was performed in cryocycles after 2–4 months. Cryoprotocols were performed using HRT and in the NC. The control group comprised 35 women with infertility due to male causes.

Results and discussion. Comparing causes of infertility in the patients with PCOS and CE, we found no significant differences between the study groups. There was no significant difference between the study groups and the control group in the frequency of surgical interventions in the anamnesis of the patients. It should be noted, however, that the structure of surgical interventions in the first and second study groups was dominated by the IUDs (respectively, in 18.60% and 19.35% of the cases) relative to the control group (2.86%). The anamnesis records of the patients show no significant differences between both study groups in the frequency of scraping of the uterine cavity walls and laparoscopy, and these values do not significantly differ from the control group. Hysteroscopy was performed in 13.95% of patients of group I and 12.90% of group II, which was higher compared to the control group (8.57%). Laparotomies comprised the least frequent type of intervention in the anamnesis of patients in both study groups and the control group. The clinical picture of chronic inflammatory disorders in patients of the study groups included asymptomatic course, chronic pelvic pain, menstrual and sexual dysfunction, and vaginal discharge. In addition to menstrual dysfunction, the patients with comorbid PCOS and CE of the study groups I and II had high frequency of vaginal discharge (respectively, in 62.79% and 56.45% of the patients) and chronic pelvic pain (30.23% and 33.87%, respectively), which was significantly higher than the results of the control group. Notably, in patients with infertility against the background of the combined PCOS and CE (comprising study groups I and II), the asymptomatic course of chronic inflammatory disorders was significantly more timely compared to the control group ($p = 0.025$).

Conclusions. Results of this study indicate that patients suffering scleropolycystosis are prone to ascending infection due to the dysregulation of the vaginal microbial environment, which ultimately becomes the causative factor of chronic endometritis. The CE process has an extremely negative effect on embryo implantation and subsequent pregnancy. Endometritis can be linked to PCOS through metabolic and endocrine pathologies.

Keywords. PCOS; chronic endometritis; infertility; endometrium; histology; anovulation; hysteroscopy; PRP-therapy of the endometrium; lipid infusions; cryocycle; NC; ET; HRT; ART; COS.

Introduction. Today, infertility is a serious and urgent problem in women with polycystic ovary syndrome; among its causes is not only anovulatory menstrual cycle [1], but also changes to the histological structure of the endometrium, which results in a negative impact on embryo implantation and subsequent pregnancy. Both chronic endometritis and polycystic ovary syndrome are among well known causative factors of repeated unsuccessful embryo implantations in assisted reproductive technology (ART) programs [2-3]. Polycystic ovary syndrome is often associated not only with infertility, but also with a high risk of miscarriage due to metabolic disorder (high BMI, insulin resistance) and endocrine dysregulation (luteal phase insufficiency, hyperandrogenism, thyroid dysfunction) [4]. All these factors deserve consideration when choosing the optimal approach for the diagnosis and treatment of patients with infertility against the background of PCOS in ART programs. Recent studies have established the relationship between endometrial pathology and scleropolycystosis. A study of patients with infertility against the background of PCOS by Sedigheh Amooee et al. [1], compared hysteroscopic and histological assessments of the endometrium depending on the hormonal status, BMI, duration of infertility, and metabolic syndrome. The main changes identified during the study were: endometrial structure disorders (mismatch with the MC phase), and endometrial hyperplastic processes (polyps and glandular cystic hyperplasia; however, no cancer changes were observed. Additionally, recent research indicates that chronic inflammatory processes (such as chronic endometritis) of the endometrium in patients with scleropolycystosis may be associated with obesity, insulin resistance and hyperandrogenism [5].

Chronic endometritis is a chronic slow-developing inflammatory process of the uterine mucosa, which is manifested by impaired blood supply, poor detachment of the endometrium left over from the previous menstrual cycle, edema of the stroma, and results in hyperplastic processes of the endometrium which, consequently, can lead to premature birth. The main biomarkers for the diagnosis of CE are the inflammation markers detected by immunohistochemistry of endometrial biopsy (+ CD 138) or diagnostic hysteroscopy. However, the informativeness of endometrial biopsy results is relatively low, only 27.1% [6]. This is because of the so-called "blind" examination of the endometrium without prior visual assessment of the uterine cavity, which is only possible through diagnostic hysteroscopy. Therefore, hysteroscopy increases the sensitivity and accuracy of the CE diagnosis [7]. Hysteroscopy allows to detect micropolyps, hyperemia (the strawberry appearance), stroma edema and hyperplasia [5].

To date, the relationship between the occurrence of chronic endometritis against the background of PCOS is insufficiently studied, which, accordingly, requires further research.

Aim of the study was to analyze clinical data of patients with infertility against the background of PCOS and chronic endometritis depending on the treatment approach in ART protocols.

Materials, methods and their discussion

The study involved 140 patients with infertility comorbid with PCOS and chronic endometritis who underwent infertility treatment using ART.

The patients were divided into three groups depending on the cause of infertility and treatment approach.

The first clinical group comprised 43 women (30.71%) with infertility against the background of PCOS and chronic endometritis, who were offered conventional treatment for chronic endometritis and delayed embryo transfer in cryocycles after 2-4 months with hormone replacement therapy (HRT) in the natural cycle (NC).

The second clinical group comprised 62 women (44.29%) with endocrine infertility against the background of PCOS and chronic endometritis. The patients received pre-pregnancy treatment with *FT 500 Plus* and *Pelvidol* for 2-4 months in IVF protocols. These preparations were prescribed to obtain good quality oocytes and embryos, normalize the menstrual cycle and as a part of treatment for chronic endometritis. The patients underwent frozen embryo transfer. The cryocycles included a modified treatment scheme with alpha-lipoic acid, endometrial plasma therapy, and lipid infusions (to reduce cytotoxicity) on the day of cryoET. Cryoprotocols were performed using HRT and in the NC.

The control group (25.0%) comprised 35 women with infertility due to male-associated causes.

Results and discussion

The mean age of women with infertility against the background of PCOS and CE who received standard treatment was 32.07 ± 4.33 years, and the age of patients with PCOS and CE who received modified treatment as well as patients in the control group was not significantly different (30.97 ± 4.00 , $p = 0.376$ and 31.74 ± 4.25 , $p = 0.937$, respectively). The age of the women included in the study ranged from 26 to 36 years. Body mass index (BMI) in the first study group was 27.83 ± 5.96 kg / m² and did not significantly differ from this index of the second study group (28.09 ± 6.15 , $p = 0.974$) and control group (24.96 ± 5.72 , $p = 0.888$). However, in the second study group, which comprised patients with PCOS and CE who received a modified treatment approach, BMI was significantly higher compared to the

control group ($p = 0.035$). In the patients of the first group normal body weight was identified in 16 women (37.21%), overweight in 13 women (30.23%), 1st stage obesity in 6 women (13.95%), 2nd stage obesity in 5 women (11.63%) and 3rd stage obesity in 3 women (6.98%). In the second study group, the respective values were, 24 women (38.71%), 18 women (29.03%), 7 women (11.29%), 9 women (14, 52%) and 4 women (6.45%).

Among the patients with infertility included in the study, the majority 65 (46.43%) were unqualified employees, 54 (38.57%) qualified employees, and 21 (15.00%) homemakers and unemployed, Fig. 1. Notably, the groups did not significantly differ in regards to the social status of the patients.



Fig. 1. Social status of women involved in the study

The duration of infertility in patients diagnosed with infertility against the background of PCOS and CE who received standard treatment, was 6.00 ± 3.29 years, and did not significantly differ from the duration of infertility in patients with PCOS and CE who received modified treatment (5.84 ± 3.56 , $p = 0.971$), as well as control group (5.34 ± 3.69 , $p = 0.690$).

The patients with polycystic ovary syndrome and chronic endometritis had similar frequencies of the types of infertility between the first and second study groups: primary infertility was diagnosed in 27.91% and 24.19% and secondary infertility in 72.09% and 75.81%, respectively, of the patients in each group. These values were not significantly different from the control group (Table 1).

Analysis of the number of sexual partners in patients with infertility against the background of polycystic ovary syndrome and chronic endometritis showed that the majority of patients in the study groups had 3 to 5 sexual partners, while in the control group, the majority had up to 3 sexual partners (Table 2).

Table 1. - Frequency of types of infertility in the patients with polycystic ovary syndrome and chronic endometritis

Infertility type	First group (n = 43), standard treatment		Second group (n = 62), modified treatment		Control group (n = 35), male-caused infertility		χ^2 , p
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Primary infertility	12	27.91	15	24.19	15	42.86	$\chi^2= 3.84$; p = 0.147
Secondary infertility	31	72.09	47	75.81	20	57.14	

Table 2 - Number of sexual partners in patients with infertility against the background of polycystic ovary syndrome and chronic endometritis

Number of sexual partners	First group (n = 43), standard treatment		Second group (n = 62), modified treatment		Control group (n = 35), male-caused infertility		χ^2 , p
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Up to 3	10	23.26	13	20.97	15	42.86	$\chi^2= 6,04$; p = 0.117
3 to 5	18	41.86	27	43.55	12	34.29	
6 and more	15	34.88	22	35.48	8	22.86	

There were no significant differences between the study groups of the patients with PCOS and CE in regards to the causes of infertility. In particular, in patients of the first group (n = 43), tubal-peritoneal cause was diagnosed in 14 women, male-linked causes in 11 women, and a combination of tubal-peritoneal and male-linked causes in 12 women, while in patients of the second group (with PCOS and CE receiving modified treatment, n = 62) was these causative factors were diagnosed found in 23, 8 and 11 women, respectively (Fig. 2).

Analysis of the anamnesis data of women with infertility against the background of PCOS and CE involved in the study, indicates previous attempts to stimulate ovulation with using *Clostilbegyt* (50 mg Clomiphene-citrat), intrauterine insemination and *in vitro* fertilization (IVF). Thus, women in the first group were more likely to undergo stimulated ovulation with *Clostilbegyt* (p = 0.007) and IVF (p <0.001) and women in the second group intrauterine insemination (p <0.001) and IVF (p <0.001), compared to the control group. It should be noted that in patients of the first group ovulation stimulations with *Clostilbegyt* were significantly more frequent compared to the second group, while the patients of the second group had more frequent intrauterine insemination procedures compared to those in the first group (Table 3).

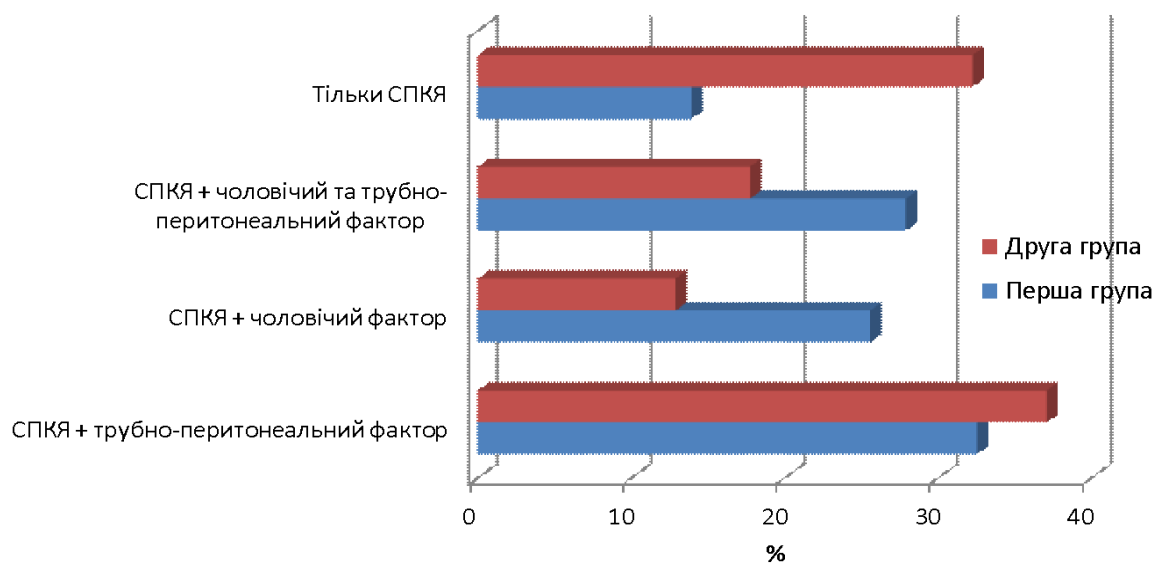


Fig. 2. Infertility causes in the patients with polycystic ovary syndrome and chronic endometritis

Table 3. - Assisted reproductive technology methods in the anamnesis of patients with infertility against the background of polycystic ovary syndrome and chronic endometritis

ART method	First group (n = 43), standard treatment	Second group (n = 62), modified treatment	Control group (n = 35), male-caused infertility	p
Stimulation of ovulation with <i>Clostilbegyt</i>	2.58 ± 1.50	2.19 ± 1.40	1.66 ± 1.03	$g_{1-2} = 0.317 *$; $p_{1-3} = 0.007 *$; $p_{2-3} = 0,145$
IUI (intrauterine insemination) in the anamnesis of	0.84 ± 1,09	1.92 ± 1.86	0.69 ± 0.80	$g_{1-2} < 0,001 *$; $p_{1-3} = 0.888$; $p_{2-3} < 0,001 *$
IVF (in vitro fertilization)	0.51 ± 0.70	0.40 ± 0.73	2.26 ± 1.52	$p_{1-2} = 0.843$; $p_{1-3} < 0,001 *$; $p_{2-3} < 0,001 *$

Note. * - statistically significant result.

Of ART methods used by the patients, ICSI process was clearly predominant in the first and second study groups, as well as in the control group (90.70%, 88.71% and 91.43%, respectively, Table 4).

During embryo transfer in the first and second study groups, as well as in the control group, 2 embryos were transferred in 65.12%, 66.13% and 62.86% of the cases, respectively. It should be noted that in 100% of women with infertility against the background of comorbid PCOS and CE, the embryo transfer was performed in a cryocycle, while in the control group

34.29% of women underwent embryo transfer in a natural cycle, which is significantly different from both study groups. Preimplantation genetic diagnosis was performed in 13.95% of cases in the first group, in 13.95% in the second group and in 11.43% in the control group (Table 5).

Table 4. - ART procedures used by the patients with infertility against the background of polycystic ovary syndrome and a history of chronic endometritis

ART procedures	First group (n = 43), standard treatment		Second group (n = 62), modified treatment		Control group (n = 35), male-caused infertility		χ^2 , p
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
IVF	4	9.30	7	11.29	3	8.57	$\chi^2= 0.22$; p = 0.897
ICSI	39	90.70	55	88.71	32	91.43	$\chi^2= 0.22$; p = 0.897
TESA	3	6.98	3	4.84	4	11.43	$\chi^2= 1.47$; p = 0.480

Table 5. - Characteristics of ART methods in patients with infertility against the background of polycystic ovary syndrome and a history of chronic endometritis

ART methods	First group (n = 43), standard treatment		Second group (n = 62), modified treatment		Control group (n = 35), male-caused infertility		χ^2 , p
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Number of embryos used in ET							
1	15	34.88	21	33.87	13	37.14	$\chi^2= 0.11$; p = 0.949
2	28	65.12	41	66.13	22	62.86	
Natural cycle	0	0	0	0	12	34.29	$\chi^2= 39.38$; p <0.001 *
Cryocycle	43	100.00	62	100.00	23	65.71	
Embryo PGD							
0	37	86.05	37	86.05	31	88.57	$\chi^2= 0.19$; p = 0.910
1	6	13.95	6	13.95	4	11.43	
Note. * - statistically significant result.							

Comparison of the frequency of somatic pathology between the study and control group shows that a significantly higher number of patients with PCOS and CE of the first and second study groups were diagnosed with the urinary system diseases compared to the control group (p <0.001). Other comorbidities, such as metabolic syndrome, were also more frequent

in the study groups, however, their frequency did not reach a significance threshold when compared to the control group (Fig. 3).

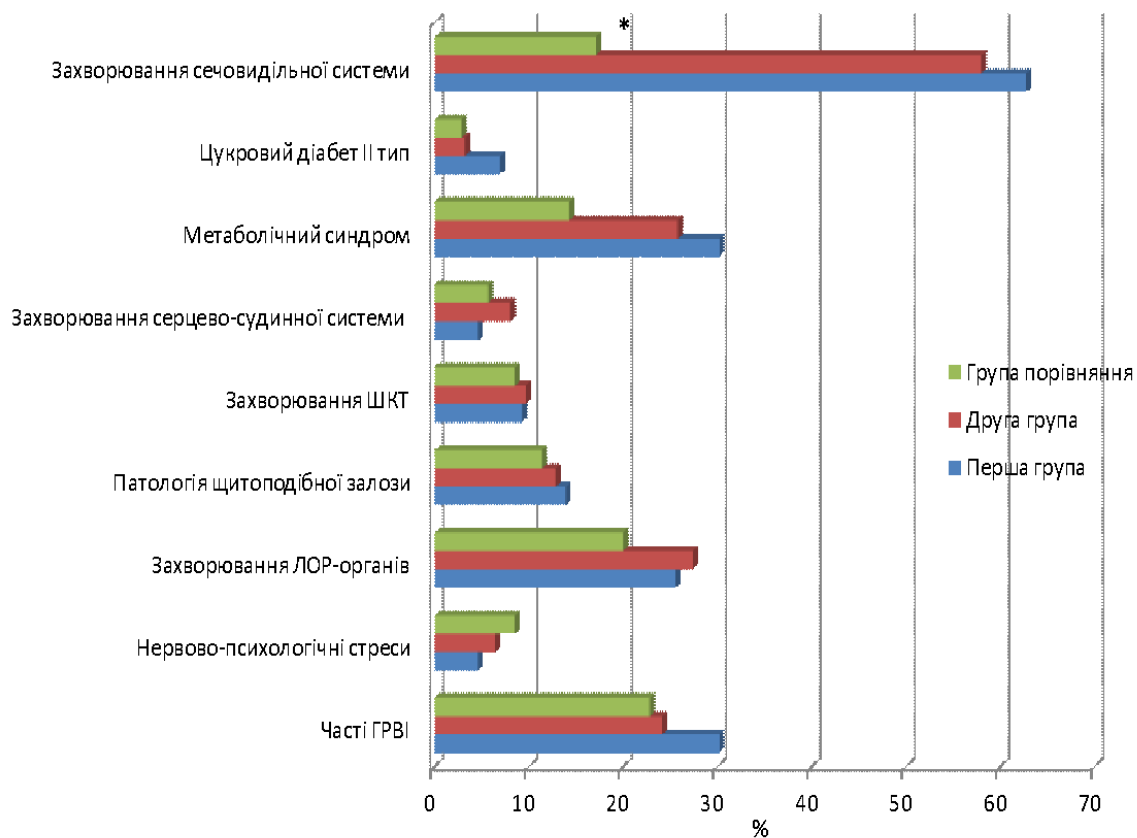


Fig. 3. Frequency of somatic pathology in patients with infertility against the background of polycystic ovary syndrome and chronic endometriosis (* - statistically significant pairwise comparisons)

Taking into account the high incidence of urinary tract pathology, we further analyzed the structure of these diseases in patients of the first and second study groups and found the predominance of cystitis (32.56% and 25.81%, respectively), chronic salpingo-oophoritis (34.88% and 35.48%, respectively), colpitis of various etiologies (39.53% and 45.16%, respectively) and bacterial vaginosis (44.19% and 40.32%, respectively) compared to the control group (Table 6).

Among the causative agents of the vaginal infections in patients with combined PCOS and CE of the first and second study groups, significantly more frequently compared to the control group were diagnosed *Chlamydia trachomatis* (25.58% and 30.65%, respectively), *Candida albicans* (44.19% and 38.71%, respectively) and *Escherichia coli* (20.93% and 22.58% respectively, Table 7).

Table 6. - Frequency of urogenital diseases in patients with infertility against the background of polycystic ovary syndrome and chronic endometritis

Disease	First group (n = 43), standard treatment		Second group (n = 62), modified treatment		Control group (n = 35), male-caused infertility		χ^2 , p
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Glomerulonephritis	0	0	3	4.84	1	2.86	$\chi^2=2.14$; p=0,343
Pyelonephritis	4	9.30	7	11.29	1	2.86	$\chi^2=2.07$; p=0.355
Cystitis	14	32.56	16	25.81	2	5.71	$\chi^2=8.43$; p=0.015*
Urethritis	9	20,93	10	16.13	2	5.71	$\chi^2=3.61$; p=0.164
Bartolinite	2	4.65	3	4.84	3	8.57	$\chi^2=0.71$; p=0.702
Hydrosalpinx	5	11.63	12	19.35	1	2.86	$\chi^2=5.52$; p=0.063
Chronic salpingo-oophoritis	15	34.88	22	35.48	4	11.43	$\chi^2=7.19$; p=0.027*
Colpitis (of various etiologies)	17	39.53	28	45.16	7	20.00	$\chi^2=6.22$; p=0.045*
Bacterial vaginosis	19	44.19	25	40.32	6	17.14	$\chi^2=7.18$; p=0.028*

Note. * - statistically significant result.

Analysis of the frequency of surgical interventions in the anamnesis of women of the study and control groups showed no significant differences between the groups. It is worth noting that in the structure of operative interventions in the first and second study groups the IUDs prevailed (18.60% and 19.35%, respectively) compared to the control group (2.86% of the cases). Proportion of the patients in the first and second study groups with a record of scraping of tissue from the walls of the uterus and laparoscopy in the anamnesis was almost equal and did not significantly differ from the control group. Hysteroscopy was found in the medical history of 13.95% of patients in the first group, and 12.90% in the second group, which was higher than in the control group (8.57% of the patients). Laparotomies were the least represented surgical interventions in the anamnesis of women in both study and control groups (Fig. 4).

Table 7. - Frequency diagnosed infectious agents of the vagina in patients with infertility against the background of polycystic ovary syndrome and chronic endometritis

Causative agents of vaginal infections	First group (n = 43), standard treatment		Second group (n = 62), modified treatment		Control group (n = 35), male-caused infertility		χ^2 , p
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
<i>Ureaplasma urealyticum, parvum</i>	12	27.91	18	29.03	4	11.43	$\chi^2=4.21$; p=0.122
<i>Mycoplasma hominis, genitalium</i>	6	13.95	9	14.52	3	8.57	$\chi^2=0.77$; p=0.680
<i>Chlamydia trachomatis</i>	11	25.58	19	30.65	2	5.71	$\chi^2=8.15$; p=0.017*
<i>Candida albicans</i>	19	44.19	24	38.71	6	17.14	$\chi^2=6.88$; p=0,032*
<i>Escherichia coli</i>	9	20.93	14	22.58	1	2.86	$\chi^2=6.75$; p=0.034*
<i>Enterococcus faecalis</i>	6	13.95	8	12.90	1	2.86	$\chi^2=3.04$; p=0.219
<i>Gardnerella vaginalis</i>	13	30.23	21	33.87	7	20.00	$\chi^2=2.11$; p=0.349
<i>Proteus sp, Klebsiella sp, S. aureus, S. agalactiae</i>	3	6.98	5	8.06	2	5.71	$\chi^2=0.19$; p=0.910

Note. * - statistically significant result.

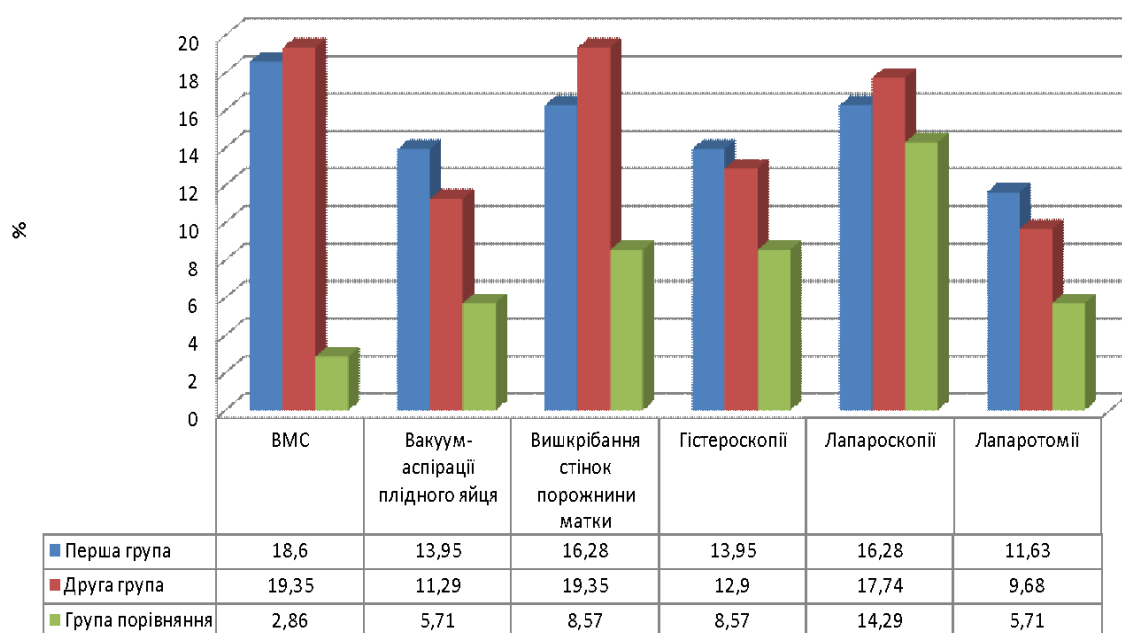


Fig. 4. Frequency of surgical interventions in patients with infertility against the background of polycystic ovary syndrome and chronic endometritis

Analysis of the incidence of gynecological disorders in patients with infertility against the background of polycystic ovary syndrome and chronic endometritis, who received standard and modified treatment, showed a significantly higher percentage of patients with STIs (gonorrhoea, chlamydia, trichomoniasis) in first group, 30.23% and second group, 33.87%, compared to the control group. Notably, there was a high incidence of cervical ectopia among the patients with PCOS and CE of the first and second study groups (Table 8).

Table 8. - Gynecological disorders and their frequency of in patients with infertility against the background of polycystic ovary syndrome and chronic endometritis

Gynecological disorders	First group (n = 43), standard treatment		Second group (n = 62), modified treatment		Control group (n = 35), male-caused infertility		χ^2 , p
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Endometrial hyperplasia	8	18.60	7	11.29	2	5.71	$\chi^2=3.08$; p=0.0214
Endometrial polyp	9	20.93	14	22.58	4	11.43	$\chi^2=1.90$; p=0.388
Uterine leiomyoma	5	11.63	6	9.68	1	2.86	$\chi^2=2.07$; p=0.1356
Follicular cysts	4	9.30	7	11.29	2	5.71	$\chi^2=0.83$; p=0.662
Ectopia of the cervix	11	25.58	18	29.03	3	8.57	$\chi^2=5.57$; p=0.062
STIs (gonorrhoea, chlamydia, trichomoniasis)	13	30.23	21	33.87	2	5.71	$\chi^2=9.95$; p=0.007*

Note. * - statistically significant result.

Among clinical manifestations of chronic inflammatory diseases in patients of the study groups were asymptomatic course, chronic pelvic pain, menstrual cycle disorders, sexual dysfunction, and vaginal discharge. Menstrual disorders occurred with a high frequency in the patients of the first and second study groups (81.40% and 83.87%, respectively), which was significantly higher than the respective frequency of the control group. The patients with comorbidity of PCOS and CE of the first and second study groups, had, in addition to menstrual dysfunction, high frequency of vaginal discharge (in 62.79% and 56.45% of the patients, respectively), chronic pelvic pain (30.23% and 33.87%, respectively), which were significantly higher than the corresponding values of the control group. Notably, chronic inflammatory diseases in patients with infertility against the background of comorbid PCOS

and CE of the first and second study groups, were significantly more likely to have an asymptomatic course, compared with the control group ($p = 0.025$, Table 9).

Table 9. - Chronic inflammatory diseases in patients with infertility against the background of polycystic ovary syndrome and chronic endometritis

Chronic inflammatory diseases	First group (n = 43), standard treatment		Second group (n = 62), modified treatment		Control group (n = 35), male-caused infertility		χ^2 , p
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Asymptomatic course	16	37.21	25	40.32	5	14.29	$\chi^2=7.41$; $p=0.025^*$
Chronic pelvic pain	13	30.23	21	33.87	3	8.57	$\chi^2=8.83$; $p=0.020^*$
Menstrual cycle irregularities	35	81.40	52	83.87	1	2.86	$\chi^2=72.02$; $p<0.001^*$
Sexual dysfunction	9	20.93	14	22.58	2	5.71	$\chi^2=4.74$; $p=0.094$
Vaginal discharge	27	62.79	35	56.45	9	25.71	$\chi^2=12.08$; $p=0.002^*$

Note. * - statistically significant result.

Results of this study indicate a high incidence of the urinary system pathology with a predominance of cystitis, chronic salpingo-oophoritis, colpitis of various etiologies and bacterial vaginosis. Among infectious agents of the vagina, *Chlamydia trachomatis*, *Candida albicans* and *Escherichia coli* were detected with a significantly high frequency. The frequent chronic inflammatory diseases were either clinically manifested by menstrual irregularities, vaginal discharge and chronic pelvic pain, or had an asymptomatic course.

Therefore, patients with scleropolycystosis are prone to ascending infection caused by dysregulation of the microbiome in the vagina, which ultimately is the causative factor of chronic endometritis.

These results allow us to conclude that chronic inflammation has an extremely negative impact on embryo implantation and subsequent pregnancy. The link between endometritis and PCOS is likely related to metabolic and endocrine pathologies.

Conclusions

1. Chronic endometritis is one of the most common causes of embryo implantation disorders and abortions in patients who become pregnant or undergo infertility treatment with ART.

2. The main causative factor of chronic endometritis is an ascending infection (most often caused by *Chlamydia trachomatis*, *Candida albicans* or *Escherichia coli*) and surgery in the uterine cavity (IUD, hysteroscopy, instrumental revision of the uterine cavity).

3. The development of chronic endometritis in patients with infertility against the background of PCOS is most often associated with obesity, insulin resistance and hyperandrogenemia.

4. Chronic endometritis requires current treatment approaches using modified schemes that include endometrial plasma therapy, alpha-lipoic acid and the use of lipid infusions in ART cycles, which ensure shorter duration of the therapy and a positive effect on the receptive function of the endometrium.

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