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## ULTRASOUND AND DOPPLEROMETRIC CHARACTERISTICS OF PELVIC ORGANS IN WOMEN WITH INFERTILITY AND THE HISTORY OF PRENATAL STRESS

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At the stage of selective examination of infertile women with prenatal stress, an ultrasound examination with Doppler examination of blood vessels was performed. The aim of the study was to increase the effectiveness of ultrasound diagnosis of genital changes of infertile women with prenatal stress, depending on the type of infertility treatment. Ultrasound is considered to be a highly informative non-invasive method, helps to establish the presence, location, structure, size of myomas, ovarian cysts, to identify concomitant pathology of the pelvic organs. Prospects for further development: the identified features of the pelvic organs will increase the frequency of natural fertile cycles and the efficiency of fertilization in *in vitro* fertilization programs.

**Key words:** infertility, stress, Doppler examination, uterus, ovaries, reproduction.

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## УЛЬТРАЗВУКОВА ТА ДОПЛЕРОМЕТРИЧНА ХАРАКТЕРИСТИКА ОРГАНІВ МАЛОГО ТАЗУ ЖІНОК З БЕЗПЛІДДЯМ ТА ПЕРЕНЕСЕНИМ ПРЕНАТАЛЬНИМ СТРЕСОМ

На етапі селективного обстеження безплідних жінок з пренатальним стресом виконане ультразвукове дослідження матки та яєчників із доплерометричним дослідженням їх судин. Метою дослідження було підвищити ефективність ультразвукової діагностики патологічних змін статевих органів у безплідних жінок з перенесеним пренатальним стресом залежно від виду лікування безпліддя. Ультразвукове дослідження вважається високоінформативним неінвазивним методом, який допомагає встановити наявність, локалізацію, структуру, розміри міоматозних вузлів, кіст яєчників, виявити супутню патологію органів малого таза. Перспективи подальших розробок: виявлені особливості стану органів малого таза дозволять збільшити частоту природних фертильних циклів та ефективність запліднення в програмах екстракорпорального запліднення.

**Ключові слова:** непліддя, стрес, доплерометричне дослідження, матка, яєчники, репродукція.

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The problem of infertility stays one of the most important in modern medicine, even given the significant advances in the diagnosis and treatment of disorders of the reproductive system and the introduction of assisted reproductive technologies.

Recently, scientists have shown considerable interest in the pathology of reproductive function, which is associated with prenatal stress (PS). The consequence of the adverse environmental situation, increasing the frequency of chronic somatic diseases, decreased immunity, the tendency to aging population, the common frequency of psychological disorders, is an increase in the number of women with diseases of the female reproductive system [1, 3].

Transvaginal ultrasound (US) with Doppler examination of the vessels of the uterus and ovaries is performed at the stage of selective examination of infertile women. Ultrasound of the pelvic organs is still not a basic "first line" study in screening examinations of the population. This study could provide an opportunity to more effective diagnostics of organic and functional pathological changes of the uterus and appendages [2, 12]. For infertile women, other laboratory and instrumental examinations and invasive interventions are planned and performed based on the results of US to confirm a clinical diagnosis and assess the extent of the pathological process in the pelvic organs.

High informativeness, non-invasiveness, possibility of use in mass examinations of the female population due to the relative simplicity and speed of execution are the main advantages of the ultrasound method of research [1]. For adequate correction of pelvic disorders requires a detailed study of body size, cervix and ovaries, ultrasound structure of the myometrium, thickness and ultrasound structure of the endometrium, cervix and ovaries [13].

The growth of all pathologies among women of reproductive age, especially among those who plan to use assisted reproductive technologies, has been a cause for concern in recent years. This is due to the fact that in modern society, most women think about having children after 35 years, and the majority of pathological processes in women begin to develop at this age. According to the literature data, for example, uterine leiomyoma (LM) is the most often found at the patients of age of 32–35 years. At the same time, in women younger than 20–30 years LM occurs in 0.9–1.5 % (9/1000–15/1000) cases [4, 10]. The presence

of myomatous nodes (MN) is characteristic of LM. These nodes are usually numerous and vary in size, at the same time, their location may be inside the uterus: intramural, subserous, submucosal; outside the uterus: extensive uterine ligament, cervix, and diffuse leiomyomatosis. Subserous localization of nodes on the leg can usually mimic appendages [3]. Significant vascularization of the ovaries is necessary to perform their various functions, such as the synthesis of sex steroids, the preservation of the follicular apparatus and the creation of conditions for folliculogenesis and ovulation. The ovaries receive arterial blood supply from two vascular branches: the ovarian arteries and the branches of the uterine arteries [11, 14].

Transvaginal ultrasonography has recently become a widely used method of diagnosis, overcoming such obstacles that limit the use of transabdominal sensors (obesity, adhesions, and flatulence). The accuracy of the method reaches 96 %; diagnosis is usually not difficult [6]. Studies by many authors show a decrease in the index of peripheral resistance in women, which indicates a greater intensity of blood flow in the vascular bed of the uterus in the presence of pathological changes in the pelvic organs. An increase in the concentration of estrogen and estrogen receptors in MN causes a decrease in vascular resistance, which in turn leads to vasodilation of the vascular network of the uterus [10]. The study of the condition of the pelvic organs of patients in the dynamics of treatment is useful in choosing the method of treatment, the possibility of using *in vitro* fertilization (IVF) to assess its effectiveness, helps to predict prospects for restoring women's reproductive health [4].

**The purpose** of the study was to increase the effectiveness of ultrasound diagnosis of pathological changes of the internal genital organs in infertile women with psycho-emotional disorders associated with prenatal stress, depending on the type of infertility treatment.

**Materials and methods.** The study was performed on the basis of the Department of Reproductive health of the municipal non-profit enterprise "Regional Medical Center for Human Reproduction" of Zaporizhzhya Regional Council. The study involved 120 patients, 80 of whom suffered from prenatal stress. They formed the main group, which was divided into: group 1A which included 41 women with a history of PS, aged 18 to 30 years, who underwent *in vitro* fertilization (IVF), group 1B consisted of 39 women with PS, aged 31 to 45 years, who underwent *in vitro* fertilization. For comparison, a control group consisted of 40 women without PS, with the presence of ovulation and tubal-peritoneal factor infertility, which were divided into subgroups: group 2A: women aged 18 to 30 years; group 2B: women aged 31 to 45 years.

When analyzing the results of the study, the complaints of patients, features of somatic and gynecological anamnesis were studied, as well as the assessment of pelvic ultrasound with Doppler characteristics of blood flow in uterine and ovarian vessels (ultrasound machine "Philips HD11XE", the Netherlands).

Each patient was issued a unified study card, which was completed by the patient only after obtaining consent to participate in the study. The ethical permission was obtained from the Institution's "Ethics Committee" prior to the study.

Negative factors that caused PS were considered to be the presence in women during pregnancy of patients who subsequently developed infertility, symptoms of severe preeclampsia and/or the birth of children from this pregnancy with signs of intrauterine growth retardation.

The mean age of patients was  $32.62 \pm 1.13$  years ( $24.45 \pm 1.43$  years in group 1A,  $36.84 \pm 1.78$  years in group 1B, and  $31.52 \pm 1.68$  years in the control group ( $p > 0.05$ )). The inclusion of the patient in the study was performed after a answering a questionnaire with an assessment of somatic and gynecological history. Exclusion criteria were: patients with acute inflammatory diseases of bacterial and viral origin, autoimmune, cancer and mental illness; with decompensated stage of somatic pathology. Clinical manifestations of diseases were carefully assessed, namely: the general condition of patients, the presence of menstrual disorders, pain in the lower abdomen and lumbar region, dysfunction of adjacent organs of the bladder and intestine. Ultrasound determined the size of the uterus, any changes in the endometrium and myometrium and the echogenicity of the ovaries, their volume. The study of blood circulation in the uterine and ovarian arteries was performed. After measuring circulatory velocity values, the systolic-diastolic ratio (SDR), pulse index (PI) and resistance index (IR) were determined.

Statistical processing of research results was performed using the statistical package of the licensed program "STATISTICA® for Windows 13.0" by the method of variation statistics, evaluating the Student's t-test. Variability at  $p < 0.05$  were considered significant.

**Results of the study and their discussion.** In patients with uterine leiomyomas, the clinical developments were quite traditional. 32.42 % of patients had abnormal uterine bleeding of varying degrees, 24.14 % had pain, and 14.7 % of women had algodysmenorrhea. All other indicators were also evaluated on a 4-point scale. The obtained data indicate that in the examined women the pain syndrome, which was

leading, was  $3.50 \pm 0.53$  points. Hyperpolymenorrhea was the next symptom of pathology of the reproductive system (score in points –  $2.40 \pm 0.45$ ), complaints of discomfort from adjacent organs were found in 65.6 % of patients (score in scores –  $2.89 \pm 0.47$  points). When talking to patients, we evaluated the intensity of pain, using a visual-analog scale of verbal evaluation (from 0 to 4 points).

Ultrasound is a highly informative and non-invasive method that helps to determine the presence, location, structure, size of myomas, ovarian cysts, as well as to detect concomitant pathology of the pelvic organs. The specific features of the anatomy of the vascular location in the uterus with leiomyoma were studied during the ultrasound of the uterine circulation, as well as the changes in the background of tumor development and different location of the nodes were noted. The vessels were more developed at the intermuscular location of the tumor and more anastomoses were found. Subserous nodes were characterized by less intensive blood supply.

When determining blood circulation, the location of the nodes and their size were important. The state of uterine and ovarian circulation was assessed on the basis of color Doppler mapping with IR and SDR analysis. In the uterine arteries in the study of blood circulation IR peripheral circulation ranged from 0.927 to 0.994. The IR of the central circulation was  $0.57 \pm 0.09$ . Thus, the analysis of the data showed that the blood circulation in the uterine artery was significantly lower than normal and was: IR –  $0.61 \pm 0.04$ ; SDR –  $3.20 \pm 0.18$  ( $p < 0.05$ ).

The circulation in the ovary was negatively affected by the fact that when the nodes were located in the corners of the uterus, the perinodular arteries of the node had a single mouth, and in the tubular corner the arteries were divided into two branches that feed the node and ovary. In favor of a perinodular artery at such topographic variant of a course of vessels there is a redistribution of blood circulation. Analyzing such data, we can conclude that the localization of nodes in the bottom and tubular corners of the uterus is considered unfavorable for the blood supply to the ovaries in LM, but the localization of nodes in the body of the uterus is considered as favorable.

The size of the ovaries did not differ from the norm – the volume of the right ovary was  $7.25 \pm 0.51$  cm<sup>3</sup>, the volume of the left ovary –  $7.31 \pm 0.52$  cm<sup>3</sup>.

Uterine leiomyoma is a tumor with abundant blood supply, with more veins and arteries, larger vessel diameter than in normal myometrium. During of the uterine circulation ultrasound diagnostics, the anatomy of the vascular location in the uterus with leiomyoma were studied, and changes in the background of tumor development and different location of the nodes were determined. The vessels were more developed at the intermuscular location of the tumor and more anastomoses were found.

Ultrasound of the ovaries, which includes Doppler study of blood flow in them, is the most informative among the biophysical methods of assessing their condition. All sizes of the right and left ovaries with a high degree of reliability in patients of the main group were larger than in patients of control group 2A (table 1).

Table 1

**Ultrasound diagnostics results of ovaries of patients of the compared groups.**

Indexes	Group 1A, n=41	Group 1B, n=39	Group 2A control, n=21	Group 2B control, n=19
Right ovary:				
Length, cm	$4.12 \pm 0.03^*$	$3.71 \pm 0.07$	$3.31 \pm 0.07$	$3.51 \pm 0.05$
Width, cm	$3.21 \pm 0.04^*$	$3.32 \pm 0.05$	$2.82 \pm 0.08$	$2.92 \pm 0.07$
Thickness, cm	$2.73 \pm 0.05^*$	$2.43 \pm 0.06$	$2.11 \pm 0.08$	$2.22 \pm 0.07$
Left ovary:				
Length, cm	$4.12 \pm 0.02^*$	$3.94 \pm 0.03^*$	$3.33 \pm 0.08$	$3.43 \pm 0.07$
Width, cm	$3.21 \pm 0.04^*$	$3.22 \pm 0.02^*$	$2.72 \pm 0.09$	$2.66 \pm 0.06$
Thickness, cm	$2.33 \pm 0.04^*$	$2.42 \pm 0.02^*$	$2.12 \pm 0.08$	$1.92 \pm 0.08$

Note: the degree of reliability of the difference of the compared indices \*  $p < 0.05$ .

Thus, in patients of the group 1A the length of the right ovary was greater by 26.4 % (the degree of reliability of the difference of the compared indicators in all the following percentage parameters  $p < 0.05$ ), width – by 24.2 %, thickness – by 25.8 % than women in the control group 2A. In patients of the 2nd group, the left ovary is larger in length – by 21.3 %, in width – by 22.4 %, in thickness – by 24.1 %, compared with the corresponding parameters in women without ovulation disorders.

In the older age group, the differences between the ovarian sizes of the patients of the main group and women of the control group were smaller than in the younger age subgroup, as can be seen from the presented data. In the group 1B, the size of the right ovary exceeded the same in women without reproductive disorders: length – by 8.6 %, width – by 4.4 %, thickness – by 3.6 %. The left ovary in women of group 1A and group 1B was larger by 11.6 % in length, 18.7 % in width and 18.7 % in thickness,

compared with the parameters of patients without a history of PS. In patients of the main group with increasing age, all major ovarian sizes tended to decrease. The right ovary decreased by 6.6 % in length, by 8.7 % – in width, while the left ovary became smaller by 5.2 % in length, by 5.4 % – in thickness. In women of the control group, the length of the right ovary increased by 6.4 %, width – by 8 %, thickness – by 2.5 %. The length of the left ovary of women in the control group increased by 3.3 % with age.

The blood flow inside the ovary was studied during the research: stromal vessels are easily identified with the help of modern equipment. In the course of the study, the analysis of blood flow in the ovaries of women of the compared groups was performed (table 2).

Table 2

**Indicators of ovarian blood flow Doppler examination in patients of the compared groups.**

Indexes	Group 1A, n=41	Group 1B, n=39	Group 2A, control, n=21	Group 2B control, n=19
<b>Right ovary:</b>				
Resistance index, RI	0.40±0.04*	0.52±0.03*	0.34±0.06	0.43±0.05
Pulse index, PI	0.73±0.06	0.81±0.06	0.65±0.05	0.73±0.08
Systolic-diastolic ratio, SDR	4.71±0.04*	4.42±0.02*	6.61±0.08	5.92±0.07
<b>Left ovary:</b>				
Resistance index, RI	0.43±0.03*	0.53±0.04*	0.37±0.06	0.40±0.06
Pulse index, PI	0.76±0.07	0.89±0.06	0.59±0.06	0.71±0.07
Systolic-diastolic ratio, SDR	4.84±0.04*	4.13±0.04*	6.92±0.07	6.24±0.06

Note: the degree of reliability of the difference of the compared indicators \* p<0.05.

Significant vascularization of the ovaries is necessary to perform their various functions, such as the synthesis of sex steroids, the preservation of the follicular apparatus and the creation of conditions for folliculogenesis and ovulation. The ovaries receive arterial blood supply from two vascular branches: the ovarian arteries and the branches of the uterine arteries. The study examined blood flow inside the ovary: with the help of modern equipment, stromal vessels are easily identified. During the study, the analysis of blood flow in the ovaries of women of the compared groups was performed.

In patients with anovulatory infertility in the arteries of the right and left ovaries in the younger and older age subgroups, the IR was significantly higher than in women in the control group. In the main group, IR was higher than in the control group, at 18–30 years in the arteries of the right ovary by 27.3 %, in the arteries of the left ovary – by 25.7 %; in 30–45 years – by 32.5 % and by 28.6 %, respectively. In comparison with the patients of the control group, the patients of the main group of PI in 18–30 years were higher in the arteries of the right ovary by 18.18 %, the left – by 19.37 %; at the age of 31–45 – by 19.46 % and 20.53 %, respectively.

The increase in IR and PI in the ovarian arteries of patients in the main group, compared with the IP and PI of patients in the control group, due to increased peripheral vascular resistance in the microvascular network of the ovaries. SDR of patients in the arteries of the right and left ovaries of group I 18–30 years and 31–45 years was significantly lower than in the control group. In patients of the main group SDR was lower than in patients of the control group, in 18–30 years in the arteries of the right ovary – by 31.3 %, in the arteries of the left ovary – by 31.7 %; at the age of 31–45 – by 30.4 % and by 30.9 %, respectively.

The decrease in SDR in the ovarian arteries of infertile women of the main group may be a consequence of the increased diastolic blood flow and decreased systolic blood flow rate compared with women in the control group. Decreased organ perfusion in the microvascular bed is accompanied by an increase in peripheral vascular resistance. In women with increasing age, there is an increase in peripheral vascular resistance and a decrease in the values of blood flow velocity in the ovaries.

Based on the obtained data, we can conclude that ovarian arterial perfusion is significantly lower in the main group than in the control group. The analysis in the main group showed a significant increase in IP values with increasing age: in the arteries of the right ovary it increased by 27.3 %, in the arteries of the left ovary – by 21.7 %.

To predict the further development of the process and the choice of further tactics of patients' treatment, it is necessary to determine blood circulation indicators, which allow obtaining the information about the activity of LM growth, ovarian cysts, and inflammatory formations in the pelvic organs.

The myomatous node has a reduced blood supply, compared with the surrounding myometrium due to the periphobroid plexus formed by arcuate and radial uterine arteries. Our research coincides with this statement of Birch Petersen [8]. According to a number of authors [9, 14], the volume of the ovaries can vary widely and normally reaches 40 \* 30 \* 20 mm in length, thickness and width, respectively, which

is 4.21–10.57 между числами без пробелов  $\text{cm}^3$ , when the normal size of the uterus is from 6 to 12  $\text{cm}^3$  ( $5.48 \pm 1.64 \text{ cm}^3$ ).

Age-related changes in the size of the ovaries of patients in the main group are characterized by a tendency to decrease, and the main ovaries size of women without PS in the anamnesis with increasing age tended to increase, which coincides with research Pirogova VI, Ferenc M. [6].

Conclusions are made that coincide with most studies on this topic based on the study of Doppler indicators of ovarian blood flow in women of the studied groups and subgroups [4]: in the main group were significantly higher indicators that characterize peripheral vascular resistance in the ovaries than in the control group; ovarian arterial perfusion in patients with a history of PS is lower than in patients without a history of PS. Ovarian aging is accompanied by a decrease in ovarian arterial perfusion, which coincides with the study of patients in the main group [13].

### Conclusions

1. In the control group, the age dynamics of peripheral vascular resistance and blood flow velocity in the ovaries is much less pronounced.

2. In patients with infertility and PS, the aging process begins earlier or is more intense than in women with tubal-peritoneal factor infertility and normal regulation of the hypothalamic-pituitary-ovarian system.

3. Timely and correct ultrasound and Doppler study of the pelvic organs, along with the evaluation of vascularization, helps to differentiate the choice of diagnostic algorithm and further tactics of choosing the method of infertility treatment (conservative or surgical) in patients with infertility and PS.

**Prospects for further research.** In the future, we plan to increase the frequency of natural fertile cycles and the efficiency of fertilization in in vitro fertilization programs due to the identified features of the pelvic organs, the assessment of ultrasound and Doppler indicators, as well as to develop treatment regimens for correction of reproductive disorders and psycho-emotional adaptive capabilities of the expectant mother, who treats infertility and has a psycho-emotional disorder associated with a history of prenatal stress.

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